# ANTIBIOTIC USE & RESISTANCE IN BANGLADESH

REPORT 2018

# SITUATION ANALYSIS & RECOMMENDATIONS ON ANTIBIOTIC RESISTANCE


The GARP-Bangladesh National Working Group

GARP-BANGLADESH & CDDEP



DGHS.MOH&FW BANGLADESH

DGDA
গণপ্রজাতন্ত্রী বাংলাদেশ সরকার
ঔষধ প্রশাসন অধিদপ্তর
স্বাস্থ্য ও পরিবার কল্যাণ মন্ত্রণালয়

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Global Antibiotic Resistance Partnership

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

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Dr. M G Mostafa Musa, International Consultant of GARP-Bangladesh, prepared the present document titled: "Antibiotic Use and Resistance in Bangladesh: Situation Analysis and Recommendations", January 2018.

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# ABBREVIATIONS

| | |
|---|---|
| ADR | Adverse Drug Reaction |
| AIDS | Acquired Immunodeficiency Syndromes |
| AMR | Antimicrobial Resistance |
| AMRC | Antimicrobial Resistance Containment |
| ANC | Antenatal Care |
| API | Active Pharmaceutical Ingredients |
| BAPI | Bangladesh Association of Pharmaceutical Industries |
| BDHS | Bangladesh Demographic Health Survey |
| BDT | Bangladeshi Taka |
| BMDC | Bangladesh Medical & Dental Council |
| CDC | Communicable Disease Control |
| CDDEP | Center for Disease Dynamics, Economics & Policy |
| CFC | Chlorofluorocarbons |
| CMSD | Central Medical Store Depot |
| COPD | Chronic Obstructive Pulmonary Diseases |
| CWG | Core Working Group |
| DCO | Drugs (Control) Ordinance |
| DGDA | Directorate General of Drug Administration |
| DGFP | Directorate General of Family Planning |
| DGHS | Directorate General of Health Services |
| DGNM | DGNM Directorate General of Nursing and Midwifery |
| DLS | Department of Livestock Services |
| DNA | Deoxyribonucleic Acid |
| DoF | Department of Fisheries |
| DOTS | Directly Observed Treatment, Short-course |
| EDCL | Essential Drugs Company Limited |
| EDL | Essential Drug List |
| ESP | Essential Service Package |
| FAO | Food and Agriculture Organization |
| GAP-AMR | Global Action Plan on Antimicrobial Resistance |
| GARP | Global Antibiotic Resistance Partnership |
| GARDP | Global Antibiotic Research and Development Partnership |
| GBD | Global Burden of Disease |
| GDP | Gross Domestic Products |
| GMP | Good Manufacturing Practice |
| HACCP | Hazard Analysis and Critical Control Points |
| HED | Health and Engineering Department |
| HEU | Health Economics Unit |
| HFA | Hydrofluoroalkane |
| HIV | Human Immunodeficiency Virus |
| HNPSP | Health, Nutrition and Population Sector Program |
| ICU | Intensive Care Unit |
| IPC | Infection Prevention and control |
| L.AmB | Liposomal Amphotericin B |
| LGD | Local Government Division |
| MDG | Millennium Development Goal |

# ABBREVIATIONS

| | |
|---|---|
| MDR-TB | Multi-drug Resistant Tuberculosis |
| M&E | Monitoring & Evaluation |
| MoA | Ministry of Agriculture |
| MoAFD | Ministry of Armed Forces Divisions |
| MoFL | Ministry of Fisheries & Livestock |
| MoHA | Ministry of Home Affairs |
| MoHFW | Ministry of Health and Family Welfare |
| MoLGRD&C | Ministry of Local Government, Rural Development & Cooperatives |
| NCL | National Control Laboratory |
| NDP | National Drug Policy |
| NGO | Non-Government Organizations |
| NIPORT | National Institute of Population, Research & Training |
| NKEP | National Kala-azar Elimination Program |
| NMCP | National Malaria Control Program |
| NRA | National Regulatory Authority |
| NSC | National Steering Committee |
| NTP | National TB Program |
| NTC | National Technical Committee |
| NWG | National Working Group |
| OOP | Out-of-Pocket |
| ORT | Oral Rehydration Therapy |
| OTC | Over-the-Counter |
| PKDL | Post-kala-azar Dermal Leishmaniasis |
| PPP | Purchasing Power Parity |
| R&D | Research and Development |
| RNA | Ribonucleic Acid |
| RR-TB | Rifampicin Resistance Tuberculosis |
| SAARC | South-Asian Association for Regional Cooperation |
| SDG | Sustainable Development Goal |
| SEARO | South-East Asia Region Office |
| STD | Sexually Transmitted Disease |
| STI | Sexually Transmitted Infection |
| THE | Total Health Expenditure |
| TOR | Terms of Reference |
| UHC | Upazila Health Complexes |
| UHFPO | Upazila Health & Family Planning Officer |
| UN | United Nations |
| USD | United States Dollar |
| UTI | Urinary Tract Infections |
| U5C | Under Five Children |
| WHA | World Health Assembly |
| WHO | World Health Organization |
| WOAH | World Organization for Animal Health |
| WPR | Western Pacific Region |
| XDR-TB | Extensively-Drug Resistant Tuberculosis |

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# FOREWORD

Antimicrobial Resistance (AMR) poses a serious public health problem leading to a reduction in the effectiveness of antimicrobial treatment and an increase in healthcare expenditure associated with bacterial disease burden. AMR causes a great threat to global public health that at present no country acting on its own will be able to adequately protect the health of its citizen against the threat of resistant microbial infections. To tackle drug resistant infections globally, the United Nations (UN), with its member countries and other UN organizations agreed upon a historical resolution to prevent AMR in 2016 in New York. The blueprint for stopping AMR was later reaffirmed through the "WHO Global Action Plan on AMR 2015".

Bangladesh, as a member state of the WHO-SEARO and United Nations, has responded to call to address AMR by preparing a National Strategy and Action Plan for AMR. Bangladesh has taken the initiative to implement integrated activities, including a national antibiotic surveillance system and laboratory network, and collaborating with the member countries of WHO-SEARO and other countries globally. GARP-Bangladesh is a member of the "Global Antibiotic Resistance Partnership (GARP)" project, which is technically supported by the "Center for Disease Dynamics, Economics & Policy (CDDEP)". It is committed to assisting with the "National Strategy and Action Plan on AMR" in preserving antibiotic effectiveness, slowing down the spread of AMR, and establishing national capacity for antibiotic policy and access.

The present report on situation analysis of AMR has attempted to analyse the scopes, extents and magnitudes of development and spread of resistant microbes and reviewed the functions, roles and responsibilities of the stakeholders. These includes (i) the pharmaceutical industry as an entity for the manufacture of antimicrobial drugs; (ii) the intermediary groups as an entity of procuring and supplying antimicrobial drugs, such as directorates, institutions, organizations, groups, business parties and whole sales/retail pharmacies to the end users; (iii) the end user groups, such as clinicians, medical practitioners and veterinarians prescribing antimicrobial drugs for patients - both for human and animal population; and (iv) the Directorate General of Drug Administration (DGDA), as a National Regulatory Authority (NRA), implementing drug regulations at all stages of productions, upto and including the dispenses of medicines in Bangladesh.

The combined efforts of these stakeholders will definitely ensure a high-level of safety, efficacy and quality of drug in the country, however, the failure of the stakeholders at any level will foster the development, multiplication and spread of AMR within the environment. Therefore, to overcome the challenge of AMR, it is necessary to bring all these key actors on the same board and ensure synergistic coordination among the vital stakeholders. Moreover, gaps in the quality of data and information on microbes and antibiotics could be generated by the research institutes to deal AMR problems in Bangladesh. GARP-Bangladesh, as a national partner of choice, has identified this issue as a major challenge, and would like to advocate among policy and decision makers to frame an antibiotic policy guideline, and to coordinate in building a comfortable synergy among the four vital stakeholders to prevent the AMR problem in Bangladesh.

This is the first report on antibiotic use and resistance to be published in Bangladesh. The report attempts to capture a brief introduction to AMR, the health system and economic context, microbial disease burden, antimicrobial resistance in humans and animals, drug regulations, supply chain management and access to antibiotic in Bangladesh. This report, I believe, with further information generated from research and study will fill the current gaps to develop an effective antibiotic policy, for guiding the health professionals to use antibiotics rationally and for advocating the policy-decision makers to capture political commitment for AMR programme activities. GARP-Bangladesh National Working Group in these regards would continue to assist its high-level technical and other expertise in the mitigation and prevention of the current AMR problem in Bangladesh.

Finally, we would like to thank Honourable Advisors, Vice Chairs and Executive Members of GARP-Bangladesh National Working Group for their initiatives, proposed future directions, valuable feedback and comments to ensure that the report is accurate, effective and credible. We would like to thank the author for the outstanding work that he has done and will continue to pursue.

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Director, Disease Control Unit, and
Line Director, Communicable Disease Control (CDC)
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# ACKNOWLEDGEMENT

The review report “Antibiotic Use and Resistance in Bangladesh: Situation Analysis and Recommendations on Antibiotic Resistance” is a combined and shared efforts of GARP-Bangladesh and Center for Disease Dynamics, Economics & Policy (CDDEP), and is a reflection of joint commitment to combat and contain AMR problems in Bangladesh. In this connection, we are pleased to acknowledge the technical and financial support received from CDDEP-Washington DC in preparing and publishing the report.

We would like to express our thanks to Mr. Md. Salahuddin, Assistant Director, DGDA for his inputs in drug regulations, supply chain and access to medicines; Dr. Rezaul Huq Khan, Upazila Livestock Officer of DLS for his contribution in livestock production, diseases and antibiotic uses in Bangladesh; Dr. Masud Hossain Khan, PhD, Chief Scientific Officer, Department of Fisheries, Ministry of Fisheries and Livestock for his contribution in fish production, fish disease, and antibiotic uses in fisheries in Bangladesh; and Mr. Iftekhar Rafiqullah, former National Coordinator of GARP-Bangladesh for his early initiative to appraise bacterial infections and antimicrobial resistance. We would also like to extend our special thanks to Dr. Jyoti Joshi Jain, Head of South Asia & GARP Asia Coordinator, CDDEP, New Delhi and Dr. Isabel Frost, Research Scholar, CDDEP, Washington DC, USA for their valuable feedback on the draft document.

We would also like to acknowledge the valuable inputs on antibiotic use and resistance that we received during our in-depth interview and consultative meeting with Professor Anwar Hossain, PhD, Department of Microbiology, University of Dhaka; Dr. Md. Ainul Haque, Director General and Dr. Hossan Md Salim, PhD of the Department of Livestock Services, Ministry of Fisheries and Livestock; and Prof. Dr. Meerjady Sabrina Flora, Director, Institute of Epidemiology, Disease Control & Research (IEDCR) of DGHS.

Our heartiest congratulation and acknowledgement goes to Dr. M G Mostafa Musa, who reviewed substantial number of published documents on antibiotic use and AMR of global, regional and national importance, and analysed the current AMR situation in Bangladesh and compiled the report at his best capacity. We would like to thank the author for his outstanding piece of work. Last but not the least, we would like to express our sincere thanks and gratitude to the advisors and executive members of the GARP-Bangladesh National Working Groups for their important contribution in reviewing the report and putting forward their valuable feedbacks to make the report accurate and credible.

While reviewing and analysing the AMR situation in Bangladesh, we have been challenged with serious gaps in the quantity data on AMR in general and quality of data in particular. With this limitation, we believe and hope that this report will provide the researchers, clinicians and other stakeholders of similar interest a baseline information to undertake further study, research and actions aiming to contain the antimicrobial resistance in Bangladesh.

With the influx of over one million Forcibly Displaced Myanmar Nationals (FDMNs) from Myanmar to Bangladesh – a population who were deprived of basic health facility back in their residence, lack of vaccine coverage, severe malnutrition and lack of health education will further raise AMR concern to Bangladesh where we hope this report will help the concern ministries some preliminary guidance on how to address AMR issues among those displaced population.

**Dr. Wasif Ali Khan**
Vice Chair Person
GARP-Bangladesh

**Professor (Dr.) Sayedur Rahman**
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# Executive summary and Recommendations

GARP-Bangladesh develops this report on "Antibiotic Use and Resistance in Bangladesh: Situation Analysis and Recommendations", which is divided in to five chapters with an executive summary that includes: Chapter-1: Introduction to Antimicrobial Resistance, Chapter-2: Health Systems and Economic Context of Bangladesh, Chapter-3: Microbial Disease Burden and Antimicrobial Resistance, Chapter-4: Drug Regulations, Supply Chain Management and Access to Antibiotics, and Chapter-5: AMR in Livestock, Fisheries and Agriculture in Bangladesh.

**CHAPTER-1: INTRODUCTION TO ANTIMICROBIAL RESISTANCE (AMR):**

This introductory chapter briefly describes the characteristics of antimicrobials, the meaning of resistance, and the intrinsic and external factors causing antimicrobial resistance (AMR). The overall impact of AMR, at global and national levels, is briefly discussed in addition to an explanation of the global response, particularly WHO and UN responses to AMR along with Bangladesh national response highlighting the objectives of National Strategy for AMR Containment in Bangladesh and the major activities of the "National Action Plan on AMR: 2016-2020". The roles of "Center for Disease Dynamics, Economics & Policy (CDDEP)" and a brief history of the "Global Antibiotic Resistance Partnership (GARP)-Bangladesh" are also touched upon.

This chapter highlights the objectives and priority activities of GARP-Bangladesh, and analyses the major phenomena driving the evolution and multiplication of AMR microbes, the spread of which is being accelerated by misuse, overuse, and the inappropriate use of antimicrobial agents. This chapter also identifies the most important factors contributing to the occurrence and spread of AMR in Bangladesh that includes: the availability of counterfeit or poor quality of antimicrobial medicines; weak laboratory capacity; inadequate drug monitoring and surveillance system; inadequate execution of drug regulations; poor treatment adherence; non-therapeutic use antibiotics for growth promotion in farm animals; use of self-medication and collection of antibiotics through over-the-counter; and inadequate or non-existent programs for infection prevention and control.

The roles and responsibilities of the four main stakeholders have been reviewed while attempting to analyse the scopes, extent and magnitude of the emergence, multiplication and spread of resistant microbes. These stakeholders are (i) the pharmaceutical industry, manufacturing antimicrobial drugs; (ii) the intermediary groups, procuring and supplying drugs; (iii) the end user groups, such as clinicians, medical practitioners and veterinarians prescribing antimicrobial drugs for patients - both in human and animal populations; and (iv) the Directorate General of Drug Administration (DGDA) as a National Regulatory Authority (NRA), implementing drug regulations at all stages of productions, upto and including the dispense of medicines. The combined efforts of these stakeholders will definitely ensure high-level of safety, efficacy and quality of drug in the country, however, the failure of the stakeholders at any level will foster development and spread of antimicrobial resistance within the environment.

**Recommendations:** GARP-Bangladesh has identified the above issue as a major challenge and would like to advocate among the policy and decision makers to frame an antibiotic policy guideline, and to coordinate to build a comfortable synergy among the four vital stakeholders to prevent antibiotic resistance in Bangladesh. The GARP-Bangladesh has made the following recommendations:

1. Review of existing documents on AMR: Provide technical assistance in reviewing and giving feedback to the national strategy and action plan in line with the proposed WHO and CDDEP strategic objectives, and

2. Antibiotic Policy Issue: Assist in implementing the antibiotic policy issues at the national level to improve awareness and understanding of AMR and educate healthcare professionals.

3. GARP-Bangladesh Website Development: Develop a central 'One Health' AMR repository (Website) to host AMR information, reports and resources including links to Bangladesh, GARP Countries, Center for Disease Dynamics, Economics & Policy (CDDEP), United Nations (UN), World Health Organization (WHO), Food & Agriculture Organization (FAO), World Organization for Animal Health (WOAH), European Antimicrobial Resistance Surveillance Network (EARS-Net) and the US National Antimicrobial Resistance Monitoring System (NARMS), European Public Health Association, and other existing international initiatives.

4. Newsletter on Common Health Issues and AMR: Develop a newsletter on common health issues and AMR especially on antibiotics, antimicrobials and antibiotic resistance and circulate among health professionals (health, livestock, fisheries, and pharmaceuticals at all levels). Three/four newsletters in a year could be published in coordination with the Disease Control Division of CDC, DGHS, Department of Livestock Services and Department of Fisheries.

**CHAPER-2: HEALTH SYSTEM AND ECONOMIC CONTEXT OF BANGLADESH:**

Chapter-2 describes the geography and demography, economic context, health system, health indicators, access to healthcare and essential medicines, health and economic policies, and healthcare financing in Bangladesh. Each sub-chapter is briefly described as follows:

This sub-chapter describes in brief the geography and demography of Bangladesh defining its location, size of landscape, seasonal variations, rainfall, temperature, population, education, ethnicity, governance, etc. The economic context of Bangladesh has been highlighted with especial emphasis on poverty reduction, growth trends, the role of agriculture, and sources of revenues earnings. The impact of agriculture sector on major macroeconomic objectives, such as employment generation, poverty alleviation, human resources development, and food security has been documented.

This sub-chapter also reviews healthcare delivery system of Bangladesh and describes the benefits of reform of the national health plan using a sector wide strategic approach, a shifting from a project basis towards a coordinated sectoral programme. The major policy level activities of DGHS and DGFP in the public health sector have been described highlighting their responsibilities in making health policy; organizing, managing and coordinating implementation of healthcare services; and regulating national health and family planning programmes. The roles of health facilities in delivering healthcare services, supplying medical and health related goods, deploying healthcare professionals, and providing healthcare services have been reviewed and explained.

It is also revealed from the review that there is a large cadre of healthcare providers in the informal sector that comprises semi-qualified allopathic providers (e.g. community healthcare providers/workers, medical assistants and midwives), unqualified allopathic providers (drug shop retailers, village doctors, birth attendants, etc.), traditional healers (practitioners of ayurvedic, unani and homeopathic medicine) and faith healers. They are not a part of the mainstream health system but a major healthcare provider for the poor rural population, especially in remote rural and hard-to-reach areas. These large healthcare cadres with no or very limited knowledge and skills have been prescribing antibiotics in an inappropriate way and they are thought to be one of the major contributors to the development of AMR in the country.

The importance of national health indicators and the role of antibiotics in reducing infant, child and maternal mortality have been reviewed. The health outcomes have shown marked improvement despite many challenges with falls in neonatal, infant, under-five child, and maternal mortality rates with significant reductions in total fertility rate. However, the quality of care in both public and private sectors is found to be poor.

**Recommendations:** It is recommended from the review that the healthcare services should be improved with provision of quality medicines with other health resources to improve the healthcare services for the citizen of Bangladesh in general and to prevent the AMR situation in particular with especial emphasis to be given in the follow issues:

1.Ensure access to healthcare services and essential medicines for all. Make availability of right kind of health provider mix, which is considered to be an important determinant measuring accessibility and hence utilization of healthcare services in Bangladesh.

2. Overcome mark shortage of doctors, nurses and medical technologists by filling-up the vacant positions of health workforce in the public sector and to make appropriate skill mix and equitable distribution of doctors, nurses and technologists with a ratio of 1.0:3.0:5.0 respectively (WHO recommended standard).

3. Implement health, economic, population, financing and nutrition policies into actions to guide desired health indicators and outcomes; to ensure people to have easy access to safe, effective and good quality drugs; to improve the overall national nutritional status for all citizens; and to increase financial protection for the entire population and decrease out-of-pocket payments.

**CHAPTER-3: MICROBIAL DISEASE BURDEN AND ANTIMICROBIAL RESISTANCE:**

The Chapter-3 is divided into five sub-chapters describing bacterial disease burden, antimicrobial resistance with description of major infectious diseases, parasitic diseases, sexually transmitted infections, prophylactic use of antimicrobial, hospital acquired infections, management of healthcare waste, education and understanding of AMR and societal factors that influence antimicrobial use.

Bacterial diseases burden and antimicrobial resistance (AMR): The bacteria causes some of the deadliest diseases and devastating epidemics including cholera, diphtheria, pneumonia, tuberculosis, typhoid fever, typhus, etc., and destroyed hundreds of millions of human lives in the past centuries. However, the epidemic has come down remarkably due to the introduction of effective antibiotics in mid

nineteen fifties and onwards, but from the beginning of the twenty first century and onward, the bacteria have shown remarkable resistance to many conventional antimicrobial agents with third and in some cases fourth generation antibiotics. In Bangladesh, this remarkable AMR is caused as a result of lack of quality in terms of patient examination due to allocation of brief consultation time, under-value in evaluating and reaching proper diagnosis to disease and use of inappropriate antibiotics.

There is no regular national surveillance on microbial infections and AMR until 2016, except in selected diarrhoeal pathogens which have been monitored and documented. The documentation of the national data on surveillance of infectious diseases and their resistance pattern; the data on major infectious diseases, their aetiologies and resistance patterns; and the risk factors causing resistance have been found to be inadequate. However, the data on AMR from few tertiary level teaching hospitals, icddr,b and few population-based surveillance studies have been analysed and found that the most of the antibiotics show resistance to wide range of the infectious agents.

In Bangladesh, the pathogens most common infectious diseases that have shown resistance to antimicrobials include acute respiratory infection (ARI), diarrheal diseases, tuberculosis (TB), urinary tract infections (UTIs), neonatal infection (sepsis), ear infections (otitis media), typhoid fever, and skin and soft tissue infections (SSTIs). The most common organisms causing infectious diseases are *Staphylococcus aureus*, Methicillin Resistant *Staphylococcus aureus (MRSA), Staphylococcus pneumoniae, Streptococcus pneumoniae, Klebsiella pneumoniae, Escherichia coli, Candida albicans, Pseudomonas aeruginosa, Enterobacter, Pseudomonas, Acinetobacter baumannii, Salmonella typhi, Salmonella Paratyphi, Stenotrophomonas maltophilia, Clostridium difficile, Mycobacterium Tuberculosis*, and Vancomycin-resistant *Enterococcus.*

Microorganisms transmitted by airborne transmission include Mycobacterium tuberculosis, *Legionella,* and the rubella and *varicella* viruses. Different studies documented that in Bangladesh hospital acquired infections are problem in public tertiary hospitals, in which E. coli, Pseudomonas sp, Proteus sp, and *Klebsiella* sp. might be a potential source of *nosocomial* infection. The isolated organisms showed high level of resistance to commonly used antibiotics. The resistance of the organisms markedly increased with the hospital stay. Patients have frequently experienced hospital-acquired respiratory infections.

Infectious diseases are the major health problems in Bangladesh. Diagnosis and treatment of the diseases are mostly on empirical decision rather than evidence based. The sensitivity patterns of pathogens causing diseases are not available in many health facilities in sub-district hospitals for selecting appropriate antibiotics. Many infectious diseases do not respond to conventional antimicrobial agents.

Societal factors that influence antimicrobial use have been identified as overstatements and misinformation about the antibiotics. Pharmaceuticals companies are the only organizations providing information on antibiotic to physicians and in some cases, the information provided are not checked on a regular basis nor recommended from public health bodies. A large number of physicians are reported to accept economic incentives from the pharmaceutical companies in the form of cash and/or kinds as gift items, which are usually printed with company's insignia and trade names of medicines, which significantly influences doctors' prescribing behaviors.

**Recommendations:**

1. Implement infection control policies, antibiotic stewardship program and effective infection prevention and control program at national and local levels health facilities; Implement the national action plan to mitigate AMR,

2. Monitoring Medicine Use: To improve medicine use and monitor medicine use in hospitals, clinics and private chambers on a regular basis, a vigilant health promotion unit should be developed and Drug and Therapeutic Committees (DTC) should be strengthen in all hospitals within the DGHS and DGDA of the MoHFW.

3. Medical Education: Provide technical assistance in introducing undergraduate training on AMR, antibiotic use, infection prevention and control, and antimicrobial stewardship for medical students, dental, veterinary, fisheries, pharmacy and nursing staff, supported by mandatory continued professional development activities throughout the practitioner's career.

4. Advocacy, Communication and Social Mobilization: Provide technical assistance in developing a coordinated, audience appropriate, healthcare system-wide, and community-wide approach to advocate, communicate, educate, and conduct awareness programs on AMR, infection prevention and control and the appropriate use of antibiotics.

5. Training of Health Professionals: Provide technical assistance in conducting training for the different health professionals at medical university, medical colleges and hospitals, medical institutes, pharmacy retailers/drug sellers; provide assistance to develop different training modules at a national level; conduct train-the-trainers workshop for healthcare professionals on antimicrobial stewardship in hospitals in Bangladesh.

6. Conduct Research and Surveillance: Provide technical assistance in conducting relevant research and surveillance of AMR and ARC, including research on a surveillance system and study on prescriptions patterns; monitoring of rational use of antibiotic drugs; and establishing a monitoring system for antimicrobial resistance;

## CHAPTER-4: DRUG REGULATIONS, SUPPLY CHAIN MANAGEMENT & ACCESS TO ANTIBIOTICS

The Chapter-4 is divided in to five sub-chapter that contains drug policies, acts, regulations, ordinance and strategies; regulatory network; pharmaceuticals (drugs/medicines) in healthcare delivery; drug safety, efficacy, quality and control mechanism; and antibiotic supply chain, supply chain management and access to antibiotic to the end users. The main points of this chapter are as follows:

This chapter describes the need and the importance of a robust drug regulations, policy, act, and ordinance, which are designed to ensure safety, efficacy, and quality of drug. The safety, efficacy and quality of drug are prerequisites for a therapeutic success. The therapeutic failure due to low quality drug aggravates disease condition in patients; low quality drug develops resistance against the microbes; and even patients may die if unsafe and low-quality drugs are used.

The National Regulatory Authority (NRA) of the Directorate General of Drug Administration (DGDA) is the responsible authority to ensure safety, efficacy, and quality of pharmaceutical products through the implementation of the relevant drug legislations and regulations including supervision and monitoring of procurement, import, export, production, sales and distribution of finished medicines, and pricing of Active Pharmaceuticals Ingredients (API).

There are number of issues related to pharmaceuticals (drugs/medicines) that are identified as a priority issues, these are: supply and selection of drug; information of drug use; implementation of drug regulation, drug policy and acts; mobilization of trained human and adequate financial resources; governance issues; development of guidelines; and fostering effective.

The roles and functions of different drug committees with terms of references (TOR) have been reviewed and found that the committees do not have specific timeframe for holding the meeting. These committees have been formed with poor articulation of TOR without considering thoughtful attention to WHO guidelines and recommendations. In addition to this, the absence of technical and skilled persons in some committees fail to set standard drug price, encounter problems in approving new manufacturing units, and fail to ensure proper drug control mechanism and hence the drug quality.

The antibiotic supply, supply chain management and access to antibiotic issues have been reviewed and analysed. The existing antibiotic supply chain and distribution system includes (i) public sector channel and (ii) private sector channel. Public sector procures antibiotics mainly from the state-owned Essential Drugs Company Limited (EDCL); whereas private sector including whole sale and retail pharmacies procures antibiotics from the private pharmaceutical companies. Public hospitals can also source from private pharmaceutical companies through tender bids.

**Recommendations:**

1. Drug Committees: Ensure that the different drug committee have adequate technical personnel with regular time schedule for holding meetings. TOR of the different drug committees should be reviewed with necessary amendments to include and adapt scientific changes in medicines and technological innovation in pharmaceutical industry in Bangladesh.

2. National Control Laboratory (NCL): Ensure that the National Control Laboratory (NCL) obtain accreditation from WHO PQ and ISO 17025 by the end 2018 and Divisional Control Laboratory (DCL) be established at eight divisions on a priority basis.

3. Recruitment of skill personnel: The DGDA should recruit adequate number of skill personnel to fill the vacant position up on a priority basis to carry forward all regulatory activities within the pharmaceutical industry in Bangladesh.
4. Prevention of Pharmaceutical Pollution: Provide technical assistance to the pharmaceutical industry to contain AMR by conducting training, seminars and workshops on AMR, improving antibiotic-waste management, and preventing pharmaceutical pollution.

## CHAPTER-5: ANTIMICROBIAL RESISTANCE IN LIVESTOCK, FISHERIES AND AGRICULTURE

The Chapter-5 is divided into six sub-chapters and describes roles of the Department of Livestock Services (DLS) and Department of Fisheries of the Ministry of Fisheries and Livestock (MoFL); brief discussion about livestock and fish production in Bangladesh; livestock and fish health and diseases; antimicrobials used and AMR in livestock and fisheries sector; and existing acts, policies, rules, regulations and strategies of livestock and fisheries.

The total livestock disease burden remains complex and is

not clearly understood and not properly documented owing to the general lack of diagnostic and disease recording system causing economic impacts analysis rather limited. The DLS has mostly engaged with treatment of sick animals, while the health preventive care has been grossly neglected. Consequently, the high mortality of the food animals as a result of epidemics like anthrax, haemorrhagic septicaemia, black quarter and foot and mouth diseases imposes huge losses to farmers.

The antibiotics are used for treatment of diseases as therapeutic reasons, prophylactic reasons for prevention and control of diseases, and growth promotion for livestock animals. Most common antibiotics used are tetracycline, penicillin, sulphonamide, fluoroquinolone, cephalosporin, macrolides, etc. Despite the widespread use of antibiotics in food animals, reliable data about the quantity and patterns of use, e.g., dose, frequency and duration are not available in Bangladesh.

Bangladesh Fish Feed and Animal Feed Act 2010 banned use of antibiotic as growth promoter, growth hormone, steroid, pesticides and other harmful chemicals in fish and animal feeds. But the research results revealed that the toxic and harmful residues of antibiotics are still present in poultry meat and eggs. Vested interest, low veterinary regulations and low enforcement of regulatory acts may be the root causes of this situation. Antibiotic resistant bacteria are being produced due to antibiotic abuse which is a big threat to human and animals and for the ecosystem.

Only limited scientific information is available about the antimicrobial resistance properties of bacteria isolated from livestock sector in Bangladesh. Small number of data published about the antimicrobial resistance properties of E. coli, and found that E. coli was highly resistant to cotrimoxazole, gentamycin, penicillin Ciprofloxacin, Rifampicin, Kanamycin, Chloramphenicol Neomycin, Streptomycin, Cefixime, Erythromycin, Ampicillin and Tetracycline.

Both local pharmaceutical companies and importers have directly involved in the supply and distribution of antimicrobial products for livestock to the wholesalers, retails pharmacies, chemists, and feed sellers and even to the commercial poultry farmers to some extent. A major portion of antimicrobials are sold directly to animal farm owners through over-the-counter and also by the quacks and fake veterinary doctors. Only a very negligible amount of total sale volume of antimicrobials is sold through prescription.

Fish Production, Fish Diseases and Antibiotics used in Fisheries: The Department of Fisheries (DoF) under the Ministry of Fisheries and Livestock (MoFL) is mandated to disseminate improved aquaculture technologies through training and demonstration; to enhance fisheries resources through enacting conservation and management measures; to assist formulating policies, acts etc.; to enforce quality control measures; to conduct fisheries resources survey and assessment of stock; to formulate and implement development projects/programs towards sustainable utilization of fisheries resources to ensure food security; and to disseminate improved aquaculture technologies through e-extension service.

A wide variety of parasites and pathogens can infect fish. Most disease agents are naturally present in low numbers and normally do not cause problems. The natural defence mechanisms of fish i.e. undamaged skin, mucus covering the skin, and various components of the immune system keep disease agents in check. However, when the crowded fish in culture operations are further stressed (by low dissolved oxygen, nutritionally inadequate feeds, excessive handling), their natural disease defence systems may be weakened and the ability of the fish to protect itself against infectious diseases may be reduced. Disease induced catastrophic mortalities are frequently the result of, and response to, a stressful experience.

Most fish diseases can be avoided with proper management. The most common causes of fish diseases are: fish with ulcer, fish with cloudy eye, dropsy, fish with white spot, bacterial diseases, fungal disease, finrot, swim bladder disorder and Lymphocystis. Despite the limited use of antibiotics and antifungal drugs in fish, reliable data about the quantity and patterns of use, e.g., dose, frequency and duration are not available in Bangladesh because of the lack availability of systematic data.

**Recommendations:**

1. Veterinary regulations and acts should be properly implemented to ensure that the antibiotics as growth promoter are not used in livestock and fisheries.

2. Vaccination program for livestock animals should be strengthened to prevent the livestock diseases. The less the antibiotics are used, the less is the risk of development of AMR in livestock population. It is therefore recommended that the DLS should produce adequate vaccines and focus more on vaccinating the livestock population to reduce the incidence of AMR microbes within the country.

3. Coordination and Collaboration: Coordinate and collaborate with multi-sectoral, inter-ministerial and different committees and forums at local, national and international levels.

# CHAPTER-1

# INTRODUCTION TO ANTIMICROBIAL RESISTANCE

## CHAPTER-1: INTRODUCTION TO ANTIMICROBIAL RESISTANCE

### 1.1. ANTIMICROBIALS AND RESISTANCE:

**1.1.1 Antimicrobials:** Antimicrobials are chemical substances, often derived from natural products, produced by the living microorganisms and characterized by distinct physical, chemical and biological properties making them ideal chemotherapeutic agents for the treatment of infections. They are active against a wide range of infectious diseases, including those caused by bacteria (antibiotics), viruses (antivirals), fungi (antifungals) and parasites (antiparasitics including antimalarials). They have capacity to inhibit and kill disease-causing microorganisms, thereby treating patients. The mode of action of antibiotics can be sub-divided into bacteriostatic inhibiting bacterial growth in the host, and bactericidal, directly killing bacteria. Antibiotics with either of these modes of action can be effective in the treatment of bacterial infections.

**1.1.2 Antimicrobial Resistance (AMR):** Antimicrobial resistance (AMR) is defined as the ability of a microorganism to survive and reproduce in the presence of an antimicrobial agent. AMR is also known as drug resistance. Clinicians and researchers have identified AMR worldwide and have further recognized AMR as one of the greatest challenges to global public health. AMR can be intrinsic (innate to a given species of microorganism), evolved through mutation or acquired. An example of intrinsic resistance would be when, a microorganism does not possess the target site that is specific to a given antibiotic drug and therefore, the antibiotic does not affect the microorganism. In addition, many microorganisms have thick cell walls, or are able to pump antibiotic out of the cell. This can make it difficult for antimicrobial agents to reach their target and result in a level of innate resistance against antimicrobials agents in certain microorganisms.

Microorganisms can become resistant to antimicrobials through various routes. Bacteria may respond to the presence of antimicrobial agents by limiting their cell permeability to a particular group of antimicrobial agents by changing the lipo-poly-saccharide composition, decreasing the porin content, or over expressing the efflux pumps. Microorganisms can also become resistant through random changes that occur in their genetic code, which enable them to withstand the destructive effects of antibiotics by chance. In addition, genetic code carrying the blueprints for antimicrobial resistance can be shared between microorganisms, thus allowing previously susceptible bacteria to acquire resistance.

**The most important mechanisms of AMR are:** (i) production by microorganism of an enzyme that inactivates the antimicrobial agent; (ii) a gene mutation within the microorganism which reduces the binding of the antimicrobial agent; (iii) post-transcriptional or post-translational modification of the microorganism which reduces the binding of the antimicrobial agent; (iv) reduced uptake of the antimicrobial agent by the microorganism; (v) active efflux of the antimicrobial agent; and (vi) overproduction of the targeted enzyme by a microorganism. [1]

The occurrence and spread of AMR is being accelerated by the misuse, overuse, and inappropriate use of antimicrobial agents. The poor quality of antimicrobial medicines; weak laboratory capacity; inadequate drug monitoring and surveillance system; insufficient drug regulations and lack of proper execution in case of production to ensure antimicrobial drug safety, efficacy and quality; poor treatment adherence by patients; non-therapeutic use for growth promotion in farm animals; self-medication and the sale of antimicrobials over-the-counter or through internet sales; availability of counterfeit or poor-quality antimicrobials; and inadequate or non-existing programs for infection prevention and control have been found to be the factors contributing to an increased incidence of AMR.[2]

### 1.2. IMPACT OF ANTIMICROBIAL RESISTANCE (AMR):

AMR is regarded as one of the most important global public health problems because it reduces the effectiveness of antimicrobial treatment. This leads to increased morbidity, mortality, disease burden and health care expenditure; negatively contributing to increased production losses, and reduced livelihoods and food security. AMR is a major threat to global public health and no country acting on its own can adequately protect its citizen against it. Jim O'Neill, et al, May 2016, in his "Review on Antimicrobial Resistance: Tackling Drug-resistant Infections Globally" reported that as many as one million people will die every year globally and estimated the tragic human cost in terms of lost global productivity, between now and 2050, would be as high as 100 trillion USD without a policy to stop the worrying spread of AMR.[3]

## 1.3 GLOBAL & NATIONAL RESPONSE TO ANTIMICROBIAL RESISTANCE:

**1.3.1 World Health Organization (WHO) Response:** WHO being the responsible technical organization acknowledged AMR as a global public health problem long before in 1998 and responded officially at World Health Assembly (WHA) in its 51st Resolution (WHA51.17, May 1998, agenda item 21.3) to urge member states to develop measures to encourage the appropriate and cost effective use of antimicrobials; to prohibit the dispensing of antimicrobials without the prescription of a qualified healthcare professional; to improve practices to prevent the spread of infection and thereby the spread of resistant pathogens; to strengthen legislation to prevent the manufacture, sale and distribution of counterfeit antimicrobials and the sale of antimicrobials in the informal market; and to reduce the use of antimicrobials in food-animal production. Countries were also encouraged to develop sustainable systems to detect resistant pathogens, to monitor volumes and patterns of use of antimicrobials and the impact of control measures.[4]

In 2010, the 63rd session of the Regional Committee of WHO South-East Asia Region Office (WHO-SEARO) approved a Regional Strategy for Prevention and Containment of AMR in Delhi. In the following year, the Health Ministers of the member states of WHO-SEARO endorsed the "Jaipur Declaration on Antimicrobial Resistance" in the WHO-SEA Regional Committee Meeting held in Jaipur, India. In the same year, the resolution of WHO Western Pacific Region Office (WHO WPRO/RC62.R3) urged member states to adopt the WHO six-point policy package to combat AMR. While some countries have taken significant steps, the local and national responses to contain AMR have been insufficient in most member states. In 2013, the Draft Action Agenda for AMR in WHO-WPRO was developed in response to analyses of AMR surveillance. In 2014, the member states of WPRO approved the draft action agenda, which was reflected in the resolution of WHO WHA-67.25, stressing the need for a global action plan.

In 2013, WHO undertook an initial survey, entitled the "Worldwide Country Situation Analysis: Response to Antimicrobial Resistance" over a period of two years, from 2013 to 2014 to determine the extent of problem, review the current practices of antibiotic prescription, and create recommendations to prevent and control AMR. This survey was conducted in 133 countries in all six WHO regions and focused on the building blocks that are considered prerequisites to combat antimicrobial resistance. They recommend that all countries should develop a comprehensive national plan; establish laboratory capacity to undertake surveillance for resistant microorganisms; ensure access to safe and effective antimicrobial medicines; control the misuse of these medicines; advocate for raising awareness and understanding of AMR among the general public; and implement effective infection prevention and control programme on priority basis.[5]

In 2014, the Regional Director of WHO-SEARO included AMR as one of her six regional flagship programs to address the problem effectively. In 2015, WHO in collaboration with its member countries and partners developed a draft global action plan to combat antimicrobial resistance, including antibiotic resistance. In May 2015, the 68th Session of WHO World Health Assembly (WHA-68, May 2015) adopted a "Global Action Plan on Antimicrobial Resistance (GAP-AMR: 2015)" with 5 objectives. Governments were asked to approve the plan and, in doing so, declared their commitment to address the problem of AMR as a threat to global health. One essential step in implementing the Global Action Plan would be to develop comprehensive national strategic and action plans in countries where they are now lacking and further develop and strengthen existing plans.

Several sessions of the WHO Regional Committee for South-East Asia adopted resolutions on the prevention and containment of antimicrobial resistance, with the last one being in Dili, Timor-Leste, in September 2015. At present many countries including Bangladesh have responded to AMR and have developed comprehensive national strategic and action plans to contain AMR.

**1.3.2 The United Nations (UN) Response:** The United Nations (UN) with its members countries represented by Heads of State and Government and other UN Organizations, in accordance with General Assembly Resolution 70/183 organized a high-level meeting at the United Nations Headquarters in New York on 21st September 2016 on Antimicrobial Resistance (AMR) and reaffirmed the blueprint for tackling antimicrobial resistance through the "WHO Global Action Plan 2015 On Antimicrobial Resistance" and its five overarching strategic objectives developed by WHO in collaboration with its members states, and subsequently adopted by

the Food and Agriculture Organization (FAO) of the United Nations (UN) and the World Organization for Animal Health (WOAH).[6]

The UN Member States have committed to work at the national, regional and global levels to develop policy initiatives, national action plans, and multisectoral programme activities; to implement national measures for strengthening appropriate antibiotic use in humans and animals; and to support the implementation of such plans. National and international collaboration is needed to assess resource and to provide sustained technical and financial investment in shared research, laboratories and regulatory capacities, as well as professional education and training, with a view to safeguarding human and animal health, and welfare for the environment as a whole.

**1.3.3. Bangladesh National Response:** Bangladesh, being a signatory of the "Jaipur Declaration-2011" for the containment of antibacterial resistance, has responded to AMR by taking an initiative to implement integrated AMR activities through a multi-sectoral approach. The Disease Control Unit, Communicable Disease Control (CDC) of Directorate General of Health Services (DGHS) of the Ministry of Health and Family Welfare (MoHFW) of Bangladesh completed the formation of different national and local level committees such as the National Steering Committee (NSC), National Technical Committee (NTC), and National Working Group (NWG), in April 2012 to contain antimicrobial resistance. The MoHFW approved all committees in October 2012. The NWG has developed the following strategic documents and these have been subsequently approved by the NSC.

(a). National Strategy for Antimicrobial Resistance Containment (AMRC) in Bangladesh: 2012-2016: The Core Working Group (CWG) prepared a "National Strategy for Antimicrobial Resistance Containment (AMRC) in Bangladesh: 2012-2016" and was approved by the NSC.[7,8,9] The Objectives of the National Strategy for AMRC are to: establish a multi-sectoral approach to planning, coordination and implementation of ARC activities; promote and ensure rational use of antimicrobial agents in human health, livestock and fisheries; promote and strengthen infection prevention and control measures to minimize the emergence and spread of antimicrobial resistance (AMR); promote and strengthen bio-safety and bio-security principles and practices and containment measures; review, update and strengthen regulatory provisions; strengthen surveillance system for AMR containment; promote operational research and education in the area of AMR; and establish Advocacy, Communication and Social Mobilization.

(b). National Action Plan on AMRC: 2016-2020: The NWC conducted a number of consultative meeting in 2016 and also developed the "National Action Plan on AMRC: 2016-2020" in November 2016 which was approved by the NSC.[7,8,9] Major activities include: ensuring rational use of antimicrobials; ensuring good manufacturing practice (GMP) at pharmaceutical industries; ensuring infection prevention and control (IPC) activities at health care facilities and at community level; establishing a surveillance system to monitor antibiotic resistance; conducting advocacy, social mobilization for health care providers, drug sellers, community members and owners of animal farms and fisheries; and ensuring adequate funding for basic and operational research.

(c). National Surveillance System and Laboratory Network: Under the National Action Plan, a well-designed, robust, web-based "National Surveillance System and Laboratory Network" to monitor antimicrobial resistance in human and animal health has been established. The primary objective of the national surveillance system is to find out the status of antibiotic resistance among frequently isolated pathogens. A central coordination body has been formed with a focal person in place. A total of 10 regional surveillance laboratories (microbiology) both from the public and private medical college hospitals have been identified. The protocol for a surveillance system has been developed and a number of trainings have been conducted. A four-day training on "Antibiotic Susceptibility Testing (AST)" for microbiologists and laboratory technicians, from 15 medical college hospitals, throughout country, conducted in November 2015. An adequate number of kits and reagents for conducting AST for 10 regional surveillance microbiology laboratories in selected medical college hospitals were distributed in early 2016 and standard method of AST have been put into operation.

A list of priority pathogens isolated from affected patients have been identified including those causing urinary tract infection, diarrhoea, wound infection,

respiratory infection and septicaemia in line with the Global Antimicrobial Resistance Surveillance System (GLASS). An internal networking system is also in progress among the participating laboratories to facilitate web-based data entry and to share information within networks. Antibiotic resistance pattern will be updated periodically as per observed data to support the evidence-based treatment of major infectious diseases in Bangladesh. At present, funding and technical supports for conducting this surveillance are being provided by Global Health Security Agenda (GHSA); the CDC Atlanta, United States; and the American Society for Microbiology (ASM) until the year 2020.

### 1.4 DEVELOPMENT AND SPREADS OF ANTIMICROBIAL RESISTANCE

In Bangladesh, the development and spreads of antimicrobial resistance can be viewed by analysing the functions, roles and responsibilities of four main stakeholders namely: (1) the pharmaceutical industry as an entity representing production house manufacturing and selling antimicrobials; (2) intermediary groups as an entity of procuring and supplying antimicrobial drugs such as, health and family planning directorates, health institutions, organizations, groups, business parties, and whole sales/retail pharmacies to end users (patients – human and animals) as per prescriptions issued by qualified medical professionals; (3) end user groups as an entity representing clinicians, medical practitioners and veterinarians prescribing antimicrobial drugs for patients, and (4) the Directorate General of Drug Administration (DGDA) as a National Regulatory Authority (NRA) ensuring drug regulation in all stages of production, upto and including the dispense of medicines, to ensure the safety, efficacy and quality of drugs in the country.

**1.4.1 Drug Regulation and the Role of DGDA:** The Directorate General of Drug Administration (DGDA), one of the most important directorates of the Ministry of Health & Family Welfare (MoHFW) of the Government of the People's Republic of Bangladesh, is the designated National Regulatory Authority (NRA). The functions of the NRA are as follows:

(i) to regulate, control, standardize and enforce all aspects of drug legislations (statutory laws, policies, rules, procedures, acts, and ordinance related to drugs) including drug productions, quality control, import and procurement of raw materials and finished drugs, good manufacturing practice (GMP), licensing, inspecting (supervision and monitoring), export, sales and pricing of all kinds of medicines including those of ayurvedic, unani, herbal and homoeopathic drugs and medicines in the country to protect consumers' health rights, safety, and wellbeing;

(ii) to ensure drugs and medical devises are an affordable price, to encourage consumers to comply with treatment regimens; and

(iii) to prevent pharmaceutical fraud (such as GMP violation, off-level marketing , best price fraud, which occurs when the manufacturer falsely self-reports as its best price, continuing medical education fraud providing inflated information, fraudulent medicaid price reporting and manufactured compound drugs.

At present, there are 55 district offices of the DGDA in the country. All 55 officers in the district level function as "Drug Inspectors" in pursuant to the drug laws and regulations, and assist the implementation of drug regulations all over the country. In addition, several committees, including (i) the Drug Control Committee, (ii) the Drug Technical Committee, (iii) the Drug Pricing Committee, (iv) the Manufacturing Project Evaluation Committee, (v) the Herbal Drug Advisory Committee; and (vi) the Standing Committee for Procurement and Imports of Raw Materials and Finished Drugs, have a role in standardizing and assisting with drug regulations within the country.

The DGDA have developed several different standard manuals of policies and procedures that provide official instructions for the internal practices and procedures to be followed by the staffs, the members of different drug committees, the drug manufacturers, the suppliers and the end users. All the terms of references (TOR) of the committees and the manuals are available on the DGDA web page.[11] The manuals clearly and explicitly highlight the regulations of

[1] *Off-label marketing is the use of pharmaceutical drugs for an unapproved indication or in an unapproved age group, dosage, or route of administration. Both prescription drugs and over-the-counter drugs can be used in off-label ways.*

antibiotic use and encourages healthcare professionals to prescribe antibiotics only when clinically necessary, and to counsel patients in the proper use of antibiotics to comply with treatment and the benefits of completing the course of antibiotics as directed.

**1.4.2 Drug Production and the Role of the Pharmaceutical Industry:** The role of the pharmaceutical industry is to discover, develop, produce, market, and promote pharmaceutical drugs for both human and animal consumption. Pharmaceutical companies may deal in generic or brand medications and medical devices. They are subjected to a variety of laws and regulations that govern the patenting, testing, safety, efficacy, quality and marketing of drugs. The pharmaceutical industry in Bangladesh is one of the most developed technology sectors within the country. This sector provides 97% of the total medicinal requirements of the local market, and the remaining 3% of medicines are imported from the foreign countries. The pharmaceutical industry also exports medicines to about 133, countries including the USA, South America, Australia, Europe, and China. Pharmaceutical companies are expanding their business and aiming to further expand into the global export market. [10,14]

As per the DGDA regulations, it is mandatory for all local and foreign companies to follow GMP as per WHO recommended guidelines. Although, the top and the medium level companies strictly follow GMP and have high-tech facilities in their premises, however, they do not have Research and Development (R&D) facilities in real sense. The top 30 local companies have well-equipped Product Development (PD) Departments, rather than full-fledged R&D. In Bangladesh, the R&D status of modern medicines, in the pharmaceutical sector, is still at an infancy stage. Recently some top pharmaceutical companies, producing high-tech biopharmaceutical products, have started real R&D activities in a limited scale, of them only a few of the active pharmaceutical ingredient (API) producers have full-fledge R&D facilities. However, most of them are manufacturing drugs under technology transfer mostly from India and China. [14]

The roles of ayurvedic, unani, herbal and homeopathic drugs in selection for antimicrobial resistance are not known in Bangladesh, nor are any quality clinical research studies, papers or review articles available on this topic. There are numbers of experts working on medicinal plants in different institutions but none of these are operated in an integrated way to develop and establish medicinal flora as safe and effective alternatives to antibiotics drugs. In Bangladesh, the teaching universities with pharmacy departments do not have R&D facilities. There is a lacking of collaboration between the local manufacturers and the researchers from public and private universities to promote R&D activities. [14]

The way antimicrobials are manufactured in factories, the waste by-products generated, and the impact of effluent from factories to select for antimicrobial resistance in the environment, is now a pressing issue which has too often been neglected in discussions of AMR. There growing evidence that the pharmaceutical industries manufacturing APIs do not adequately treat API waste products, and as a result, high concentrations of active antibiotic ingredients are disposed into the local environment creating 'reservoirs' of antibiotic resistant bacteria, which can then be transferred into hospitals and the community.

More than 200 antibiotic production facilities located mainly in China and India; an estimated 30,000 to 70,000 metric tons of antimicrobial waste is generated by the antibiotics manufacturing industry; more than 95% of antibiotic manufacturing waste is disposed of in liquid form causing contamination in the environment (surface water of rivers, lakes and ponds). It is, therefore, highly recommended to treat waste before release to the environment; if not treated properly, environment polluted with untreated waste can create reservoirs of antibiotic resistance bacteria. The additional cost to prevent untreated waste release into the environment is approximately US$ 0.50 per kilogram of active ingredient. [13]

In Bangladesh, only 3% of the active pharmaceutical ingredient (API) is produced nationally and the remaining 97% of APIs are imported from foreign countries. The pharmaceutical industry should purchase potent and quality API when importing antibiotics from the global market. The DGDA should establish evidence-based, enforceable targets for maximum levels of efficacy for API associated with the manufacture of pharmaceutical products.

Pharmaceutical companies should improve monitoring

of API emissions from directly-operated manufacturing facilities as well as those of third party suppliers, and support the installation of proper waste processing facilities to reduce or eliminate API discharge. Such efforts should be based in voluntary, transparent and auditable commitments, with a globally consistent 'quality mark' applied to end products produced on 'environmentally responsible' basis.

Figure-1 below illustrates the emergence and spread of drug-resistant microbes (bacteria, parasites, fungus and virus) due to misuse of antimicrobial agents affecting the general population of human and farm animals

child welfare centers; (ii) Local Government Division (LGD) of the Ministry of Local Government, Rural Development & Cooperatives (MoLGRD&C) for providing healthcare services to the urban population under the Urban Primary Health Care Project in 10 City Corporations and 210 Municipalities throughout the country; (iii) Ministry of Fisheries and Livestock (MoFL) using drugs for cattle farms, fish farms and poultry; (iv) Ministry of Armed Forces Division for Army, Navy and Air Force personnel; (v) Ministry of Home Affairs for such as (i) Private Medical College & Hospitals, (ii) Private Hospitals and Clinics, and (iii) Non-Government Organizations (NGO); (iv) Retail Pharmacy owners.[11]

**Figure-1: Emergence and Spread of Resistant Microbes (Bacteria, Parasites, Fungus and Virus)**

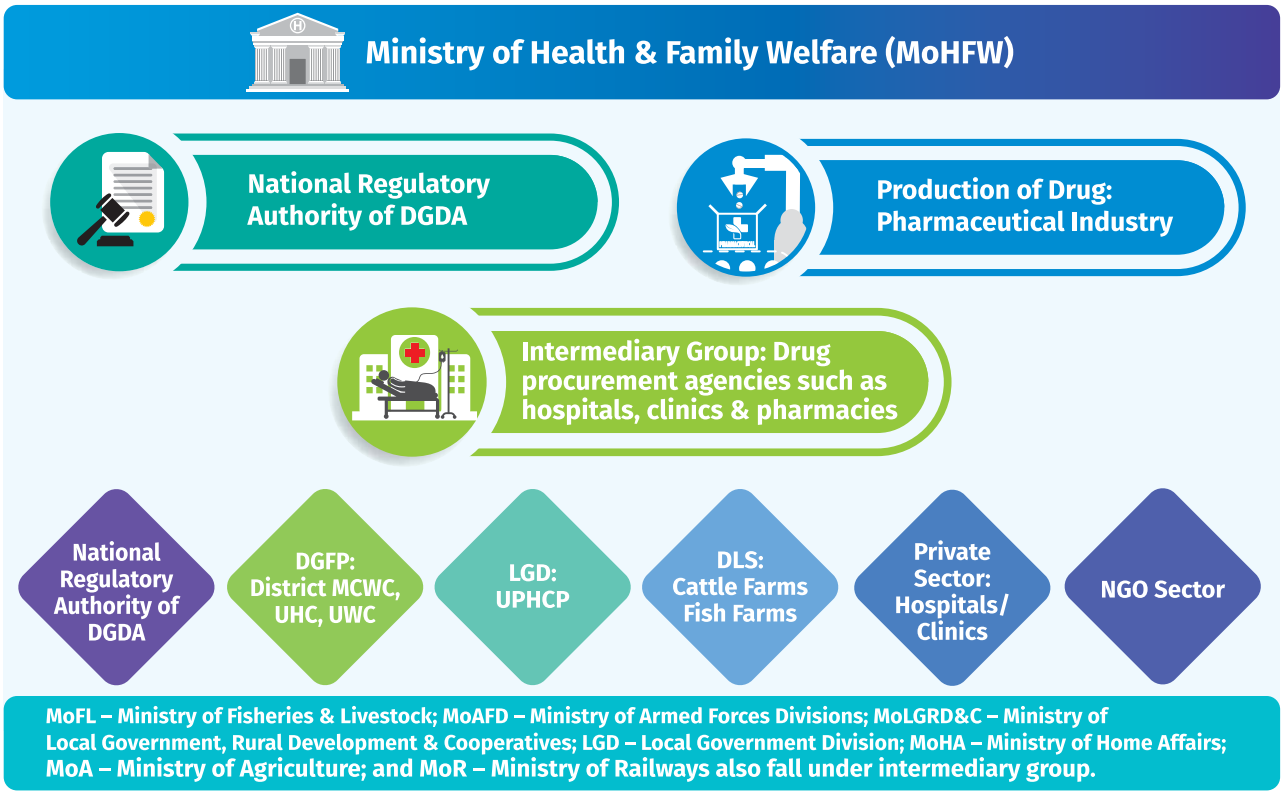

**1.4.3 Procurement of Drugs and the Role of Intermediary Agents:** The drugs produced by the pharmaceutical industry are procured and dispensed both by the public and private sectors. The stakeholders consuming drugs in the public sector include: (i) two directorates of the MoHFW namely DGHS and DGFP, who consume the bulk amount of drugs for tertiary hospitals, district hospitals, upazila health complexes, and maternal &

**1.4.4 Development and Spread of Antimicrobial Resistance in Microbes:** Antibiotics are consumed clinically and/or misused either by oral, intravenous, intramuscular, intradermal or topical application by the patients (human and animal) as the end users at hospitals, clinics, homes, cattle farms, fish farms, and poultry farms and in agricultural farms. Figure-2 below shows the relationships between different

stakeholders in drug regulation, production, marketing, supply and consumption of antibiotics, and the development of antimicrobial resistance against the different types of antimicrobial agents.

production company does not follow proper methods of disposing antibiotic waste resulting environmental pollution, then the pharmaceutical company produces low quality drugs containing a lower stated antibiotic dose

**Figure-2: Relationships between different stakeholders in using antibiotics and the development of AMR**




Microbes may become resistant if the antibiotics consumed by the treated human or animal are low in quality and quantity at production level; overused, underused, inappropriately used or irrational used by patients, physicians or on and farms; and if the drug regulations are implemented poorly at national regulatory authority level. Therefore, the development and spread of antimicrobial resistance may occurred at three levels as follows:

**(a) Production level:** (i) if the API used for the production of antibiotics are low in quality and low in quantity; (ii) if the production company uses expired API; (iii) if the production industry does not invest in new drug discovery; (iv) if the pharmaceutical industry practices unfairness at all stages of production of antibiotics, such as GMP violation, off-level marketing , best price fraud, which occurs when the manufacturer falsely self-reports its best price, continuing medical education (CME) fraud, fraudulent medicaid price reporting, and manufactured compound drugs; (v) if the which in turn increase selection for drug resistant microbes. This issue presents a major public health threat with serious implications for national as well as global health as antibiotic resistance genes spread around the world through travel and trade all over the world. [15,16]

**(b) Intermediary level:** The end users (patients – both human and animals) usually get the antibiotics through written prescriptions from registered health professionals, who are acting as a clinically and technically qualified intermediary dynamic force between production houses and the patients. Although the physician is expected to pursue "Standard Treatment Guidelines", the study conducted in 2014 revealed that only 60.9% key prescribers are aware of Treatment Guidelines.[18] In Bangladesh, National Drug Policy (2016) has prohibited the sales and distribution of antibiotics without prescription.[17] However, before 2016, patients procured antibiotics over-the-counter (OTC) from retail pharmacy shops, where the retail pharmacy owners/pharmacists/sales personnel

dispensed antibiotics directly without prescriptions.

Patients may collect antibiotics from over-the-counter (OTC) and consume them in improper doses for an inappropriate duration, in order to avoid physician consultation fees, both in rural and urban areas. These irrational uses of antibiotics by patients results in selection for drug-resistant bacteria; the patient with an infection that is resistant to antibiotic treatment is forced to attend hospitals and clinics, from where the drug-resistant bacteria may spread to other patients through poor hygiene and unclean facilities. Drug-resistant bacteria may further spread to the general public through environmental pollution. Antibiotics are given for curative, prophylactic and growth promotion to the livestock animals and crops; animals in turn develop drug-resistant bacteria in their gut. The drug-resistant bacteria reach humans through food, environment (water, soil, air) and by direct human-animal contact causing drug-resistant bacteria to spread among the general population.[20]

**(c) Regulatory level:** The DGDA is supposed to ensure proper and effective implementation of drug regulations within the country by enforcing that the pharmaceutical industry produces and markets high quality medicines, disposes their APIs properly by treating waste effectively through effluent treatment plants (ETP) before it reaches the environment, maintains GMP by following guidelines, stops all kinds of pharmaceutical fraud, and invests in drug discovery.

The consumption of antimicrobials (social factors, influencing use and contributing to antimicrobial resistance), is associated with many dynamic features such as inappropriate and excessive use of antibiotics. People earning a low-income tend to forgo physician consultation fees, depend on a pharmacist's free consultation, and collect medicines including antibiotics, over the counter from the pharmacy.

### 1.5 THE GLOBAL ANTIBIOTIC RESISTANCE PARTNERSHIP (GARP):

The Center for Disease Dynamics, Economics & Policy (CDDEP), an international organization based in Washington DC, which was established with the objective of using research to support better decision-making in health policy. CDDEP conducts actionable, policy-oriented research on antibiotic resistance, malaria, disease control priorities, environmental health, alcohol and tobacco, and other global health priorities. CDDEP has developed and designed a project called "Global Antibiotic Resistance Partnership (GARP)" with a view to establishing local policy analysis and policy development capacity related to antibiotic resistance in selected low- and middle-income countries.

The GARP-Project has supported the creation of multi-sectoral national-level working groups whose mandate is to understand and document antibiotic use and antibiotic resistance in human and animal population and to develop evidence-based proposals to encourage the introduction of measures to preserve antibiotic effectiveness, slow the spread of antibiotic resistance, and improve antibiotic access. The GARP Secretariat at CDDEP in Washington DC provides technical support to each working group, creates links within the GARP network, and involves the working groups in global discussions and policy development.

More than just establishing this capacity in eight diverse countries in Asia and Africa, CDDEP has developed a modus operandi for establishing a local capacity for antibiotic policy that is not duplicated by any other programs, recognizing that country's strengths and situations will take them in somewhat different positive directions. CDDEP has launched GARP-Phase-1 by establishing GARP-India, GARP-Vietnam, and GARP-Kenya in 2009; and GARP-South Africa in 2010. GARP-Phase-2 began its journey by establishing GARP-Tanzania and GARP-Mozambique in 2012, GARP-Nepal in 2013, and GARP-Uganda in 2014. GARP entered Phase-3 in July 2016 and has expanded the current GARP network in East and South Africa and in South and South-East Asia.

As a part of expansion of GARP in South-East Asia, CDDEP inaugurated a meeting held on 14-15 July 2016 at Kathmandu, Nepal and GARP-Bangladesh emerged as a new country to become a member of the Global Antibiotic Resistance Partnership to act as a technical member in combating antimicrobial resistance. A delegation consisting of seven members from Bangladesh, participated in the GARP-Bangladesh Inaugural Meeting, discussed the challenge of antimicrobials resistance, shared the experiences with other GARP countries, and reiterated its commitment to contain antibiotic resistance. GARP-Bangladesh will continue to utilize tools and technical support to ensure that the partnership continues to grow for the containment of antimicrobial resistance both at national and international levels.

From Bangladesh, two papers on the "National Strategy for Antimicrobial Resistance Containment in Bangladesh" were presented in the GARP inaugural meeting in Kathmandu identifying background activities and progress in combating in AMR in Bangladesh. The major social causes of

antimicrobial resistance such as misuse, overuse, underuse, and inadequate and inappropriate use of antibiotics in human, veterinary and fishery fields were identified. Operational research, advocacy, communication, social mobilization, education, surveillance and M&E were identified as the major key activities to make an effective AMR containment program in Bangladesh[3].

GARP-Bangladesh is committed to fostering four core functions by supporting a high-level coordinating mechanism on AMR as follows: (i) advocacy: to raise the awareness of both the lack of access to antibiotics and drug resistance at national and local levels, (ii) M&E: to establish, monitor, and report on national targets, (iii) resource mobilization: to finance implementation of national level action plans, and (iv) coordination of multisectoral action: to support national level, multisectoral action for the implementation of the action plan on AMR along with national efforts to improve access to effective antimicrobials.

### 1.5.1 GARP-Bangladesh Objectives:

- Mobilize a critical mass of national and local expertise across various sectors for the development of policies for antimicrobial resistance, prevention and control.
- Develop the evidence base for policy action on antimicrobial resistance; identify policy opportunities where research dissemination, advocacy, and information can have the greatest impact in slowing down the development and spread of resistance.
- Collaborate and cooperate with global, national and local initiatives to develop and implement actionable national strategies to address the challenge of antibiotic resistance.

### 1.5.2 Priority Activities of GARP-Bangladesh:

In response to global and national AMR, GARP-Bangladesh will provide technical support as a partner of choice to the national program and perform important activities on a priority basis.

Formation of GARP-Bangladesh National Working Group: The GARP-Bangladesh National Working Group (NWG) has already been formed. The members of the GARP-Bangladesh NWG includes representation from multi-sectoral, inter-ministerial, health policy maker, public health specialist, microbiologist, pharmacologist, clinician, researcher, professional bodies, as well as pre-eminent education scholars. The GARP-Bangladesh will provide overall direction for the organization and meet on a regular basis to discuss policy issues and the progress of activities.

**Conduct Situation Analysis:** As a part of national response to AMR, GARP-Bangladesh is undertaking the situation analysis on the current status of AMR, identifying gaps in existing practices and processes, and providing recommendations on antibiotic use and to prevent antibiotic resistance in Bangladesh. The situation analysis includes health and economics context of the country; antimicrobial disease burden, prevalence and incidence of bacterial diseases and antibiotic resistance; antibiotic supply chain, management and implications of antibiotic access, veterinary use of antibiotic, and conclusion and recommendations.

Review and assist in the implementation of the National Strategic and Action Plan: GARP-Bangladesh will provide technical support by reviewing the national action plan to define what strategic actions need to be taken to address the gaps and meet the strategic objectives. GARP-Bangladesh will review the action plan in line with the proposed WHO and CDDEP strategic objectives as follows:

(i) Improve awareness and understanding of AMR and educate health care professional including risk communication; (ii) Reduce the incidence of infection through effective immunization, sanitation, hygiene and infection prevention and control (IPC); (iii) Strengthen knowledge through surveillance; and ensure sustainability through funding, research and development; (iv) Improve access to antibiotics to treat infections; (v) Optimize the use of antimicrobial medicines in human and animal health; and (vi) Change incentives that discourage over use and enforce rational use.

[3] *Maj. Gen. Md. Mustafizur Rahman, Advisor, GARP-Bangladesh & DG, DGDA and Dr. M G Mostafa Musa, Executive Member, GARP-Bangladesh & Ex. Technical Advisor, CDC, DGHS presented the papers in the GARP inaugural meeting held at Kathmandu, Nepal on 14-15 July 2016.*

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# CHAPTER-2

# HEALTH SYSTEM AND ECONOMIC CONTEXT OF BANGLADESH

## CHAPTER-2: HEALTH SYSTEM AND ECONOMIC CONTEXT OF BANGLADESH

### 2.1 GEOGRAPHIC AND DEMOGRAPHIC CONTEXT:

**2.1.1 Geography of Bangladesh:** Bangladesh is a low-lying, riverine country situated in the South Asian Region. The land is hilly and dry in the north and south east parts of the country. The Ganges, the Jamuna, the Meghna, the Karnafuli and the Brahmaputra are the main rivers of Bangladesh, carrying tons of silt from the Himalayans that eventually improves the fertility of the land. The country has only 17.5 percent forest land. Bangladesh has a tropical monsoon climate characterized by heavy seasonal variations in rainfall, high temperatures and high humidity. Three distinct seasons are generally recognized: a dry, hot and warm summer from March to June; a hot, humid and rainy monsoon season from July to October; and a dry, cold winter season from November to February. In general, maximum summer temperatures range between 38 °C and 41 °C (100.4 °F and 105.8 °F). [1]

**2.1.2 Demography of Bangladesh:** The demography of Bangladesh is fairly homogeneous, with very little variation in race, ethnic background, income level, and school achievement. According to Census 2011 of Bangladesh Bureau of Statistics, the total adjusted population of Bangladesh was 149.77 million in 2011. The male population was 74.98 million and female 74.79 million. The sex ratio of Male vs. Female is almost 1:1. Taking inter-censal growth rate of population as 1.37 per annum, the estimated total population stands 162.46 million in 2017 with a density of 1,077 per square kilometre. The population household size is 4.7 per family unit. A total of 67.3% of the population lives in rural Bangladesh, while 32.7% lives urban areas. Table-1 below shows population statistics in Bangladesh. [1]

**Governance:** Bangladesh has a parliamentary form of government; the President is the head of state, while the Prime Minister is the Chief Executive of the government. Dhaka is the capital of Bangladesh and is the largest city located almost in the centre of the country. For convenience of administration, the country is divided into eight administrative divisions; each is placed under a Divisional Commissioner. Each division is further sub-divided into 64 districts and each district is headed by a Deputy Commissioner. Each district is further divided into 489 upazila(s) (sub-districts) and each upazila is headed by an Upazila Executive Officer.[1,2]

Fertility and Contraceptive Use: The total fertility rate (TFR) is 2.3 per woman of reproductive age in Bangladesh. The TFR has declined steadily from 6.3 births per woman in 1971 to 2.3 births per women in 2014.[3] In rural area, the age-specific fertility rate is 142 per 1,000 women of reproductive age in 20-24 years age group. However, the age-specific fertility rate in urban areas is higher reaching 196 per 1,000 women in 20-24 years of age group. The peak of childbearing age has remained high in this 20-24 age group and the largest absolute change in fertility also occurred in this age group, declining from 192 births per 1,000 women in the 2004 to 142 births per 1,000 women in 2014. [3]

Universal Primary Education: Bangladesh has adopted universal primary education as a fundamental goal. The literacy rate of population aged 7+ years in both sexes reached 63.6% in 2015. The adult literacy rate among population aged 15+ years in both sexes reached 64.6% in 2015 [2] The country has formulated a National Action Plan for Education to realize the goals of Education for All. With a view to spreading and augmenting the quality of education, the government has nationalized 26,193 primary schools in January 2013; furthermore, jobs of 104,776 teachers have been nationalized. [5]

**Table-1: Population Statistics in Bangladesh**

| Population Statistics | | |
|---|---|---|
| 1. | Total population in 2017 in million | **162.46** |
| 2. | Gross national income per capita (PPP international $, 2013) | **2** |
| 3. | Life expectancy at birth m/f (years, 2015) | **71/73** |
| 4. | Average life expectancy at birth (year, 2015) | **71.8** |
| 5. | Probability of dying between 15 and 60 years m/f (per 1 000 population, 2015) | **151/105** |
| 6. | Total expenditure on health per capita (Intl USD, 2014) | **88** |
| 7. | Total expenditure on health as % of GDP (2014) | **2.8** |

Latest data available from the Global Health Observatory

## 2.2 BANGLADESH ECONOMIC CONTEXT:

**2.2.1 Poverty Reduction and Growth Trends:** Bangladesh has made commendable progress in respect to the eradication of poverty and hunger. It sustained a gross domestic products (GDP) growth rate of 7.05% in 2016 and the per capita GDP is 1,384 USD.[6] Healthy growth has been accompanied by corresponding improvements in several social indicators, such as increased life expectancy at birth (71.8 years) and lower total fertility rate (2.3 births per woman). The national poverty headcount ratio declined from 56.7% in 1991-92 to 24.8% in 2015. The incidence of poverty has declined by an average of 1.74 percentage points in Bangladesh during 2000-2010 against the target of 1.20 percentage points. [5]

The poverty headcount ratio for 2015 is estimated to be 24.8% indicating that the target fixed at 29.0 for 2015 has been achieved. The poverty gap ratio has declined from 17 in 1991-92 to 6.5 in 2010. Bangladesh has already met one of the Millennium Development Goal (MDG) indicators of target-1 by bringing down the poverty gap ratio to 6.5 against the 2015 target of 8.0. The estimated figures suggest that the MDG target of halving the population living below the poverty line (from 56.7% to 29.0%) has been achieved well ahead by 2012.

Unemployment as well as underemployment still persists especially among young people between 15 and 24 years of age. This age group comprises nearly 8.5% of the country's total population and 22% of the total labour force. Bangladesh has demonstrated its capacity for achieving the goal of poverty reduction within the target timeframe. However, attaining food security, ensuring nutritional wellbeing, and reducing income inequality are some of the major concerns the country continues to strive for.[5] Table-2 below shows the progress in eradicating extreme poverty and hunger.

**2.2.2 Agriculture and Poverty Alleviation:** Bangladesh is a predominantly agricultural country. About 80% of the inhabitants directly or indirectly are involved in agricultural activities for their livelihood. Agriculture is the largest employment sector in Bangladesh. As of 2016, it employs 47% of the total labour force and comprises 16% of the country's GDP. Pluralities of Bangladeshis earn their living from agriculture. Although rice and jute are the primary crops, wheat is assuming greater importance. The performance of this sector has an overwhelming impact on major macroeconomic objectives like employment generation, poverty alleviation, human resources development, and food security. The recent economic crisis has reemphasized the need to build more dependable food security system with increased productivity.

**2.2.3 Sources of Revenues in Bangladesh:** The sources of revenues collected by the government for public use are various taxes such as income taxes including personal and corporate income tax, taxes on payments to non-residents, mining and logging tax; non-tax revenue such as interest, dividends, profits, etc; capital receipt in the form of loans and borrowing; consumption taxes such as general sales tax, alcohol tax, tobacco tax, land transfer tax, etc; and value added tax (VAT), which is regarded as the single largest source of domestic revenue in Bangladesh. Government revenue has increased steadily from US$ 2.5 billion in 1995 to US$ 23.7 billion in 2016. Revenue increased by an average of US$ 8.3 billion per year from 1995 to 2016. The National Board of Revenue (NBR) is the apex authority of tax administration operated under the Internal Resources Division (IRD) of the Ministry of Finance.[7,8]

## 2.3 BANGLADESH HEALTH SYSTEM CONTEXT:

The Bangladesh "Ministry of Health & Family Welfare (MoHFW)" seeks to create conditions whereby the people of Bangladesh have the opportunity to reach

**Table-2: The progress in eradicating extreme poverty and hunger in Bangladesh.**

| | Development Indicators: Poverty and Hunger | Base Year 1990/91 | Target 2015 | Current Status |
|---|---|---|---|---|
| 1 | Population living below US$ 1 /day (Purchasing Power Parity (PPP), % | 70.1 | 35.1 | 43.3 |
| 2 | Population below national upper poverty line (2,122 kcal), % | 56.7 | 29.0 | 24.8 |
| 3 | Population below minimum level of dietary energy consumption (2,122 kcal), % | 48.0 | 24.0 | 40.0 |
| 4 | Poverty Gap Ratio (mean shortfall of total population from the poverty line), % | 17.0 | 8.0 | 6.5 |
| 5 | Growth rate of GDP per person employed, % | 0.9 | --- | 3.6 |
| 6 | Employment to population ratio (15+ years), % | 48.5 | 100.0 | 57.1 |
| 7 | Employed people living below US$ 1/day (PPP), % | 70.4 | --- | 41.7 |
| 8 | Prevalence of underweight children U5C of age 6-59 months, % | 66.0 | 33.0 | 32.6 |

**Sources:** MDG-Bangladesh Progress Report 2015, Ministry of Planning, Government of the People's Republic of Bangladesh.

and maintain the highest attainable level of health. To realize this aim, the MoHFW has set the goal of achieving "Good Health and Well-being of Sustainable Development Goals-3 (SDGs-3)" by 2030 through the promotion of health and well-being for all. [9] The health system in Bangladesh comprises four-key actors. These are the public sector, private sector, non-governmental organizations (NGOs) and development partners who will work together to achieve the SDGs-3.

**2.3.1 Organization of Public Health Sector:** Governance and Stewardship: The MOHFW to perform its responsibilities relies on entities directly under its control including DGHS, DGFP, DGDA, DGNM, NIPORT, HEU, HED and different other statutory bodies such as BMDC, SMF, PCB, BNC, BHB, and BU&AB. During the 4th Sector Program, major activities for improving the governance and stewardship functions of the MoHFW involve: updating regulatory instruments; reviewing of the structure, organogram and mandate for regulatory bodies; reviewing of Nursing Council Ordinance; amending of BMDC Act; enacting of proper regulations for SMF; and introducing an accreditation system for assessing the quality of private medical colleges that will also be extended to government medical colleges. Other governance issues relating to service delivery improvement will also be pursued through the implementation of the 4th Sector Program. The MoHFW has established an organizational structure and built adequate healthcare infrastructure at the country administrative level.

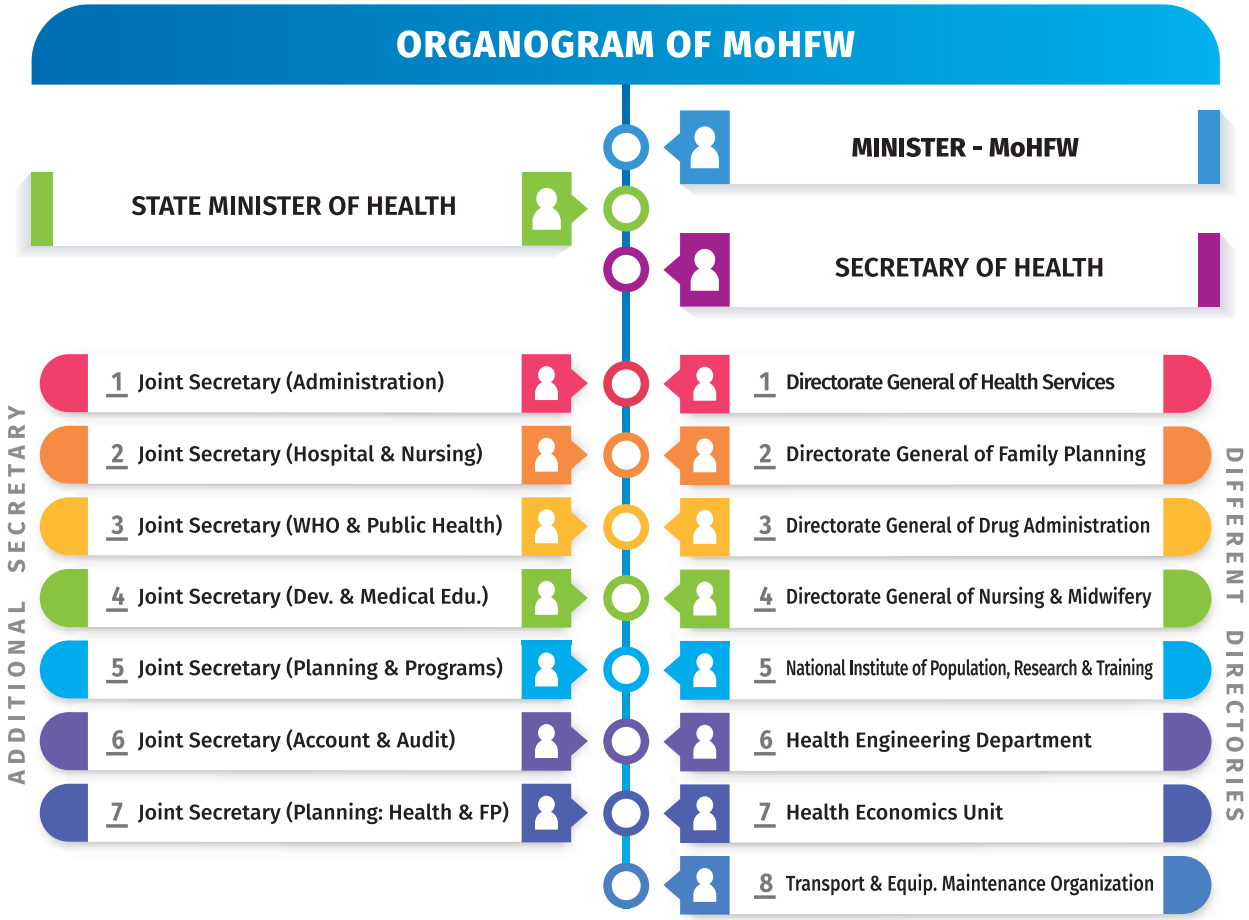
**Directorate General of Health Services (DGHS):** The DGHS executes different policies and strategies, develops annual plans, and manages and implements different health programs and activities across the country. The Director General is the head of DGHS and is assisted by two Additional Director Generals. There are 31 major disease control programs executed under DGHS. Medical college hospitals and divisional health offices are staffed with directors who are responsible for delivering all kind of healthcare services functions. In all medical colleges, principals are the academic heads ensuring medical teaching and learning. At district level, the Civil Surgeon (CS) and at Upazila level, the Upazila Health & Family Planning Officers are program heads who ensure healthcare services delivery.

**Directorate General of Family Planning (DGFP):** The DGFP is headed by Director General and is primarily responsible for ensuring quality and equitable health care services by improving access to and utilization of family planning; clinical and non-clinical contraceptives; and maternal, child, reproductive and adolescent health services throughout the country. The DGFP developed its first Population Policy in 2004, aiming to achieve replacement level fertility and a net reproduction rate of 1 (NRR=1) by 2010. The population policy was updated in 2012 and was renamed the "Bangladesh Population Policy 2012" with an objective of achieving a total fertility rate (TFR) of 2.1 and NRR=1 by 2015 along with the improvement of the other health indicators. The major strategies of the Bangladesh Population Policy 2012 are focused on client-centred services, urban health care services; area-based plans and strategies for low performing areas; and a behavior change communication (BCC) program.[38]

**Directorate General of Drug Administration (DGDA):** The DGDA, headed by the Director General, is the Drug Regulatory Authority of the country supervising and implementing all activities related to import and procurement of raw and packing materials; production and import of finished drugs; and export, sales, and pricing of all kinds of medicines. At present, there are 55 district offices under the DGDA in the country. All the officers at the district level function as "Drug Inspector" in compliance with drug laws and assist the licensing authority in performing their responsibilities. Besides a number of committees, such as the Drug Control Committee (DCC); Drug Technical Committee; Drug Pricing Committee; Manufacturing Project Evaluation Committee; Herbal Drug Advisory Committee; and Standing Committee for Imports to uphold regulatory activities and to advocate for the improvement of the quality of drugs, vaccines, biological products and other medicines for human, veterinary and aquaculture use. Figure-1 illustrates the organizational structure of MoHFW at national level.

**2.3.2. Healthcare Service Delivery System in Bangladesh:** The MoHFW is responsible for the provision of comprehensive healthcare services. To ensure healthcare affordable for all, the MoHFW has built adequate infrastructure at country's administrative levels (national, divisional, district, upazila, union, and ward levels) and is responsible for making policy; organizing, managing and coordinating implementation; and regulating national health and family planning–related activities and programs. Figure-2 below shows the public healthcare services delivery system.

**Figure-1 below illustrates the organogram of MoHFW with different directorates.**




The MoHFW delivers healthcare services through two separate executing authorities, the Directorate General of Health Services (DGHS) and the Directorate General of Family Planning (DGFP) using health facilities such as medical college hospitals, specialized hospitals, district hospitals, upazila health complexes, community clinics and other health facilities; ensures supply of medical and health related goods (e.g. drugs, instruments, equipment, laboratory reagents); deploys trained healthcare professionals (clinicians, surgeons, doctors, researchers, nurses, lab technicians, auxiliary health staff); and provides healthcare services (e.g. primary, secondary and tertiary healthcare, mental healthcare, diagnostic laboratory services, etc.) for the people of the country.

Although the health ministry has an extensive healthcare infrastructure, healthcare facilities further need an adequate supply of skilled health professionals, drugs, instruments and other necessary supplies. To bring healthcare services closer to the population, the MoHFW has developed a Community Clinic for every 6,000 population which provides primary health care, especially in rural areas. [35] The Bangladesh public health system remains highly centralized, with planning undertaken by MoHFW and little authority delegated to local levels. The Health Information System suffers from the bifurcation of the Ministry into DGHS and DGFP, with separate and distinct reporting systems for each directory.

**2.3.3 Private and NGO Healthcare Sectors:** The private and NGO sectors have emerged, as partner of choice, to develop healthcare facilities and provide healthcare services for the urban and rural populations in Bangladesh. The private sector provides modern and traditional health services through a range of facilities from hospitals to clinics, laboratories and drug stores; and the informal private sector, which largely consists of untrained providers practicing modern, homeopathic and traditional medicine.

**2.3.4 Health Workforce Situation:** Health annual report documented that there were 106,162 employees working, compared to the sanctioned 127,841 positions in June 2016 indicating only 83.0% of posts were filled at

**Fiqure-2: Public Healthcare Service Delivery System**

| PUBLIC HEALTHCARE SERVICES DELIVERY SYSTEM<br>RESPONSIBLE MINISTRY – MINISTRY OF HEALTH & FAMILY WELFARE (MoHFW) | | | | |
|---|---|---|---|---|
| **Health Facilities** | **DGHS** | | **DGFP** | |
| Medical Colleges: (Public (22) & Private (54); Specialized hospitals with post-graduate institutes (7) | Principal & Institute Director | | Director | |
| Division (8)<br>Specialized Hospitals (30) | Divisional Director-Health | | Divisional Director-FP | |
| District (64)<br>District Hospitals (62); MCWC (97) | District Civil Surgeon | | District Deputy Director-FP | |
| Upazila (492)<br>UHC (492); Hospital (34) | Upazila UH&FO | | Upazila Upazila FP Officer | |
| Unions (4,501)<br>UH&FWC (3,863); USC (1,382) | HI/AHI | MT-Lab & MA | FPI/AFPI | FWV/SACMO |
| Wards (40,509)<br>Community Clinic (12,394) | HA | CC-CHCP | FWA | |

**Source:** Universal Health Coverage for Inclusive and Sustainable Development. Country Summary Report for Bangladesh, Sep. 2014[35]

DGHS in 2016. The DGHS has to fill 17.0% vacant positions. In DGFP, there have been a total of 29,116 employees working compared to the sanctioned number of 32,512, with a total of 3,396 (10.5%) vacant positions as of December 2014. Under the Directorate General of Nursing and Midwifery (DGNM), there have been a total of 16,082 nurses working compared to the sanctioned 21,234 positions with 5,152 vacancies, which constitutes 24.3% of the total number of sanctioned positions in June 2015. [2]

There is a large cadre of health care providers in the country in the informal sector. This comprises semi-qualified allopathic providers (e.g. community health workers, medical assistants, and trained and untrained midwives), unqualified allopathic providers (drug shop retailers, rural doctors, etc.), traditional healers (practitioners of Ayurvedic, Unani and homeopathic medicine) and faith healers. They are not a part of the mainstream health system but a major health care provider for the poor rural population, especially in remote and hard-to-reach areas.

**2.3.5. National Health Plan - Sector Wide Strategic Approaches:** The Bangladesh Government through the MoHFW, started reforming the health sector by developing a health and population sector wide strategy, in 1997. The sector wide strategy had advocated a number of institutional and governance reforms, notably the shift from a project basis towards a coordinated sectoral programme. These reforms were then implemented through a series of five year sectoral programmes. MoHFW developed the following National Health Plan:

(i) First National Health Plan (1998-2003): The First 5-year Sector Wide Approach (SWAp) National Health Plan entitled "Health and Population Sector Program (HPSP: 1998-2003)", replaced 128 discrete health projects in the health ministry. (ii) Second National Health Plan (2003-2011): The Second SWAp National Health Plan entitled "Health, Nutrition and Population Sector Program (HNPSP: 2003-2011)", was implemented over a period of seven years.

(iii) Third National Health Plan (2011-2016): The Third SWAp National Health Plan entitled "Health, Population and Nutrition Sector Development Program (HPNSDP: 2011–2016)", ended in December 2016 with remarkable achievements of the MDGs. (iv) Fourth National Health Plan (2017-2022): The Fourth SWAp National Health Plan has been developed, and entitled the "4th Health, Nutrition and Population Sector Program (4th HNPSP: 2017-2022)", it has been in operation since January 2017 and will continue operating for a period of five and half years, ending in June 2022.[9]

**2.3.6 Challenges in Healthcare Provision:** From the point of view of health rights, all the citizens of Bangladesh have the right to receive health care

services according to need; however, low government investment in public facilities, some user charges and payments for medicines, and the high cost of the private sector have resulted in significant inequity in access to healthcare services. Existing reforms such as community clinics and maternal care vouchers, provide access to only limited services, while the proposal for health insurance for formal sector workers will not address the majority of those engaged in the informal and rural sector. In relation to user experience and equity of access, the general public perception of the public health system is poor, with complaints of long waiting times, absenteeism, poor behavior of providers, and exclusion of some marginalized groups. Access to care demonstrates higher rates of utilization of public and private services by the wealthier quintiles, but there has been some improvement in equity in access over the last decade.

### 2.4 NATIONAL HEALTH INDICATORS:

Health indicators are dimensions measuring different aspects of the health of a population within a community or a group or a state, tracking it over time, and comparing it with other populations. There are two main types of national health indicators: (i) health status indicators and (ii) health determinant indicators. These are briefly described below:

**2.4.1 Life Expectancy at Birth:** Prevention and control of infectious diseases in Bangladesh has contributed to the increase in life expectancy at birth, which measures the health status across all age groups. In Bangladesh, the life expectancy at birth in both sexes has improved steadily from 47.0 years in 1972 to 71.8 years in 2015, which is slightly higher than the world average. The life expectancy at birth is 73.1 years for women; on the other hand, the life expectancy at birth for men is 70.6 years, which is 2.5 years lower than their female counterparts. Bangladesh has undergone consistent improvements to life expectancy at birth (71.8 years in both sex) compared to other GARP and SARC countries whose values are below 70 years with the lowest in Mozambique, which is only 57.6 years in both sexes.[36,37]

**2.4.3 Maternal and Child Health Status:** A total of 64% of women, who gave birth, received antenatal care from a medically trained provider in 2014 compared to 55% in 2011. The percentage of women who had four or more antenatal visits, over the course of pregnancy increased from 26% in 2011 to 31% in 2014. About 42.1% of births were assisted by a medically trained provider in 2014. The percentage of births attended by a skilled provider has increased by 2.6 times since 2004, due to an increase in deliveries at medical facilities; 37% of births were delivered in the health facility and 36% of women received postnatal care from a medically trained provider within two days of their delivery. [3]

A total of 80% children age 12-23 months had been fully vaccinated against measles, in 2014. Only 6% of children under-five had diarrhoea in 2014, of them 36% of children were taken to a health facility or health provider for treatment. Among children with diarrhoea, 77% received Oral Rehydration Salts (ORS), A total of 5% of the children under-five had symptoms of Acute Respiratory Infection (ARI) in 2014; 42% of these children received treatment for ARI from health facility or health provider, and 34% children received antibiotics to treat the illness. 37% of children under-five had a fever in 2014; of these children, who had fever, 55% were taken to a health facility or health provider for treatment. Among those who received treatment, 9% received antibiotics; among the children who received antibiotics, 45% of these children received antibiotics that were prescribed by the non-health professionals.[3]

**2.4.4 Nutritional Status of Children and Women:** Bangladesh has given nutrition a high priority and developed first the "National Food and Nutrition Policy" in 1997, to improve the nutritional status of the general population of the country. This policy was subsequently reviewed in 2015 and lead to the "National Nutrition Policy 2015" to improve overall national nutrition and to align with global and national policies in the areas of health, education, agriculture, and environment.[44]

Bangladesh Demographic Health Study (BDHS) 2014 documented that a total of 36% of under five children (U5C) were stunted (height-for-age), 14% were wasted (weight-for-height), and 33% were underweight (weight-for-age). The targets set in the third national health plan (HNPSDP: 2011-2016) to improve the nutritional status for children (with stunting and wasting) have been achieved. Breastfeeding is almost universal in Bangladesh; 96% of children are breastfed during the first year of life and 87% of children are breastfed until aged 24 months. 51% of children are breastfed within one hour after birth, and 89% are breastfed within one day after delivery. 55% of children

under age 6 months are exclusively breastfed. 27% of Bangladeshi children receive a pre-lacteal feed. Bottle feeding is common in Bangladesh; 22% of infant aged 6-9 months are fed with a bottle with a nipple. Bottle feeding is most common in children aged 4-5 months (26%. Complementary foods are not introduced in a timely fashion for all children. 70% of breastfed children aged 6-9 months receive complementary foods. 62% of children received vitamin A supplementation.[3]

31% of ever-married women aged 15-19 years are undernourished (BMI <18.5). However, women's nutritional status has improved considerably in the last 10 years. The percentage of women undernourished (BMI<18.5) has declined from 34% in 2004 to 19% in 2014. On the other hand, being overweight or obese (BMI ≥25) among ever-married women aged 15-49 years has been increased over the past decade from 9% in 2004 to 24% in 2014. Using a lower cut-off point, of BMI ≥23 as a measure of overweight or obese among ever-married women aged 15-49 years, the proportion has increased from 17% in 2004 to 39% in 2014.[3]

**2.4.5 Infant and Child Mortality:** Data from the "Bangladesh Demographic and Health Survey 2014 shows that the neonatal mortality rate (NMR) was 28 deaths per 1,000 live birth, the infant mortality rate (IMR) was 32 deaths per 1,000 live birth, and the under-5 child mortality rate was 46 deaths per 1,000 live birth in the five years preceding the survey (Calendar Years 2010-2014). The BDHS survey has recorded a steady decline in IMR from 87 deaths per 1,000 live birth in 1990 to 32 deaths per 1,000 live birth in 2014. The mortality rate in children under five was 151 per 1,000 live birth in 1990, and this decreased to 46 per 1,000 live birth in 2014. As a consequence of declining rapid childhood deaths, Bangladesh has achieved its MDG-4 target for under-five mortality (48 per 1,000 live birth by 2015).[3,5] Table-3 below shows the child mortality rates and ratio indicating improvement in child health.

**Table-3: Health Indicator: Reduce Child Mortality**

| | Health Indicator: Reduce Child Mortality | Base Year 1990/91 | Target: 2015 | Current Status |
|---|---|---|---|---|
| 1 | Neonatal Mortality Rate (NMR per 1,000 live births) | --- | --- | 28 |
| 2 | Infant Mortality Rate (IMR per 1000 live births) | 87 | 31 | 32 |
| 3 | Under-five Child Mortality Rate (U5CM per 1000 live births) | 151 | 48 | 46 |
| 4 | Proportion of 1 year-old children immunized against measles, % | 54 | 100 | 80 |
| 5 | Prevalence of underweight children under-five years of age (6-59 m), % | 66.0 | 33.0 | 33.0 |

**Trends in Childhood Mortality:** Since 1993-1994, the BDHS surveys in Bangladesh have obtained childhood mortality rates for the five-year period preceding the survey. Over the last two decades, the data confirm a steady downward trend in childhood mortality (Table-4). Between the 1989-1993 and 2010-2014 periods, infant mortality declined by 56% from 87 deaths per 1,000 live births to 38 deaths per 1,000 live births. Even more impressive is the 71% decline in postnatal mortality and 65% decline in U5C mortality over the same period. As a consequence of this rapid rate of decline in childhood mortality, Bangladesh has achieved its MDG-4 target for U5C mortality of 48 deaths per 1,000 live births by 2015.[3,5]

The success of programs on immunization, control of diarrhoeal diseases and Vitamin-A supplementation are considered to be the most significant contributors to the decline in child and infant deaths; a large part of this can be attributed to conscious investment by the government, in addition to steady economic and social development. Bangladesh is a global leader in

**Table-4: Trends in Early Childhood Mortality**

| Neonatal, postnatal, infant, child and U5C mortality rates for five-year periods preceding the BDHS survey | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Data Sources | Reference Period | Neonatal Mortality | Post-natal Mortality | Infant Mortality | Child Mortality | U5C Mortality |
| 1 | BDHS 2014 | 2010 -2014 | 28 | 10 | 38 | 8 | 46 |
| 2 | BDHS 2011 | 2007 -2011 | 32 | 10 | 43 | 11 | 53 |
| 3 | BDHS 2007 | 2002 -2006 | 37 | 15 | 52 | 14 | 65 |
| 4 | BDHS 2004 | 1999 -2003 | 41 | 24 | 65 | 24 | 88 |
| 5 | BDHS 1999 -2000 | 1995 -1999 | 42 | 24 | 66 | 30 | 94 |
| 6 | BDHS 1996 -1997 | 1992 -1996 | 48 | 34 | 82 | 37 | 116 |
| 7 | BDHS 1993 -1994 | 1989 -1993 | 52 | 35 | 87 | 50 | 133 |

Computed as the difference between the infant and neonatal mortality rates

developing low-cost interventions such as the use of zinc in the treatment of childhood diarrhoea, oral rehydration solution, delivery kits, tetanus vaccinations for pregnant women, and iodized salt.

**2.4.6 Maternal Mortality:** The Maternal Mortality Ratio (MMR) in Bangladesh was 574 per 100,000 live births in 1990/91, declining from 322 in 2001 to 194 live births per 100,000 in 2010 (BMMS 2010) and further declining to 170 in 2013. [3,4,5] The overall proportion of births attended by skilled health personnel increased by more than eight-fold in the last two decades, from 5.0% in 1991, to 42.1% in 2014. Over the same period, antenatal care (ANC) coverage (at least one visit) increased to 51 percentage points; 27.5% in 1993-94 to 78.6% in 2014. However, challenges remain in the area of access to reproductive health. Table-5 below shows the improvement in maternal health as measured by different maternal health indicators.[3,5]

**Table-5: Health Indicator: Improve Maternal Health**

| | Health Indicator: Improve Maternal Health | Base Year 1990/91 | Target: 2015 | Current Status |
|---|---|---|---|---|
| 1 | Maternal Mortality Ratio, (MMR per 100,000 live births) | 574 | 143 | 170 |
| 2 | Proportion of births attended by skilledhealth personnel, % | 5.0 | 50 | 42.1 |
| 3 | Adolescent birth rate, (per 1000 (women) | 79 | 83 | --- |
| 4 | Antenatal care (ANC) coverage (at least one visit by skilled health provider), % | 27.5 | 100 | 78.6 |
| 5 | Antenatal care (ANC) coverage (at least four visits by skilled health provider), % | 5.5 | 50 | 31.2 |
| 6 | Contraceptive Prevalence Rate (CPR), % | 39.7 | 72 | 62.4 |
| 7 | Unmet need for family planning, % | 21.6 | 7.6 | 12.0 |

These interventions have been rolled out locally, scaled up and even used in other developing countries. Despite these improvements, there are challenges ahead. While mortality rates have improved, major inequalities within segments of population still need to be addressed. Childhood injuries, especially drowning, have emerged as a considerable public health problem responsible for a full quarter of the deaths among children 1-4 years of age.

**2.4.7. Combat HIV/AIDS, Malaria and Tuberculosis (TB):** HIV/AIDS: Report on "UNAIDS DATA 2017" shows that the HIV incidence rate (measuring only new cases) is very low, less than 0.01 per 1,000 population (<1 case per 100,000 population) in Bangladesh, as measured in 2016. The HIV prevalence (measuring both new and old cases) is also low, less than 0.1% in high-risk populations. In 2016, a total of 3,900 known HIV/AIDS cases were reported in Bangladesh; of them a total of 1,800 cases (46.1%) were on antiretroviral treatment (Table-4). There was a total of 1,000 AIDS related mortalities. Sex workers, people who inject drugs, gay men and other men who have sex with men, transgender people, and prisoners have been identified as the most vulnerable populations at risk of HIV/AIDS. [5,32]

**Malaria:** There has been a significant improvement in the reduction of malarial deaths as a result of the implementation of the National Malaria Control Program (NMCP). In 2014, a total of 57,480 positive cases of malaria were found, with two major types of parasites (P. falciparum and P. vivax); of the positive cases, only 45 deaths have occurred. Malaria prevalence was recorded an estimated 777 cases per 100,000 population, in 2008, which declined to 434 cases per 100,000 population in 2014, constituting a reduction of almost half in malarial prevalence. The MIS data of NMCP show that the percentage of U5C sleeping under insecticide-treated bed nets in the high risk malarial zones was 81% in 2008 and this percentage increased to 92.2% in 2014. Only 60% of U5C with a fever had been treated with appropriate anti-malarial drugs in 2008; however, this percentage increased to 99.9% indicating that almost all children had been treated with anti-malaria in 2014.

**Tuberculosis (TB):** TB prevalence was 501 cases per 100,000 population in 1990, which had reduced to 402 cases in 2014, against the target of 250 cases, in 2015, under the National TB Program (NTP). The death rate associated with TB was 80 cases per 100,000 population in 1990, which had come down to 51 cases in 2014. The overall TB case notification rate was 53 cases per 100,000 populations in 2014. The NTP adopted the Directly Observed Treatment Short-course (DOTS) strategy and started field implementation in November 1993. The programme has been maintaining over 90% treatment success rate since 2006, and has successfully treated 92% of the new smear-positive cases registered in 2014. Table-6 below shows the overall performance in combating HIV/AIDS, Malaria and TB.

**Table-6 Health Indicator: HIV/AIDS, Malaria and TB**

| | Health Indicator: HIV/AIDS, Malaria and TB | Base Year 1990/91 | Target: 2015 | Current Status |
|---|---|---|---|---|
| 1 | HIV prevalence among population, % | 0.005 | 0.00 | <0.1 |
| 2 | Proportion of population with advanced HIV infection with access to antiretroviral drugs, % | --- | 100 | 46.1 |
| 3 | Prevalence of Malaria per 100,000 population (777 cases /100,000 in 2008) | --- | 311 | 434 |
| 4 | Deaths of Malaria per 100,000 population | 1.8 | 0.6 | 0.34 |
| 5 | Proportion of Children under-5 sleeping under insecticide treated bed nets (13 high risk malaria districts), % | 81 | 90 | 92.2 |
| 6 | Proportion of children under 5 with fever who are treated with appropriate anti-malarial drugs, % | 60 | 90 | 99.9 |
| 7 | Prevalence of TB per 100,000 population | 501 | 250 | 402 |
| 8 | Deaths of TB per 100,000 population | 80 | 30 | 51 |
| 9 | Detection rate of TB under DOTS, % | 59 | 100 | 53 |
| 10 | Cure rate of TB under DOTS, % | 73 | 90 | 92 |

**Sources:** MDG-Bangladesh Progress Report 2015, and MICS (2012-2013).

**2.4.8. Safe Drinking Water and Sanitation:** Bangladesh "National Policy for Safe Water Supply and Sanitation-1998" aims to improve the public health and to improve the environment.[33] Water supply and sanitation in Bangladesh are characterized by a number of achievements and challenges. However, the populations of Bangladesh have had access to an improved water source since 1993 largely due to the construction of tube-wells with the support of external donors. Bangladesh "Multiple Indicators Cluster Survey (MICS-2014)" data show that without considering the issue of arsenic contamination, 98% of the population of Bangladesh is using an improved/safe drinking water.

The MICS 2014 result shows that 25.6% of households have used appropriate water treatment methods to make the water safe; 56% population have used improved sanitation in 2012-13; the last stool of 38.7% children age 0-24 months has been disposed safely; 59.1% of the households have a specific place for hand washing with soap or other cleansing agents; and 94.0% households could afford to have soap and/or other cleansing agents.[34] However, access to safe water for all is a challenge, as arsenic and salinity intrusion, as a consequence of climate change, impair access to safe water especially for the poor. Table-7 shows the progress of using safe drinking water at national level.

**2.4.10. Outcomes of Health Indicators:** Despite many challenges, health outcome indicators have shown a marked improvement, with falls in neonatal, infant, under-five child, and maternal mortality rates and a significant reductions in the total fertility rate. In comparison with MDG targets, infant and under-five child mortality and total fertility rates are on track to reach the 2015 targets; maternal mortality and prevalence of underweight are not on track to reach targets despite significant reductions; while targets for HIV, malaria and TB are still potentially achievable.

These outcomes have been achieved by improvements in coverage with key interventions, such as delivery of healthcare services, childhood immunization, and the management of diarrhoea with oral rehydration salts. Quality of care in both public and private sectors is poor and should be improved with provision of quality training for services providers. The supply of quality medicines and other health resources should be ensured in healthcare facilities to improve healthcare services in Bangladesh.

**Table-7: Health Indicator: Safe Drinking Water and Basic Sanitation**

| | Health Indicator: Safe Drinking Water and Basic Sanitation | Base Year 1990/91 | Target 2015 | Current Status |
|---|---|---|---|---|
| 1 | Population using improved drinking water sources, % | 68 | 100 | 98.0 |
| 2 | Households using appropriate water treatment methods, % | --- | --- | 25.6 |
| 3 | Population using an improved sanitation facility, (%) | 34 | 100 | 56.0 |
| 4 | Safe disposal of faeces children age 0-24 months, % | --- | --- | 38.7 |
| 5 | Households with a specific place for hand washing with soap/cleansing agent, % | --- | --- | 59.1 |
| 6 | Households with availability of soap/cleansing agent, % | --- | --- | 94.0 |

**Sources:** MDG-Bangladesh Progress Report 2015, and MICS (2012-2013).

## 2.5 ACCESS TO HEALTHCARE AND ESSENTIAL MEDICINES:

**2.5.1 Access to Healthcare Services:** When healthcare services are available and when there is an adequate supply of services and resources with qualified health professionals in place, then the opportunity to obtain healthcare services exist in the community, and the population in the country in real sense may have "access to healthcare services". The extent and scope in which the population "gain access to healthcare services" is also dependent on financial, economical, governance, organizational, social and cultural dimensions that would either facilitate and/or limit the utilization of health services.

**Availability of Health Professionals:** The availability of the right kind of health providers is considered to be an important determinant measuring accessibility and hence utilization of healthcare services. Data from the "World Bank's World Development Indicators (2008-2015)" on the health system in Bangladesh, indicates that the number of physician is low, at only 0.4 per 1,000 population (1 physician per 2,500 population); the number of nurses is 0.2 per 1,000 population (1 nurse per 5,000 population); and the number of hospital beds is only 0.6 per 1,000 population (1 bed per 1,670 population). This suggests that there is an inadequate supply of health professionals and a lack of sufficient hospital beds in public facilities reducing the level of utilization of healthcare services in urban and at rural areas. [46]

The DGHS Health Bulletin 2016 has documented that 17.0% of doctor positions and 18.5% of medical technologist positions are vacant in DGHS; 10.5% of staff positions are vacant in DGFP; and 24.3% of nurse positions are vacant in DGNM. This indicates marked shortage of health workforce in the public health sector, together with an inappropriate skill mix and unequal distribution skewed towards doctors over nurses and technologists, with a ratio of Doctors vs. Nurses vs. Technologist of 1.0 : 0.4 : 0.25 (4 doctors vs. 1.6 nurses vs. 1.0 technologist) in contrast to the WHO recommended ratio of 1.0 : 3.0 : 5.0. [2,5] This inappropriate skill mix and unequal distribution are considered to be one of the major determinants limiting access to healthcare. [2,10]

Availability of Basic Laboratory Diagnostic Services: The Bangladesh Health Facilities Survey 2014 measured the availability of basic diagnostic capacity in 1,548 health facilities country wide and found that the District Hospitals (97%), Upazila Health Complexes (75%), MCWC (29%) and Union Health Centre (8%) have been offering haemoglobin testing; the majority of NGO facilities (70%) and private hospitals (81%) also have the capacity to conduct haemoglobin testing.[49] The availability of five basic laboratory tests for ANC services such as blood for haemoglobin, urine for protein, urine for glucose, blood grouping and Rhesus factor, and syphilis are lacking in most health facilities. The proportion of facilities ranges from a low of 2% with the capacity to do blood grouping and Rhesus factor to a high of 31% with the capacity for urine protein testing.[49]

A total of 42% of health facilities had blood glucose testing capacity, 40% had urine protein testing capacity, and 38% offered urine glucose testing. The most common systems for TB diagnosis were x-ray, available only in 33% facilities and TB smear microscopy available in 27% facilities; 20% facilities had TB rapid diagnostic test kits, and 7% facilities had culture medium for diagnosing TB. The low level and in some cases lack of laboratory diagnostic services limits the access to healthcare services in both rural and urban areas of Bangladesh.[49]

Availability of Essential and Primary Healthcare Services: In Bangladesh, a total of 93% of health facilities provide out-patient curative care for sick children; about 80% of health facilities offer vaccination services, and only 62% provide growth monitoring services; seven in ten facilities provide Vitamin A supplementation to children; More than 97% of health facilities offer ANC services; only 16% provide the tetanus toxoid vaccine at the time of ANC services. Only 4% of facilities are ready to provide quality ANC services according to the WHO recommended criteria. About 50% of upgraded Union Health and Family Welfare Centers (UHFWCs), 28% of union level public facilities, and 7% of CCs offer normal delivery services. TB services are provided primarily in District Hospitals (94%), Upazila Health Complexes (93%), and private hospitals (62%).[49]

**2.5.2 Access to Essential Medicines:** Availability of Essential Medicine Supply: Majority of health facilities, offering curative care for children, had the six essential medicines (Oral Rehydration Salts, Amoxicillin syrup, Paracetamol syrup or suspension, Vitamin A capsules,

Mebendazole/Albendazole syrup, and Zinc tablets) in stock. A total of 80% of public facilities had amoxicillin syrup/suspension available. Among the public sector facilities that offer curative care for sick children, MCWCs (92%) and USCs/RDs (69%) had this essential medicine.[49] Each of the four priority medicines (Ampicillin powder for injection, Ceftriaxone powder for injection, Gentamycin injection, and Benzathine benzyl-penicillin injection) were available in less than 10% of all facilities that offer curative care for sick children. [49]

BHFS 2014 provided information that only 28-36% of health facilities, most often in district and private hospitals, had availability essential medicines. One fourth of facilities that offer normal delivery services have all six essential items for infection control. The availability of four essential medicines for new-born care at the service delivery site was assessed and 78% of facilities were found to have amoxicillin syrup or suspension available. [49] A 2005 World Bank study found that the majority of patients were able to get medications on-site (83% at a public UHC, 80% at a public district hospital, and 64% at a public national hospital). [49] There is also evidence of frequent and persistent unavailability of drugs in district and medical college hospital, which showed that only 8% of outpatients reported receipt of the prescribed medicines. Almost 86% of the inpatients reported paying for drug from outside hospital.[50,51]

Access to essential medicines does not depend on only medicine availability, but also on ability to pay for the drugs and the data on whether people are paying in the public sector in Bangladesh. For example, the above-mentioned study also reported findings that 48% of antibiotics were purchased in quantities of a single day dose or less, suggesting that clients often find a full course unaffordable.[50] Prices for essential medicines are highly variable (by 500% or more) for many medications, and the cost of standard antibiotic regimens prescribed for common symptoms ranged from 7% to 20% of weekly incomes. Out-of-pocket expenditures on drugs make up 70% of total out-of-pocket health expenditures.[49]

**Essential Medicines and The National Drug Policy:** The first "National Drug Policy 1982" ensured access to essential drugs within the country and identified a total of 150 products as essential drugs. Since 1993, the number of the price-controlled drugs has been reduced to 117 as primary health care drugs. Since then, the growth of the local drug production has been accelerated. According to the DGDA records in 2002, all the essential drugs were produced locally and about 44.8% of local drug production was related to essential drug. In 2008, the list of essential drug had been increased to 209. The list of essential drug has been further reviewed under the "National Drug Policy 2016" and a total of 285 essential drugs have been finally approved; of them only 39 drugs can be obtained over-the-counter (OTC) without medical prescription. No antibiotics are allowed to sell from OTC. [42]

The price of medicines in Bangladesh is currently low. The DGDA has acted as a drug regulatory authority fostering an effective business policy within the pharmaceutical industry. The DGDA has the role of supervising and implementing drug regulations, and ensuring easy access to useful, effective, safe and good quality modern medicines including vaccines, biological, traditional, homeopathic and herbal medicines at affordable prices. Despite all these efforts, the majority of the population are not able to buy the complete medicines package as prescribed by their physician, either in public health facilities or in the private health facilities.[42,43]

**2.5.3. Access to Healthcare Services and 4th HNP SP: 2017-2022:** From the above perspective and the dimensions of access to healthcare services, the Government of the People's Republic of Bangladesh, through its ministry (MoHFW), has given the highest priority to equity of access to national healthcare services and aims to: (i) provide access to healthcare services, (ii) ensure access to safe and effective medicines and vaccines for all, and (iii) achieve quality, equity and efficiency towards universal healthcare coverage by 2030, ensuring the attainment of sustainable development goals-3. The SDGs-3 should be realized by strengthening primary healthcare and emergency care for all; expanding the availability of client-centred, equity-focused and high quality healthcare services; and motivating people to seek healthcare based their right to health.[9]

## 2.6 HEALTH AND ECONOMIC POLICIES OF BANGLADESH:

**2.6.1. National Health Policy:** The MoHFW reviewed the "National Health Policy 2008" in terms of its health, nutrition and population status; rural and urban health services delivery; health governance; gender equity; healthcare financing; health workforce; medical supplies; and waste management; and subsequently developed "National Health Policy-2011 (NHP-2011)" for the purpose of providing standardization in daily operational activities and clarity. The NHP-2011 sets out a general plan of action to guide desired indicators and outcomes, and is a fundamental guideline to aid health managers and policy makers in making decisions. The purpose of the NHP-2011 is to communicate to health managers and employees the desired outcomes. They help employees understand their roles and responsibilities within the healthcare organization. [24]

**2.6.2 Bangladesh Population Policy:** The first Bangladesh population policy was formulated in 2004 and was updated in 2012; it was renamed as "Bangladesh Population Policy 2012" with an objective of lowering the total fertility rate (TFR) to 2.1 and NRR=1 by 2015 along with the improvement of the other health indicators such as family planning methods; reproductive health, reproductive tract infections and HIV/AIDS, counselling services, maternal and infant mortality, health care for mothers and children, gender quity and women's empowerment, gender discrimination. The major strategies of the Population Policy 2012 have focused on client-centred services, urban healthcare services; area-based plans and strategies for low performing areas; and the behavior change communication program.[38]

**2.6.3 National Drug Policy:** In 1976, the Drug Regulatory Authority (DRA) was established under the MoHFW of the Government of the People's Republic of Bangladesh.[43] Following the establishment of DRA, the first "National Drug Policy-1982" (NDP-1982) was formulated in 1982 to improve the health and drug sector in the country and to ensure adequate supply and availability of essential drugs. The "Drug (Control) Ordinance 1982" was also promulgated in the same year. Guided by the objectives articulated in NDP-1982, the DRA controlled the price of the medicines. The NDP-1982 and Drug (Control) Ordinance 1982 had effectively brought to an end to transfer pricing and over-invoicing for the imports of capital machineries, raw materials, and packaging materials.[40,]

In October 2001, the MoHFW reviewed and amended the NDP-1982 and Drug (Control) Ordinance 1982; updated the policy and ordinance with new elements in order to properly deal with the changing of new technologies in the drug sector over a period of time; and formulated "National Drug Policy 2005 (NDP-2005)" to meet the requirement of the current needs of the country. The NDP-2005 ensured useful, effective, safe and good quality essential and other drugs at an affordable price; adapted the remarkable technological advancements; guided the drug sector to perform better in the competitive world market; and made the country a producer and an exporter of good quality drugs in the world.[41]

The MoHFW has further reviewed the NDP-2005 in December 2016 and updated, and come up with a new version of the "National Drug Policy 2016 (NDP-2016)" with the following objectives: to ensure people have easy access to safe, effective and good quality drugs at an affordable price; to ensure rational and safe use of drugs and proper dispensing; to achieve self-sufficiency in the manufacture of drugs and raw materials by providing services and facilities on a priority basis to all local drug manufacturing companies; to expand the export of drugs that are manufactured in the country; and to establish an effective surveillance system of medicines. One of the key components of the NDP-2016 is to strengthen DGDA into a fully functional National Regulatory Authority (NRA).[41,42,43]

**2.6.4. National Nutrition Policy:** In response to the basic human right to nutrition, Bangladesh has given nutrition a high priority and developed first the "National Food and Nutrition Policy" in 1997 to improve the nutritional status of the general population in the country. This policy was subsequently reviewed and updated to create the "National Nutrition Policy 2015", to improve the overall national nutritional status of all citizens including children, adolescent girls, pregnant women and lactating mothers; ensure availability of adequate, diversified and quality safe food and promote healthy feeding practices; strengthen nutrition-specific, or direct nutrition interventions; strengthen nutrition-sensitive, or indirect nutrition interventions; strengthen multi-sectoral programs and increase coordination among sectors to ensure improved nutrition; and to align it in support of global and national policies in the areas of health, education, agriculture, and environment.[44]

## 2.7 HEALTHCARE FINANCING IN BANGLADESH:

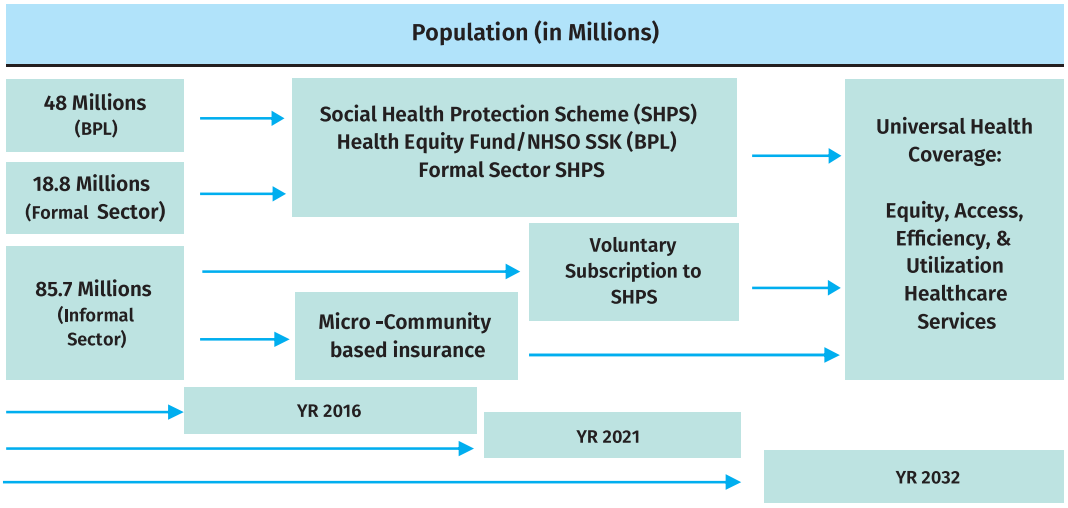
**2.7.1 Healthcare Financing Strategy:** The "Health Care Financing Strategy: 2012-2032" has been designed to provide a framework for developing and advancing health financing in Bangladesh. The strategy is aligned with (i) the vision of the 4th national health plan "HNPSP: 2017-2022", (ii) the universal coverage as defined by WHO, and (iii) the National Health Policy 2011.

The goal of the financing strategy is to strengthen financial protection and extend healthcare services country wide to create full coverage especially of poor and the vulnerable segments of the population, with the long-term aim of achieving universal healthcare coverage. The role of healthcare financing is to: (i) provide all people with access to needed healthcare services of sufficient quality; and (ii) ensure that the use of these services does not expose the user to financial hardship. Figure-3 below shows the timeline of proposed reforms to the healthcare financing strategy in Bangladesh.

The first or initial phase, started from 2012–2016, it was planned to pilot Health Protection Fund (HPF) among the households whose incomes have fallen below the poverty Line (BPL). In the second phase, that starts from 2016–2021, the HPF has been launched, with the intent to cover all households below the poverty line (31.5% of the population) through a non-contributory regime, and formal sector households (12.3% of pop.) through a contributory regime. During this interim period, community-based insurance will be promoted for households lacking coverage (56.2% of the population).

By 2032, it hopes to achieve UHC and integrate all households under the national HPF. Over its 20-year implementation period, the strategy aims at reduction of out-of-pocket payments from 67% to 32% of total health expenditure, increase in government expenditure from 23% to 30%, increase in social protection from 1% to 32%, and reduce the dependence on external funds from 8% to 5%.[13]

**Figure-3: Timeline of the Proposed Reforms of Healthcare Financing Strategy**




**Source:** Universal Health Coverage for Inclusive and Sustainable Development. Country Summary Report for Bangladesh. Health, Nutrition and Population Global Practice, World Bank Group, Sep. 2014 [35]

The 20-year health financing strategy proposes to cover the poor and is progressively extending the coverage to the all segments of the population by 2032. To increase financial protection for the entire population and decrease out-of-pocket payments, the following three strategic objectives have been proposed: (i) generate more resources for effective health services, (ii) improve equity and increase health care access especially for the poor and vulnerable, and (iii) enhance efficiency in resource allocation and utilization. [13]

**2.7.2. Bangladesh National Health Accounts:** Total Health Expenditure (THE) is the sum of public and private health expenditure. It covers the provision of health services (preventive and curative), family planning activities, nutrition activities, and emergency aid designated for health but does not include provision of water and sanitation. The Bangladesh National Health Accounts (BNHA) tracks THE between the fiscal years 1997 to 2012, reports on the basis of

cross-stratification and categorization by financing classifications, and describes the expenditure spent by the providers on health and other purpose on the annual basis. Its main goal is to inform national policymakers and other stakeholders of the magnitude and profile of health spending. It also serves in institutionalizing the monitoring of health outlays.

THE in Bangladesh is estimated as Taka 325.1 billion (US$4.1 billion) in 2012, Taka 153.9 billion (US$2.2 billion) in 2007, Taka 81.5 billion (US$1.4 billion) in 2002 and Taka 46.4 billion (US$1.1 billion) in 1997. In recent years, the THE grew at an annual average of around 14% in nominal terms. In real terms, the growth level has been approximately 8% annually. Figure-4 below describes the summary of Bangladesh National Health Accounts 1997-2012.[6,11]

Comparing health expenditure between urban and rural areas, it was found that urban expenditures on health are 33% of the total health expenditure constituting US$ 40.0 per capita per year, while the rural expenditures are less, at US$ 24.0 per capita. The government financing of urban health expenditures is 17% of urban health expenditure, while that of rural health expenditures is 26% of rural health expenditure. Chronic under spending of the MoHFW's budget indicates inefficiency in utilization of resources as observed in the public sector review and should be overcome by implementing health care financing strategy.[10,11, 12]

OOP payments are not used for prepayment mechanisms, and instead they are primarily used in direct spending in pharmacies and drug shops (70%),


**Figure-4: Summary: Bangladesh National Health Accounts 1997-2012**

According to the latest Bangladesh National Health Accounts (BNHA-V, Sep. 2017), it is estimated that total health expenditure (THE) remains at 2.8% of GDP (US$ 3.4 billion) spending only US$ 37.0 per capita per year (which was US$ 27.0 per capita in 2012), of which 67% comes through out-of-pocket (OOP) payments making up the largest share from the individual level; however, the OOP expenditure was 63% in 2012. Public funding for health is the main prepayment mechanism with scope for risk pooling, which constitutes only 23% of THE from the government side. The remaining 10% of the health expenditure source is being contributed by NGO (3%) and international development partners (7%). In comparison with the countries of South-Asian Regional Cooperation (SARC), the Bangladesh spends highest OOP (67%) in 2017 followed by India (62%), Pakistan (56%), Nepal (47%), Sri Lanka (42.1%), Bhutan (25%) and Maldives (18%) respectively. hospital for curative treatment (11.5%), hospital out-patient department (10%), diagnostic laboratories facilities (8.2%), and for other self-treatment options (8%).[11] There is no purchaser-provider split in the public health care system. The MoHFW directly provides care. Budget allocations are made in five-year increments and supported by the sector-wide approach program funded by several donors.

The financial protection and universal health coverage will ensure adequate healthcare services including vaccination to the people in general and the lower incoming group in particular. The patient's compliance to treatment regimens is expected to high; the misuse and irrational use of medicines particularly antibiotics will be low; and the overall impact of universal health coverage will lead to prevent the AMR in Bangladesh.

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# CHAPTER-3

# MICROBIAL DISEASE BURDEN AND ANTIMICROBIAL RESISTANCE

## CHAPTER-3: MICROBIAL DISEASE BURDEN AND ANTIMICROBIAL RESISTANCE

### 3.1 BACTERIAL DISEASE BURDEN AND ANTIMICROBIAL RESISTANCE

**3.1.1 Bacterial Disease Burden: Global Context:** Disease burden is the impact of a health problem, which is measured by incidence, prevalence, morbidity, mortality, financial cost and economical cost, or other indicators. It is often quantified in terms of Quality-Adjusted Life Years (QALYs) or Disability-Adjusted Life Years (DALYs), both of which quantify the number of Years Lost due to Diseases (YLDs). One DALY can be thought of as one year of healthy life lost, and the overall disease burden can be thought of as a measure of the gap between current health status and the ideal health status (in which cases, the individual lives to old age free from disease and disability).[1,2,3]

The Global Burden of Disease 2015 revealed that the low back pain and major depressive disorder were among the top ten causes of YLDs and was the cause of more health loss than diabetes, chronic obstructive pulmonary disease, and asthma combined. The study was based on data from 188 countries and was considered to be the largest and the most detailed meta-analysis to quantify levels, patterns, and trends in ill health and disability. The analysis concluded that the proportion of DALYs due to YLDs increased globally from 21.1% in 1990 to 31.2% in 2013.[4] These measures allow for the comparison of disease burdens, and have also been used to forecast the possible impacts of health interventions. By 2014, DALYs per head were 40% higher in low-income and middle-income regions compared to high income countries.[6]

The World Health Organization (WHO) has provided a set of detailed guidelines for measuring disease burden at local and national level.[3] In 2004, the health issue leading to the highest YLD for both men and women was unipolar depression;[6] however, the lower back pain was found to be the primary YLD in 2010.[7] According to an article in the Lancet published in November 2014, disorders in those people aged 60 years and older represent "23% of the total global burden of disease"; and the Lancet also documented that the leading contributors to disease burden were "cardiovascular diseases (30.3%), malignant neoplasms (15.1%), chronic respiratory diseases (9.5%), musculoskeletal diseases (7.5%), and neurological and mental disorders (6.6%)".[6] The leading causes of death and disability have changed from communicable diseases in children to non-communicable diseases in adults.

The Global Burden of Disease 2010 (GBD 2010) found that the leading causes of premature death and disability, or DALYs have evolved dramatically over the past 20 years with changes in the leading causes of DALYs in 1990 and 2010. Communicable, newborn, maternal, and nutritional diseases have fallen in rank during this period; while causes associated with ill health and death in adults such as ischemic heart disease, stroke, and lower back pain increased in rank between 1990 and 2010; Meanwhile causes and diseases that primarily affect children, such as preterm birth complications, lower respiratory infections, and neonatal encephalopathy increased in rank. However, diarrhoeal diseases in children decreased dramatically from rank one in 1990 to rank six in 2010.

Unlike most of the leading communicable diseases, HIV/AIDS and malaria increased by 351% and 21% respectively. Since 2005, however, premature mortality and disability from these two causes have begun to decline. Four main trends have driven changes in the leading causes of DALYs globally: aging populations, increases in non-communicable diseases, shifts toward disabling causes and away from fatal causes, and changes in risk factors.[8] Bangladesh is holding almost middle position in an epidemiologic transition where the burden of disease is shifting from a disease profile dominated by infectious diseases, under-nutrition and conditions of childbirth to one increasingly characterized by non-communicable chronic diseases.

**3.1.2 Bacterial Disease Burden: Bangladesh Context:** The levels and trends of health loss due to diseases, injuries, and risk factors in Bangladesh were quantified; and premature death, preterm birth complications, lower respiratory infections, and neonatal encephalopathy (birth asphyxia and birth trauma) were identified as the highest ranking causes contributing to the number of Years of Life Lost (YLLs).[8]

Taking all–cause mortality rate into account, the Figure-1 below shows the decline in mortality rate at

every age range. The higher points on the chart indicate that declines in mortality rates were faster in those age groups between 1990 and 2010. The greatest reductions in all-cause mortality rate were experienced by females aged 1-4 years (79%). Males aged 80+ years saw the smallest decrease in mortality rate (7%).[8]

by weighting the prevalence of different conditions based on severity. The top five leading causes of YLDs in Bangladesh have been identified as low back pain, iron deficiency anaemia, major depressive disorder, chronic obstructive pulmonary disease (COPD) and anxiety disorders.

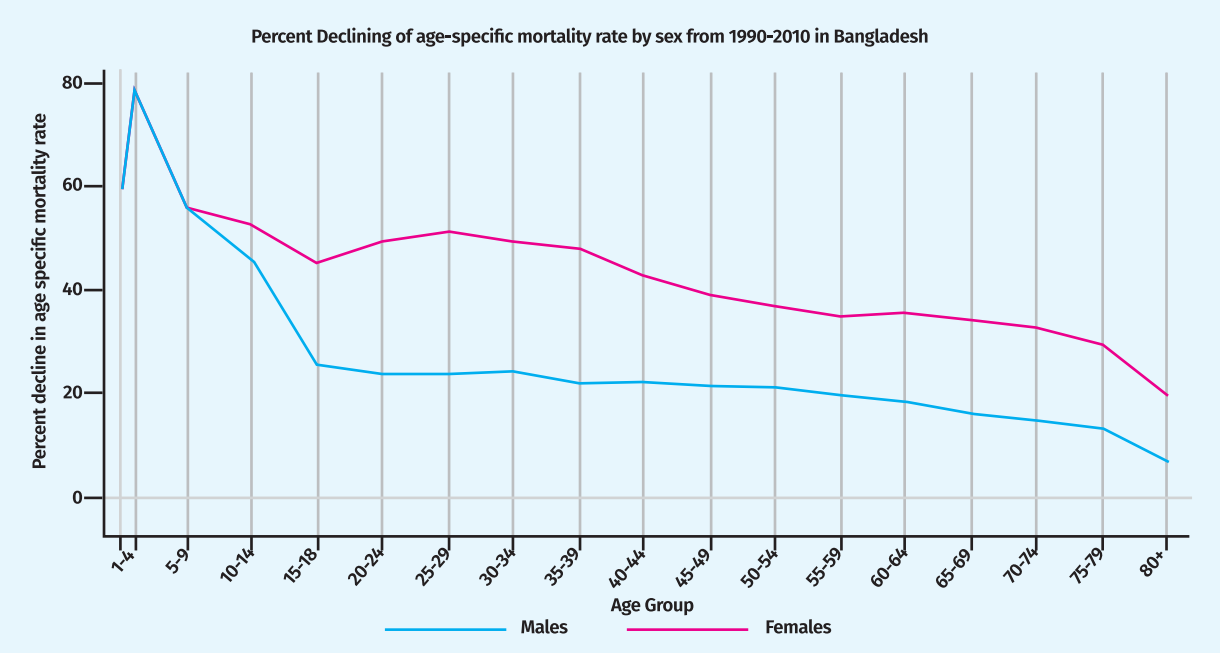



**Figure-1: Declining of age-specific mortality rate by sex from 1990-2010 in Bangladesh**

The Table-1 below shows the leading top 10 causes of Years of Life Lost (YLLs) and quantifies premature mortality by weighting younger deaths more than older deaths in 1990 and 2010 in Bangladesh.

Disability-Adjusted Life Years (DALYs): The number of DALYs quantifies both premature mortality (causing YLLs) and disability (causing YLDs) within a population. In Bangladesh, the top five causes of DALYs in 2010 were

**Table-1: Rank for top 10 causes of YLLs in 1990 and 2010 in Bangladesh[8]**

| Rank for Top 10 Causes of YLLs in 1990 | | | |
|---|---|---|---|
| Sl | Disease Profiles in 1990 | # YLL thousands | % |
| 1 | Diarrheal diseases | 8,491 | 13.5 |
| 2 | Preterm birth complications | 7,348 | 11.7 |
| 3 | Lower respiratory infection | 6,617 | 10.5 |
| 4 | Drowning | 3,071 | 4.9 |
| 5 | Neonatal encephalopathy | 3.037 | 4.8 |
| 6 | Protein-energy malnutrition | 2,934 | 4.7 |
| 7 | Tuberculosis | 1,314 | 2.1 |
| 8 | COPD | 1,186 | 1.9 |
| 9 | Tetanus | 1,170 | 1.9 |
| 10 | Congenital anomalies | 1,120 | 1.8 |

| Rank for Top 10 Causes of YLLs in 2010 | | | | |
|---|---|---|---|---|
| Sl | Disease Profiles in 2010 | # YLL thousands | % | % Change |
| 1 | Preterm birth complications | 2,915 | 8.5 | - (58) |
| 2 | Lower respiratory infections | 2,310 | 6.7 | - (65) |
| 3 | Neonatal encephalopathy | 2,289 | 6.6 | - (26) |
| 4 | Drowning | 1,344 | 3.9 | - (59) |
| 5 | COPD | 1,170 | 3.4 | - (1) |
| 6 | Diarrheal diseases | 1,155 | 3.4 | - (86) |
| 7 | Ischemic heart diseases | 1,086 | 3.2 | 244 |
| 8 | Tuberculosis | 999 | 2.9 | - (22) |
| 9 | Chronic kidney disease | 809 | 2.4 | - (10) |
| 10 | Cirrhosis | 744 | 2.2 | 1 |

**Note: COPD – Chronic Obstructive Pulmonary Diseases**

Of the 10 most important causes of disease burden, as measured by Disability-Adjusted Life Years (DALYs), diarrhoeal diseases showed the largest decrease, falling by 86% from 1990 to 2010.

Years Lived with Disability (YLDs): In 2010, the number of Years Lived with Disability (YLDs) has been estimated

preterm birth complications, neonatal encephalopathy (birth asphyxia and birth trauma), lower back pain, lower respiratory infections and chronic obstructive pulmonary diseases. In 2010, the ischemic heart disease was the only cause to appear in the top 7 leading causes of DALYs shifting from rank 30 in 1990.[8]

Risk Factors for Disease Burden: Overall, the seven risk factors that account for the most disease burden in Bangladesh are tobacco smoking, household air pollution from solid fuels, dietary risks, occupational risks of adults aged 15-49 years, high blood pressures, iron deficiency, and childhood underweight. The other leading risk factors for adults were high fasting plasma glucose, ambient particulate matter pollution, and suboptimal breastfeeding, in 2010.

Country Benchmarking of Burden of Disease: Bangladesh demonstrates a relatively satisfactory performance against 15 comparison countries and displays key insights into public health successes, though there are some areas where Bangladesh might be falling behind. However, in 2010, Bangladesh ranked 3rd for age-standardized death rate, age-standardized YLLs, life expectancy at birth, and health-adjusted life expectancy at birth; and ranked 5th in age-standardized YLD rate among the 15 comparator countries.[8]

**3.1.3. Impacts of Disease Burden:** The impact of disease burden is viewed by the combination of direct costs of medical care along with travel costs and the indirect cost due to loss of workforce productivity both in the household and at government level. At a household level, the incidence of a disease and/or injury has two immediate potential effects; firstly, the diseased or injured person may have to reduce their normal level of productive activity, whether paid or unpaid; and secondly, the household may need to increase its consumption of health services or goods at the expense of other goods and services. The impact at the society level is to increase the transfer of payment costs to meet social security expenditures because of the disease and/or injury from which the patients are suffering.[11]

The impact at company level: The financial and economic impacts of health origin are sustained losses in the case of companies' returns and a reduction in wealth; and an increase in both direct and indirect costs and a reduction in firm earnings. The reduction of earnings translates into lower future dividends paid and reduced shareholder wealth and consumption. Losses might also force reductions in profit retention and investment activities. The disease burden may impact negatively on macroeconomic performance through a number of different channels, which include increased health expenditure, incurred losses in labour and productivity, and reduced investment in human and physical capital formation.[11]

**3.1.4 Antibiotic Resistance –** A New Challenge: Bacteria are tiny single-cell living microorganisms with a defined cell wall, which do not have an organized nucleus and organelles. They are usually a few micro meters in length and often exist together in communities of millions of cells. Bacteria can be found in soil, water, plants, human, animals, deep in the earth's crust, organic material, hot springs, ocean depths, and elsewhere in the environment. According to bacteriologists, bacteria are found absolutely everywhere, even in places where temperatures may be extreme for other forms of life, or where they may be exposed to a high concentration of toxic chemicals. They can be spherical, rod like or spiral in shape. Humans and plants need bacteria to survive and to grow; bacteria in the digestive system are crucial for the breakdown of certain types of nutrients, such as complex sugars, into forms the body can use. Not all bacteria cause disease. Some bacteria protect their host against pathogens. When the pathogenic bacteria overpower, the bacteria that are usually present in a host, such a human or animal, they are able to produce an infection called bacterial disease, within the human or animal.

The bacteria which are pathogenic to humans can cause some of the most deadly diseases and devastating epidemics, such as diarrheal diseases including cholera and dysentery, diphtheria, pneumonia, tuberculosis, typhoid, typhus, etc., and have taken hundreds of millions of human lives in the past centuries. This epidemic has seen a remarkable reduction in the present time, due to the implementation of effective prevention and control programs, both worldwide and at a country level. In the past centuries pneumonia, tuberculosis and diarrheal diseases were the three biggest killers, both in Bangladesh and worldwide. As the supply of safe drinking water improved, well-designed national vaccines and immunization programs were implemented, and antibiotic treatment became more advanced, these interventions caused the human death toll to drop significantly.

Currently, more than 700,000 people worldwide are estimated to die each year due to antimicrobial

resistant (AMR) infections; this has been predicted to rise to 10 million deaths by 2050 if the situation continues unchecked. Bangladesh is not an exception to this trend. The rate of antibiotic resistance in Bangladesh is growing. In this context, it is important to understand the national situation in Bangladesh, find a way to preserve effective antimicrobials for future use, and shape health policy to slow down the spread of AMR. Figure-2 below shows the deaths attributable to AMR worldwide.[12]

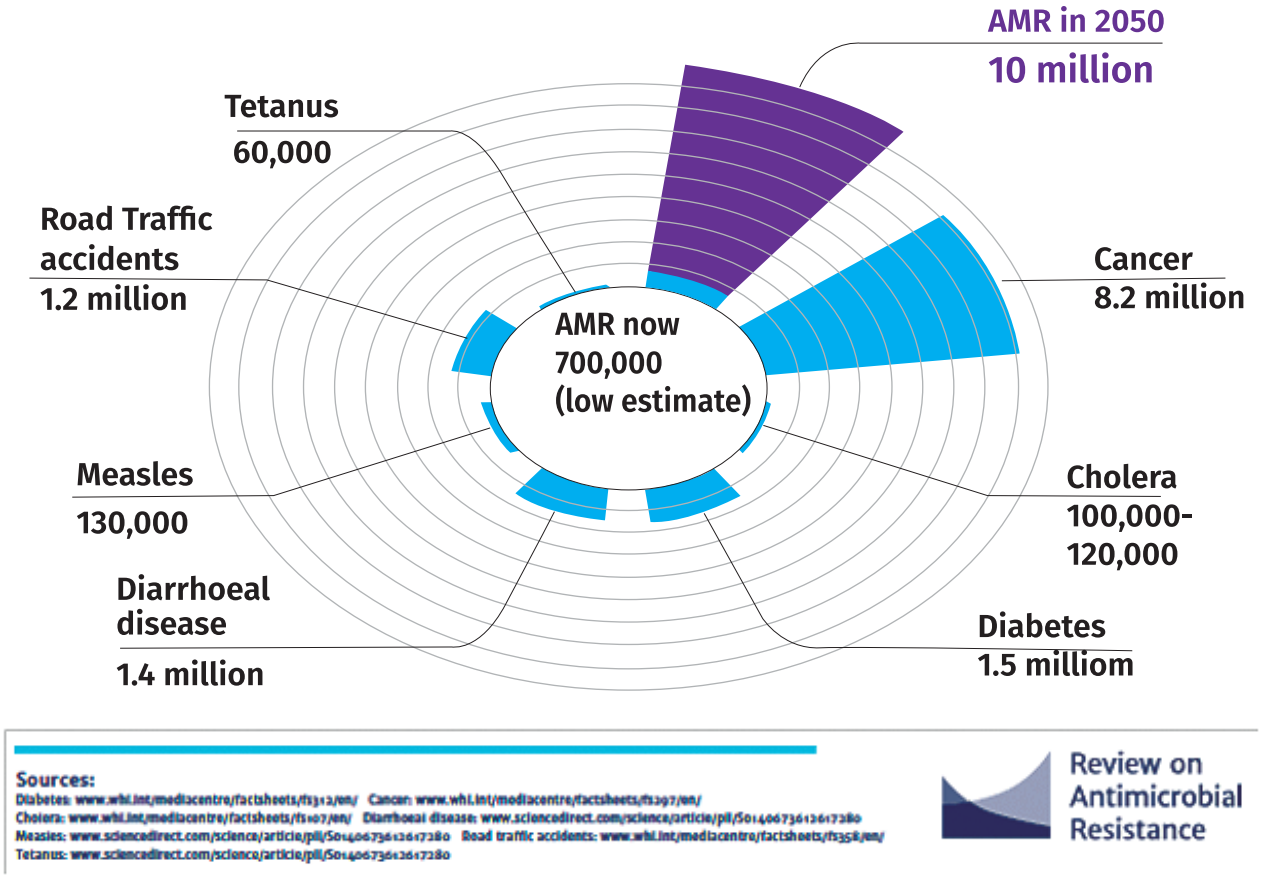



**Figure-2: Comparative analysis of death attributable to AMR and other common diseases every year**

It is estimated that more than half of antimicrobials are inappropriately prescribed, dispensed or sold in Bangladesh.[14] Brief consultation time, lack of quality in terms of patient examination, under-value in evaluating and reaching proper diagnosis to disease and use of inappropriate antibiotics by physicians is another important factor contributing to AMR.[15] A highly disproportionate physician to patient ratio [1] physician per 2,500 populations] exists in Bangladesh.[121] In addition, rural patients often travel long distances and incur expensive medical care in many cases; they are not willing to wait for laboratory results and less likely to return for follow-up visits, and prefer to receive immediate treatment and cure. Moreover, many drugs are expensive, and as a result low-income patients may purchase incomplete regimens and in most cases they discontinue treatment when their symptoms disappear, even when the pathogen has not been completely eliminated. A complete analysis is required to understand current trends and to set priority areas for policy development for decision makers.

**3.1.5 Major Bacterial Diseases, Aetiologies, and Resistance Patterns:** Systematic data on antibiotics from 2000 to 2012 have been collected for review and the mean antibiotic resistance, for 35 antibiotics, in Bangladesh, has been analyzed. The highest rates of antibiotic resistance were found in cloxacillin (100%), ampicillin (80%), oxacillin (78%), tetracycline (77%) and metronidazole (78%). The lowest rates were reported to imepenem (5%) and linezolid (4%).[13] Irrational use of antimicrobials both in urban and rural areas is documented and is found to be widespread in the community.[16,17] However, the organized data on the irrational use of antimicrobials in health centres is scarce.

There was no regular national surveillance conducted on AMR until 2016, except in selected diarrhoeal pathogens, monitored and documented by the research organizations like icddr,b, Dhaka. Despite the inadequacy of national surveillance data on infectious diseases and their resistance patterns, the data on major infectious diseases, their aetiologies, resistance patterns and risk factors, contributing to resistance to available antimicrobials, have been searched and reviewed. The AMR data from icddr,b, a few tertiary level teaching hospitals, and few population-based surveillance studies, both inside and outside Dhaka, have been collected to understand the patterns of resistance.

The available literature, medical journals, and research reports from the Government of Bangladesh, icddr,b, WHO-Bangladesh and other available national and international sources have been reviewed; and the data and information have been analysed to understand the pattern of antibiotic resistance. The most common bacterial, parasitic and viral diseases as categorized by the GBD 2010 for Bangladesh will be described. These are as follows:

(i) Major bacterial diseases, aetiologies, and resistance patterns such as acute respiratory infection (ARIs), diarrhoel diseases, tuberculosis (TB), urinary tract infections (UTIs), neonatal infection (sepsis), ear infections (otitis media), typhoid fever, and skin and soft tissue infections (SSTIs); (ii) Parasitic disease burden and antimicrobial resistance such as malaria and kala-azar; (iii) Sexually transmitted infections (STIs) disease burden and antimicrobial resistance such as chlamydia, gonorrhoea, syphilis and HIV/AIDS will be discussed in more detail.

**1. Acute Respiratory Infections (ARIs):** Data from the Bangladesh Demographic Health Survey 2014 (BDHS-2014) shows that children under-5 (U5C) mortality in the five years preceding the survey (which corresponds approximately to the calendar years 2010-2014) is 46 per 1,000 live birth. The BDHS 2011 estimated that the ARIs were responsible for up to 22% of deaths of U5C and 13% of neonatal deaths.[50,51] Several studies have examined ARI disease burden throughout country in which seven hospitals found that a total of about 37,300 children met the criteria for pneumonia, meningitis, and severe respiratory infections. Of the 16,505 children enrolled in the study, 135 had pneumococcus isolated from blood or cerebrospinal fluid samples.[49,52]

Considering the bacterial infection, lower respiratory infections (LRIs) were found to be the highest contributor to Years of Life Lost (YLLs) after preterm birth complications as reviewed in GBD 2010 for all age groups.[9,18] LRIs are the leading cause of mortality among infectious diseases for all age groups in Bangladesh, accounting for 2,310 thousand YLLs, followed by neonatal encephalopathy (2,289 thousand YLLs) and diarrheal diseases (1,155 thousand YLLs) in 2010.[9,19] Pneumonia, the major LRI, is the leading cause of mortality in all infectious diseases among the under five children in Bangladesh.[20,21]

*Streptococcus pneumoniae* is responsible for most cases of bacterial pneumonia in children worldwide, followed by Haemophilus influenzae type b.[21] The incidence of pneumonia among preschool children in Bangladesh is higher than in developed countries.[22,23] Bangladesh alone stands 4th in the world in terms of estimated absolute number of new cases of clinical pneumonia (0.41 episodes per child per year). The estimated child mortality rates is 27 per 10,000 in under-five populations which places Bangladesh among the top 10 countries, ranked by volume of pneumonia-induced deaths in the world.[24]

Moreover, increasing trends of AMR are a big concern for *S. pneumoniae*; especially resistance to macrolides and β-lactam antimicrobials, which are the first therapeutic choice for *S. pneumoniae* infections.[25,26] One recent review found high levels of penicillin resistance among *S. pneumoniae* strains in different Asian countries.[27] However, only a small rise was observed in penicillin resistance from 4% in 2005 to 8% in 2014 in Dhaka, Bangladesh over a period of 10 years.[28]

Another study found that resistance to penicillin against *S. pneumoniae* ranged from 0% to 3%, when considered in terms of the syndrome-specific cut-off for non-meningitis [Minimal Inhibitory Concentration (MIC) is <4.0 µg/mL) and for meningitis (MIC >0.12 µg/mL].[29] Additionally, variable levels of resistance were detected against macrolides (5% to 55%) at icddr,b, Dhaka, though ampicillin and ceftriaxone were found to be susceptible. Ampicillin and penicillin might be considered the drugs of choice for eating *S. pneumoniae*

in these settings as ceftriaxone is more expensive. [28]

Table-2 below shows a summary of AMR from LRIs isolated pathogens in Bangladesh.

A significant portion of pneumonia infections are of viral origin (40% to 50%).[30] Measles virus, RSV,

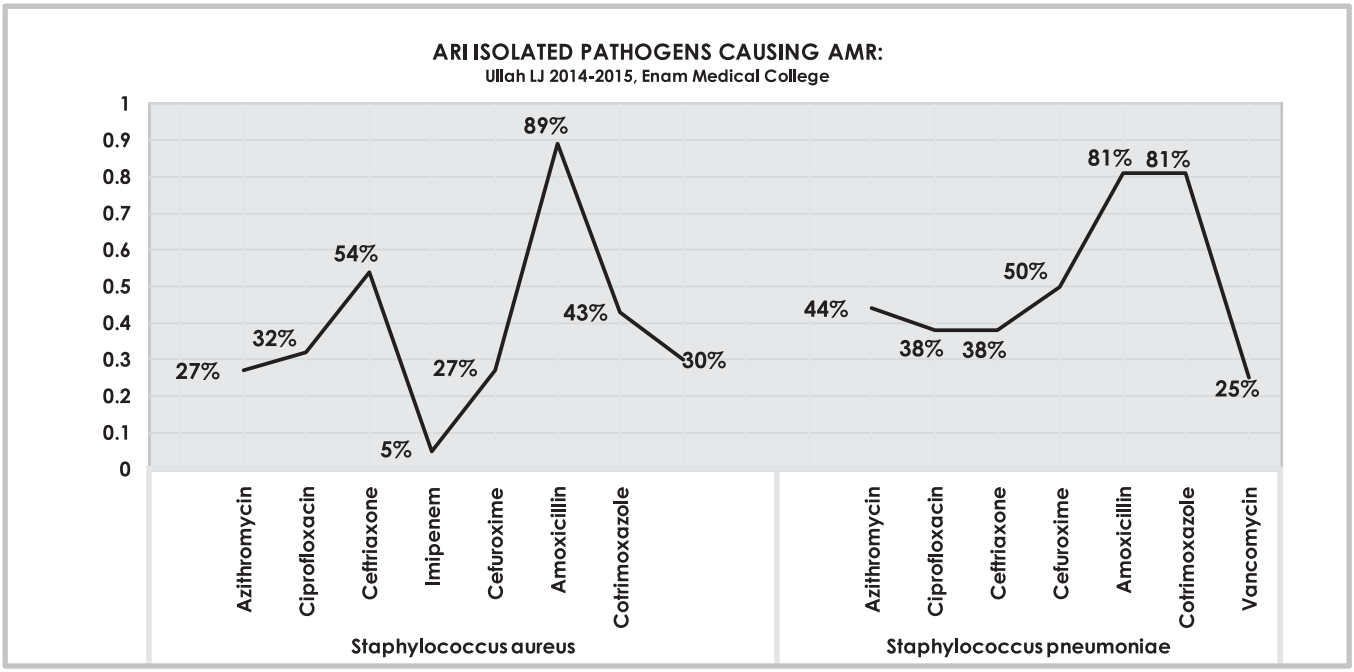
**Table-2: Summary Table of AMR from ARIs Isolated Pathogens in Bangladesh**

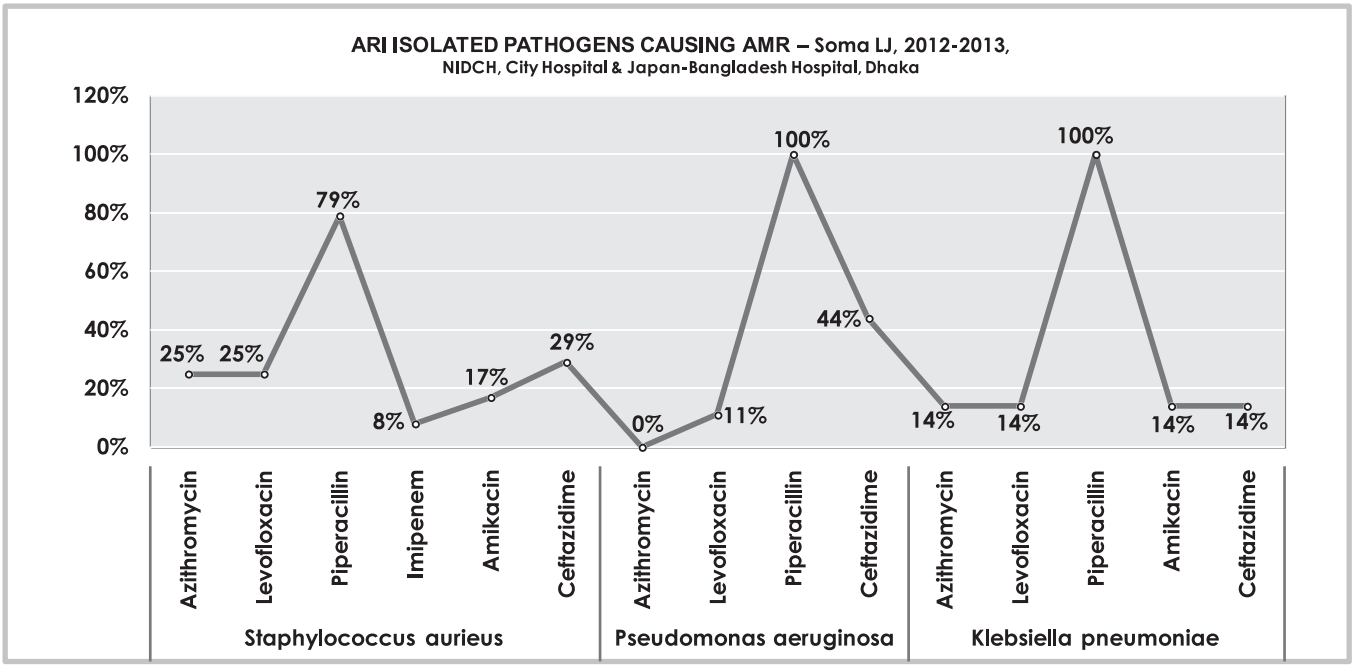
| Author, n=sample size | Study Site | Study Population | Major Pathogens, number of isolated pathogens | Antimicrob ials and Resistance patterns | |
|---|---|---|---|---|---|
| | | | | Resistant Rate | (%) |
| Ullah et al. (2016), n=100<br><br>Study Period: 2014-2015 | Enam Medical College Hospital, Savar-Dhaka | Indoor patient | Staphylococcus aureus (37) | Azithromycin | 27% |
| | | | | Ciprofloxacin | 32% |
| | | | | Ceftriaxone | 54% |
| | | | | Imipenem | 5% |
| | | | | Cefuroxime | 27% |
| | | | | Amoxicillin | 89% |
| | | | | Cotrimoxazole | 43% |
| | | | | Vancomycin | 30% |
| | | | Streptococcus pneumoniae (16) | Azithromycin | 44% |
| | | | | Ciprofloxacin | 38% |
| | | | | Ceftriaxone | 38% |
| | | | | Cefuroxime | 50% |
| | | | | Amoxicillin | 81% |
| | | | | Cotrimoxazole | 81% |
| | | | | Vancomycin | 25% |
| Soma et al. (2014) n=58<br><br>Study Period: 2012-2013 | 1. National Institute of Diseases of the Chest and Hospital (NIDCH)-Dhaka;<br><br>2. City Hospital- Dhaka;<br><br>3. Japan Bangladesh Friendship Hospital-Dhaka | Hospital patients | Staphylococcus aureus (24) | Azithromycin | 25% |
| | | | | Levofloxacin | 25% |
| | | | | Piperacillin | 79% |
| | | | | Imipenem | 8% |
| | | | | Amikacin | 17% |
| | | | | Ceftazidime | 29% |
| | | | Pseudomonas aeruginosa (9) | Azithromycin | 0% |
| | | | | Levofloxacin | 11% |
| | | | | Piperacillin | 100% |
| | | | | Ceftazidime | 44% |
| | | | Klebsiella pneumoniae (7) | Azithromycin | 14% |
| | | | | Levofloxacin | 14% |
| | | | | Piperacillin | 100% |
| | | | | Amikacin | 14% |
| | | | | Ceftazidime | 14% |
| Ahmed et al. (2017) n=103,679<br>Study Period: 2005-2014 | Dhaka Hospital-Dhaka | Hospital attending patients | Streptococcus pneumoniae (49 and 26 pathogens isolated in 2005 and 2014 respectively) | Azithromycin | 31% |
| | | | | Pen G | 8% |
| | | | | Ceftriaxone | 0% |
| | | | | Cotrimoxazole | 73% |
| Saha et al. (2016), n=42,964 | (1.) Dhaka Shishu (Children's) Hospital-Dhaka; | Under-five children | Streptococcus pneumoniae (752) | Penicillin | 3% |
| | | | | Erythromycin | 13% |
| | | | | Cotrimoxazole | 13% |

Study Period: 2007-2013. (2.) Shishu (Children) Shasthya Foundation Hospital (SSFH)-Dhaka; (3.) Chittagong Mother & Child Hospital-Chittagong; and (4.) Kumudini Women's Medical College Hospital (KWMCH)-Kumudini.

Despite a high pneumonia burden, a decreasing trend in isolation of *S. pneumoniae* was observed throughout the study period of 2005-2014 at icddr,b, Dhaka[28] and of 2007-2013, in a WHO designated sentinel site the network for Vaccine Preventable Invasive Bacterial Disease (VP-IBD) surveillance in Bangladesh.[29] Policy makers decided to add the pneumococcal PCV-10 vaccine to the extended program on immunization (EPI) in 2015 in response to the increasing levels of antimicrobial resistance and high burden of neumonia-attributable deaths of children under five.

parainfluenza viruses, influenza type A virus, and adenoviruses are the leading agents causing viral pneumonia. It is challenging to differentiate between viral and bacterial pneumonia radiographically, partly because the lesions look similar and partly because bacterial super infection occurs with influenza, measles, and RSV infections. Antimicrobials are commonly used to treat respiratory viral infections due to inaccurate diagnoses, increasing the risk of adverse drug effects, enhancing the cost of care and contributing to the problem of antimicrobial resistance.




**2. Diarrhoeal Diseases:** Diarrhoeal disease is considered to be one of the most important public health problems because the disease incidence, prevalence, morbidity and mortality are very high ranking as the 4th most common causes of global disability-adjusted life years (DALYs) in 2010.[8] Childhood diarrhoea, causing three or more loose or liquid stools per day, is the second leading cause of U5C mortality and morbidity among all infectious diseases worldwide.[31] Globally each year diarrhoea kills around 525,000 U5C and there are nearly 1.7 billion cases of childhood diarrhoeal diseases every year. Diarrhoea is a leading cause of malnutrition in U5C.

Rotavirus and Escherichia coli are the two most common etiological agents of moderate-to-severe diarrhoea in low-income countries. Other pathogens such as cryptosporidium and shigella species may also be important. There are three clinical types of diarrhoea: acute watery diarrhoea – lasts several hours or days, and includes cholera; acute bloody diarrhoea – also called dysentery; and persistent diarrhoea – lasts 14 days or longer (WHO, 2005).[122]

In 2015, a total of 2,560,598 diarrhoea cases and 24 related deaths were reported in Bangladesh. The case fatality rate due to diarrhoea thus remains at around 0.001%, as in previous years. The Diarrhoeal Disease Surveillance System of the International Centre for Diarrhoeal Diseases Research, Bangladesh (icddr,b) has systematically enrolled every 50th individual with diarrhoea irrespective of age, sex, socioeconomic status and disease severity since 1979. Diarrhoea is the only such illness that has been under systematic surveillance in the country for such a long period of time. [32]

Diarrhoea can be caused by both viral and bacterial infections. Rotavirus, *Shigella* spp., *Vibrio cholerae* and Enterotoxigenic *Escherichia coli* (ETEC) are the predominant pathogens isolated from diarrhoeal patients in Bangladesh. Rotavirus was responsible for the majority of diarrhoeal infections in urban children under-five during the periods of 1993 to 1997 (25%) and 2008 to 2012 (42%). This rose to 68% in 2012 from 1993 ($p<0.001$).[33] Higher rates of co-infection with Shigella (3% vs. 1%); V. cholerae (4% vs. 1%); and ETEC (13% vs. 7%) were detected in 1993 to 1997 compared to 2008 to 2012.[33]

Another study from icddr,b conducted in 2013 found that rotavirus was predominant in all four study sites in Bangladesh, with the highest rates in Mirzapur (28%) followed by Dhaka (24%), Matlab (19%) and Mirpur (18%).[34] Despite the high burden of rotaviral infection, a significant portion of these patients received antimicrobials before coming to the hospital. Use of antimicrobials before hospital visits was found to be 30 to 84%, with the lowest rates in urban areas and highest rates in suburban and rural areas of Bangladesh.[34]

Another study showed a change in species distribution and antimicrobial resistance patterns of Shigella over a 29-year period from 1980–2008 in hospitalized patients.[35] Shigella prevalence decreased steadily from 8 to 12% in the1980s to 3% in 2008. Endemic *S. flexneri* was the most commonly isolated species (54%) during this period. Epidemic *S. dysenteriae* type 1 had two peaks, in 1984 and 1993, but was not detected after 2000, except for one case in 2004.

Therapeutic options are now limited for bacterial pathogens causing diarrhoea due to increasing rates of resistance. Studies at different hospitals (Dhaka, Mirpur, Mirzapur and Matlab) in Bangladesh found that 28 to 35% of Shigella isolates were resistant to ciprofloxacin, while 8 to 57% were resistant to mecillinam.[34,35] Resistance of Shigella to azithromycin and ceftriaxone in Dhaka was 26% and 5% respectively, and in Mirpur 12% and 8% respectively.[34] High resistance to other available drugs left only azithromycin and ceftriaxone as drugs with proven efficacy in the management of shigellosis.[35]

*V. cholerae* showed the highest resistance to trimethoprim-sulfamethoxazole (100%) and the lowest resistance to ciprofloxacin (as low as 0 percent) and azithromycin (7 to 30%).[34] Reduced susceptibility of *V. cholerae* to ciprofloxacin has been reported, which was attributed to the widespread use of ciprofloxacin during the study period (1994-2012). [36]

Table-3 (see page: 55) shows the summary of AMR from pathogens isolated from diarrhoeal patients.

A recent analysis of resistance patterns of Enterotoxigenic *Escherichia coli* (ETEC) described the emergence of ciprofloxacin-resistant ETEC strains.[37] Between 2005 and 2009, a total of 8,580 stool specimens from diarrhoeal patients attending the icddr,b Dhaka hospital were screened for ETEC. Among the 1,067 (12%) were identified as ETEC and AMR of the ETEC strains was observed as follows: to ampicillin (66%), azithromycin (27%), ciprofloxacin (27%), ceftriaxone (13%), cotrimoxazole (46%), doxycycline (44%), erythromycin (96%), nalidixic acid (83%), norfloxacin (27%), streptomycin (48%) and tetracycline (42%). Resistance to ciprofloxacin increased from 13% in 2005 to 34% in 2009. None of the strains were resistant to mecillinam. However, resistance may result in a major challenge to current treatment strategies for ETEC diarrhoea.

**3. Tuberculosis (TB):**

Tuberculosis (TB), a disease caused by Mycobacterium tuberculosis bacterium, has been a major public health problem in Bangladesh. In 1965, the TB program was mainly confined to providing curative services and was only available to TB Clinics and TB Hospitals. Under the second Health and Population Plan (1980-86), TB curative services were expanded to 124 Upazila Health Complexes (UHC). During the third Health and Population Plan (1986-91), the Mycobacterial Disease

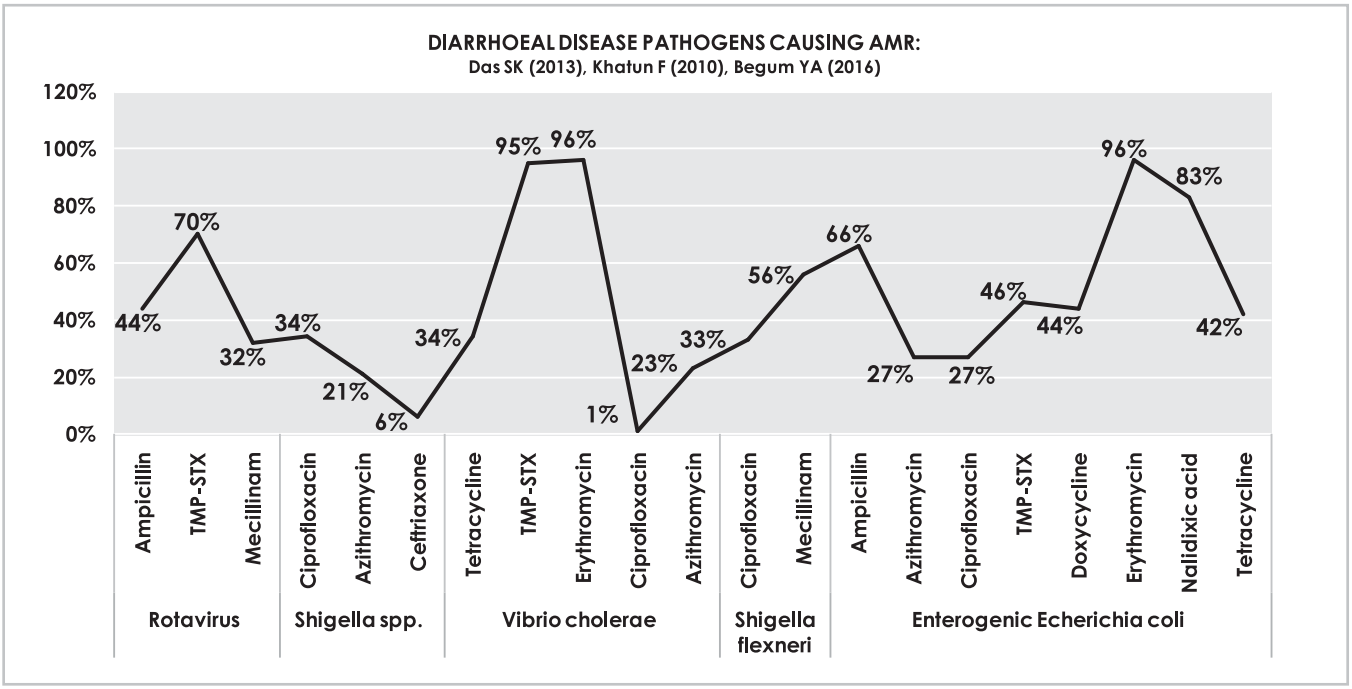
**Table 3: Summary of AMR from Diarrhoeal Disease Pathogens**

| Author, n= Sample size | Study Site | Study Population | Major Pathogens | Antimicrobials & Resistance Patterns (%) | | Comments |
|---|---|---|---|---|---|---|
| | | | | Resistance | % | |
| Das et al. (2013)<br>N=13,959<br><br>Study Period: 2010-2011 | 1. Kumudini Hospital -Mirzapur;<br>2. Dhaka Hospital-Dhaka;<br>3. Matlab Hospital -Matlab;<br>4. Mirpur Treatment Center-Mirpur -Dhaka | Under-five children | Rotavirus (2,812)<br><br>Shigella spp. (534)<br><br>Vibrio cholerae (275) | Ampicillin<br>TMP-STX<br>Mecillinam<br>Ciprofloxacin<br>Azithromycin<br>Ceftriaxone<br><br>Tetracycline<br>TMP-STX<br>Erythromycin<br>Ciprofloxacin<br>Azithromycin | 44%<br>70%<br>32%<br>34%<br>21%<br>6%<br><br>34%<br>95%<br>96%<br>1%<br>23% | The isolation rates and antimicrobial resistance differed significantly in certain geographical areas |
| Sarker et al. (2014)<br>n=5357<br>Study Period: 1993-1997, 2008-2012 | Dhaka Hospital -Dhaka | Under-five children | Rotavirus | NA | | Rota viral diarrhoea increased gradually |
| Khatun et al. (2010)<br>n=83,073<br>Study Period: 1980-2008 | Dhaka Hospital -Dhaka | All age group | Shigella flexneri (4157) | Ciprofloxacin (2008),<br>Mecillinam (2008) | 33%<br>56% | Hospitalization for Shigellosis decreased gradually |
| Khan et al. (2015)<br>n=161<br>Study Period: 1994-2012 | Dhaka Hospital -Dhaka | Adult | Vibrio choleraeO1 (275) | In 1994 -2008, $MIC^{90}$ to Ciprofloxacin was 0.01 µg/ml and 0.475 µg/ml respectively<br>In 1994 2008, $MIC^{90}$ to Nalidixic acid was 21 µg/ml and >256 µg/ml respectively | | Diminished susceptibility to ciprofloxacin observed over the years |
| Begum et al. (2016)<br>N=8580<br>Study Period: 2005-2009 | Dhaka Hospital -Dhaka | All age group | ETEC (1067) | Ampicillin<br>Azithromycin<br>Ciprofloxacin<br>TMP-STX<br>Doxycycline<br>Erythromycin<br>Nalidixic acid<br>Tetracycline | 66%<br>27%<br>27%<br>46%<br>44%<br>96%<br>83%<br>42% | Diverse clones were identified from all ciprofloxacin resistant strains |

Control (MBDC) Unit of DGHS integrated TB services operationally with the leprosy control program.

The National TB Program (NTP) of Bangladesh adopted the Directly Observed Treatment Shots (DOTS) during the fourth Health and Population Plan (1992-98) under the project "Further Development of TB and Leprosy Control Services". In July 1998, the NTP was integrated into the Communicable Disease Control (CDC) component of the Essential Services Package under the Health and Population Sector Program (HPSP: 1998-2003). The subsequent sector wide approach has run from 2003-2016 and onwards, all national health and population plans including the current health plan "HPNSP: 2017-2022" have endorsed NTP as a priority program. [39]

Bangladesh has made significant achievement in controlling tuberculosis through its National TB Control Program (NTP). However, TB continues to be the most important communicable diseases in Bangladesh in terms of incidence, prevalence and mortality rates. The disease has been infecting more than 360,000 people and claiming more than 80,000 lives annually. There are about 168,834 cases, which remain undetected and/or unreported annually. Bangladesh ranks 7th among high burden 22 TB countries and ranks 10th among the 27




high burden Multi-Drug Resistance TB (MDR-TB) countries in the world.[38,39,47,53]

The inequity in access to TB services, delay in diagnosis, slow introduction of new diagnostic technology, shortage of skilled human resources, lack of well-designed diagnostic facilities at UHCs and hospitals level, and inadequate financial resources, have been identified as some of the important challenges to the TB control program in Bangladesh. There are also issues of high urban transmission, co-morbidity with diabetes mellitus, Chronic Obstructive Pulmonary Diseases (COPD), HIV/AIDS,

A total of 191,166 cases of TB (both new and relapse cases) was notified in 2014, with a rate of 120 cases per 100,000 population with a case detection of 52.3%. However, an estimated 47.7% of cases of TB are not detected, accounting for about 168,834 undetected cases (Table-4).[32] This 2010-11 study shows, the prevalence of Multi-Drug Resistant TB (MDR-TB) in new TB cases was 1.4%, and in re-treatment cases, it was 28.5%.[39] Rates of MDR-TB with fluoroquinolone resistance are rapidly rising.[40] However, Extensively-Drug Resistant TB (XDR-TB) was not reported in 2014. TB cases were reported in the most recent national annual report. Only two cases of XDR-TB were detected in Dhaka in 2013 and were attributed to inappropriate patient treatment.[41] Table-4 shows TB cases notification in 2014.

**Table-4: TB Cases Notification in 2014** [47]

| Sl | TB Notification Cases (New and Relapse cases) | Pulmonary TB | | Extra-Pulmonary TB | Total (TB Cases) | Rate/(100,000 pop.) | % of Case all form |
|---|---|---|---|---|---|---|---|
| | | Bacteriological Confirmation | Clinically Diagnosed | Bacteriological & Clinical | | | |
| 1 | New Cases of TB | 106,767 | 42,832 | 37,406 | 187,005 | ---- | ---- |
| 2 | Relapse Cases of TB | 2,989 | 863 | 309 | 4,161 | ---- | ---- |
| 3 | Detected TB Cases (1+2) | 109,756 | 43,695 | 37,715 | 191,166 | 120 | 52.3% |
| 4 | Undetected TB cases | ---- | ---- | ---- | 168,834 | ---- | -(47.7%) |
| 5 | Estimated # Total TB Cases | ---- | ---- | ---- | 360,000 | ---- | 100% |

**Note: Among 187,005 case of new TB, 6262 (3.3%) cases are aged <15 yrs. Number of TB previously treated, excluding relapses was 5631.**

Kala-azar, TB branding and social mobilization, and insufficient evidence regarding trend of MDR-TB and XDR-TB . Keeping these as the priority issues, the government set up the objectives of NTP in 4th HNP SP: 2017-2022 to ensure diagnosis and treatment of over 80% of TB cases. [38]

National TB Reference Laboratory (NTRL): Bangladesh has established the NTRL, located at the National Institute of Diseases of Chest Hospital (NIDCH), Dhaka on 27th June 2007 for the effective diagnosis and management of MDR-TB. The NTRL is the WHO recommended TB reference laboratory dedicated for culture and drug sensitivity testing (DST).

[4]*MDR-TB: Multi Drug Resistance TB, when TB is resistant to Rifampicin and Isoniazid.*
[5]*XDR-TB: Extensively-Drug Resistant TB. XDR-TB is resistant to the same drug as MDR-TB in addition to being resistant to any of the fluoroquinolones, such as Levofloxacin or Moxifloxacin, and to resistant to at least one of the three injectable second-line drugs like Amikacin, Capreomycin or Kanamycin.*

The NTP administered a program to improve the sensitivity and specificity of TB diagnoses and introduced GeneXpert/MTB-Rif (WHO-endorsed automated technology to diagnose TB) equipment in 2012. These are now available in 38 NTP/GF supported centers across the country.

As a part of the Programmatic Management of Drug Resistance TB (PMDT) plan, the NTP has established five Regional TB Reference Laboratories (RTRL), in the country located at Chest Disease Hospitals (CDH) at Rajshahi (2008), Chittagong (2011), Pabna (2013, Khulna (2013 and Sylhet (2014); and a total of 3,702 MDR-TB patients have been managed from May 2007 to December 2014. In addition to five RTRL, the Damien Foundation, an international organization has been operating three hospitals in the greater Mymensingh District with a shorter regimen of 9 months since 2005, and has been managing a total of 1,393 MDR-TB patients including 230 new patients in 2014. The overall trend of treatment of MDR-TB patients is an increase in success rate. The treatment for MDR-TB patients enrolled under a 24 months regimen shows an increased success rate from 64.4% in 2008 to 72.9% in 2012. [48]

Despite making substantial progress in cases notifications between 2012 and 2013, the NTP needs to overcome considerable challenges that remain in the control and prevention of TB epidemic. The challenge is to expand and to establish the diagnostic services countrywide; to ensure full involvement of private sector providers in TB care; and to improve the detection of MDR-TB among all age groups especially children. The Joint Monitoring Mission (JMM) report on TB, by WHO, described a general lack of political commitment to TB control, as reflected in allocating limited government funding, both at central and peripheral levels, and a "human resource crisis" reflected in a general lack of adequate staffing at all levels of the NTP in Bangladesh.[45]

Drug-Resistant TB: Drug-resistant TB continues to threat Bangladesh and remains a major public health problem in many parts of Dhaka and Chittagong Divisions in the country. The NTP conducted the first countrywide national drug resistance survey in 2010-2011 to generate drug resistance data and reported that the proportion of new TB cases with MDR-TB was 1.4% (Global estimate was 3.3% in 2014) and that of re-treatment cases with MDR-TB was 28.5% (Global estimate was 20% in 2014).[48,46]

In 2014, among the 27 highest MDR-TB burden countries globally, Bangladesh identified (bacteriologically confirmed) a total of 12,573 (12.0%) new TB cases tested for RR-/MDR-TB; the number of retreatment cases notified, previously treated for TB, testing positive for RR-/MDR-TB was 4,959 (51.0%); and the number with DST result confirmed MDR-TB cases was 182 (19.0%) in Bangladesh.[47] The estimated number of MDR-TB among notified pulmonary cases was 4,800; of them the total number of confirmed RR-/MDR-TB cases notified as pulmonary cases was 994 (21.0%); the number of cases enrolled on MDR-TB treatment was 945 (95.1%) as against the confirmed cases in 2014.[47] Table-5 below shows the Drug Susceptibility Testing (DST) and estimation, detection and enrolment for treatment of MDR-TB and RR/MDR-TB in 2014.

**Table 5: Drug-Susceptibility Testing (DST) for TB cases; Estimated MDR-TB among notified TB cases; RR/MDR-TB cases detected, and enrolment on MDR-TB treatment, 2014** [47]

| | Indicators | New Cases | | Re-Treatment | | Total |
|---|---|---|---|---|---|---|
| | | n | % | n | % | |
| 1. | Confirmed TB cases tested for RR-/MDR-TB | 12,57 | 12.0% | 4,959 | 51.0% | 43,360 |
| 2. | Drug Sensitivity Testing (DST) confirmed MDR-TB | 182 | 19% | --- | --- | 182 |
| 3. | MDR -TB Cases among notified Pulmonary TB | 2,100 | 1.4% | 2,700 | 28.5% | 4,800 |
| 4. | Confirmed RR-/MDR-TB cases notified as Pulmonary TB | 994 | 21.0% | --- | --- | 994 |
| 5. | Cases Enrolled on MDR-TB for Treatment | 945 | 95.1% | --- | --- | 945 |

**4. As against the estimated cases of 4,800 in 2014 5. As against the confirmed cases of 994 in 2014;**
**RR – Rifampicin Resistance; MDR-TB: Multi-drug Resistance TB (Resistance to both rifampicin & Isoniazid)**

**TB Disease Burden:** TB disease burden that includes incidence, prevalence, morbidity and mortality rates of TB continues to improve since the implementation of Bangladesh National Tuberculosis Control Programme (NTP) since 2008. In 2014, the assessment of available data showed that there were confirmed 187,005 incident cases of TB (new TB cases) with confirmed 4161 relapse cases of TB in the country. The TB disease prevalence (old & new cases) declined from 501 per 100,000 population in 1990 to 250 per 100,000 populations achieving MDGs in 2015.

The death rate associated with TB was 80 per 100,000 population in 1990. The rate has come down to 51 per 100,000 population in 2014. The new TB cases have been segregated by sex, showing the percent of male cases (60.5%) is much higher than their female (39.5%) counterparts. New cases of TB notified among the children is much lower; the rate of TB per 100,000 populations is higher in the higher age group of both male and female populations in the country.[8,39]

**TB/HIV Co-Infection:** TB/HIV Co-infection usually represents a deadly combination, since they are more destructive together, killing a larger number of people than either disease can do alone. HIV affects the immune system of the human body and increases the likelihood of people acquiring new TB infection. HIV also promotes latent TB infection to an active disease progression and increases relapse of the disease in previously treated patients. On the other hand, the presence of TB bacteria in the body of a HIV infected person accelerates the progress of HIV infection to AIDS. TB is one of the leading causes of death in HIV-infected people. Table-6 below shows the TB burden, TB incidence, notification and cases detection. [47]

**Table-6: Estimated TB Burden; TB Incidence, Notification and Case Detection, 2014**

| | Variables: Population in millions - 162.5 | Number (in Thousands) | Rates (Per 100,000 pop) |
|---|---|---|---|
| 1 | TB Notification Cases | 191,166 | 120 |
| 2 | Mortality (excludes HIV+TB) | 81 (59 –110) | 51 (37 –68) |
| 3 | Mortality (HIV+TB only) | 0.18 (0.14 – .22) | 0.11 (0.09 –0.14) |
| 4 | Prevalence (includes HIV+TB) | 640 (340–1 000) | 404 (211 –659) |
| 5 | Incidence (includes HIV+ TB) | 360 (320–410) | 227 (200–256) |
| 6 | Incidence (HIV+TB only) | 0.57 (0.45 –0.71) | 0.36 (0.28–0.45) |
| 7 | TB Mortality (HIV Positive + HIV Negative People) | 82 | 51 |

in 2014, the number of TB cases with known HIV status was identified as 1,110 in Bangladesh (Table-7). Of these TB cases, 45 cases were found HIV positive representing 4.1% of the total. All 45 HIV Positive TB patients have been covered under co-trimoxazole preventive therapy (CPT) and antiretroviral therapy (ART). However, the data on initiation of isoniazid preventive therapy (IPT) for people newly enrolled in HIV care are not available in Bangladesh. The provision of IPT was reported just by 23% of countries globally, including only 13 of the 41 high TB/HIV burden countries. Table-7 below shows HIV testing for TB patients; provision of CPT and ART of HIV positive patients and initiation of IPT for people newly enrolled in HIV care, in 2014. [47]

Preventing TB deaths among HIV-positive people requires an intensified scale-up of TB prevention, diagnosis and treatment interventions, including earlier initiation of ART among people living with HIV and those with HIV-associated TB. Increased efforts in joint TB and HIV programming could facilitate further scale-up and consolidation of collaborative TB/HIV activities.

**4. Urinary Tract Infections (UTIs):** The most common UTIs occur mainly in women and affect the bladder (cystitis) and urethra (urethritis); and when it affects the upper urinary tract, it is described as kidney infection (pyelonephritis). Cystitis (infection of the bladder) is a form of UTI and is usually caused by Escherichia coli (E. coli), a type of gram-negative coliform anaerobic bacteria accounting for 80% to 85% of the infection commonly found in the gastrointestinal (GI) tract. However, sometimes other bacteria are also

**Table-7: HIV Testing for TB Patients; Provision of CPT and ART of HIV Positive Patients and Initiation of IPT for People Newly Enrolled in HIV Care, 2014**

| | TB Cases With Known HIV Status | Number (n) | % |
|---|---|---|---|
| 1 | Number of TB cases with known HIV status | 1,110 | 0.58% |
| 2 | HIV Positive TB Patients | 45 | 4.1% |
| 3 | HIV Positive TB Patients on CPT | 45 | 100% |
| 4 | HIV Positive TB Patients on ART | 45 | 100% |
| 5 | HIV Positive people screened for TB | 726 | ---- |
| 6 | HIV Positive people provided IPT | 00 | ---- |

**CPT – Co-trimoxazole Preventive Therapy; ART – Anti-Retroviral Therapy;**
**IPT – Initiation of Isoniazid Preventive Therapy for people newly enrolled in HIV care.**

responsible for UTIs such as Staphylococcus species constituting 10% to 15% of infections.[61] In addition, bacterial Klebsiella, Pseudomonas, Proteus and Enterococcus species can also cause these types of infection. Sexual intercourse may lead to cystitis, but one doesn't have to be sexually active to develop it. Symptoms from a lower urinary tract include pain with urination, frequent urination, and feeling the need to urinate despite having an empty bladder. Symptoms of a kidney infection include fever and flank pain usually in addition to the symptoms of a lower UTI. Rarely the urine may appear bloody. In the very old and the very young, symptoms may be vague or non-specific.

**Antibiotic use in the treatment of UTI:** The physician usually prescribes antibiotics as the first line treatment for UTIs. Antibiotics are chosen depending on the health of the patient and the type of bacteria found in the urine. Drugs commonly recommended for simple UTIs include: Trimethoprim and sulfamethoxazole in combination (co-trimoxazole), Fosfomycin, Nitrofurantoin, Cephalexin, and Ceftriaxone.

**Antibiotic Resistance in UTIs:** Antimicrobial resistance is common in urinary pathogens and is increasing at an alarming rate, as a result of the overuse and misuse of antibiotics. Resistance patterns vary by geographic location, but are rising nationwide and globally. Therapy for UTIs is usually begun before the results of microbiological tests are known. In women with acute uncomplicated cystitis, therapy without a pre-urine culture is often used. The rationale for this approach is based on the highly predictable spectrum of etiologic agents causing UTIs and their antimicrobial resistance patterns. However, AMR among uropathogens causing UTIs, both cystitis and pyelonephritis, is increasing. Most important has been the increasing resistance to cotrimoxazole, the current drug of choice for treatment of acute uncomplicated cystitis in women.

A hospital-based study (n=50) conducted in 2008 detected *Escherichia coli (E. coli)* as the most frequently isolated (70%) pathogen, in Mymensingh Medical College Hospital, Bangladesh.[54] Resistance of *E. coli* to ceftriaxone, levofloxacin, amikacin and nitrofurantoin was less than 20%. Resistance to cotrimoxazole, ampicillin, cephradine and ciprofloxacin were found to be high. Similar findings in AMR patterns were observed in other studies.[55,56] Due to its higher efficacy and lower rates of resistance, nitrofurantoin is widely used against all types of UTIs. A syndromic approach is used for managing UTIs in outpatient settings and in drop-in centers and sub drop-in centers (n= ~70) for sex workers in Bangladesh using a relatively old guideline and is found to be beneficial.

Sabita et at., (2014) in a study, found that the bacteriuria was present in 42 (9%) of 462 patients. *Escherichia coli* (69%), *Streptococcus* spp. (15%) and Pseudomonas aeruginosa (7%) were the most frequently isolated organisms found from the urine samples. The E. coli isolates showed complete resistance to commonly used antibiotics, and 58% of these isolates were multidrug resistant (MDR). Isolated strains of *E. coli* exhibited an equal extent of ciprofloxacin resistance irrespective of the presence or absence of plasmid in them. The study concluded that the extent of drug resistance among the uropathogens if ignored may render them uncontrollable. This study suggests regular monitoring of the drug resistance phenotype of UTI pathogens to reduce the morbidity of female UTI patients and offer better treatment strategies in the healthcare sectors in Bangladesh.[58]

Begum et at., (2006) conducted a cross sectional study on UTIs among female workers, in a selected garment industry of Dhaka City, and documented the resistance pattern of organisms. 67.7% of isolates were resistant to Ampicillin and 45.4% were resistant to Cotrimoxazole and Cephalexin. Resistance to Nalidixic acid was 11.1% and that of Nitrofurantoin was 33.3% in isolated organisms. However all 18 positive cases were 100% sensitive to Ciprofloxacin and Ceftriaxone.[59]

Gram-negative bacteria produce enzymes called carbapenemases against Carbapenems, a broad-spectrum antibiotic used for empirical treatment in severe UTIs. The enzyme carbapenemases produce extensive resistance against Carbapenem antibiotics. As resistance is becoming more widespread, careful use of antimicrobials is imperative and as asymptomatic bacteriuria is typically benign in the elderly, antibiotics should not be prescribed without clinical signs of a UTI. The use of antibiotics, as suppressive therapy or long-term prophylaxis, may no longer be defensible in UTIs.[60]

A recent study in Bangladesh shows high resistance to antibiotics against the urinary tract pathogens, the clinicians and the researchers recommend testing

sensitivity before prescribing any antibiotic. Islam et al., (2017) conducted a study at Dhaka Children's Hospital, Bangladesh and evaluated a total of 147 culture-positive UTI children; in which *E coli* was found to be the most prevalent in 103 (70%) children, who had responded well to Imipenem (97.27%), followed by Colistin (94.6%), Meropenem (93.9%) and Amikacin (91.8%).[62] On the other hand, Khatri et al., (2012) documented that the most frequent causative organisms isolated were *E coli* (82.3%) and Nitrofurantoin was found to be the most effective drug against the *E. coli* isolates.[63] Ranganathan Vasudevan (2014) in his review article on urinary infections documented that among the bacterial species, *E coli* account for 80% to 85% of infections followed by *Staphylococcus* species that constitute 10% to 15%. In addition, bacterial species such as Klebsiella, *Pseudomonas, Proteus* and *Enterococcus* species play a minor role in conferring infection.[61]

The studies above suggested periodic evaluation of antimicrobial activity of different antibiotics to observe variation in the patterns of antibiotic sensitivity. The study strongly recommended that there has been a great need for antimicrobial resistance surveillance at the local, national, and international levels; and has been a need for laboratory analysis of the commonly used antibiotics that are prescribed to treat UTIs in children.[62,63]

Table 8 below shows a summary of AMR from UTIs caused by *E coli*

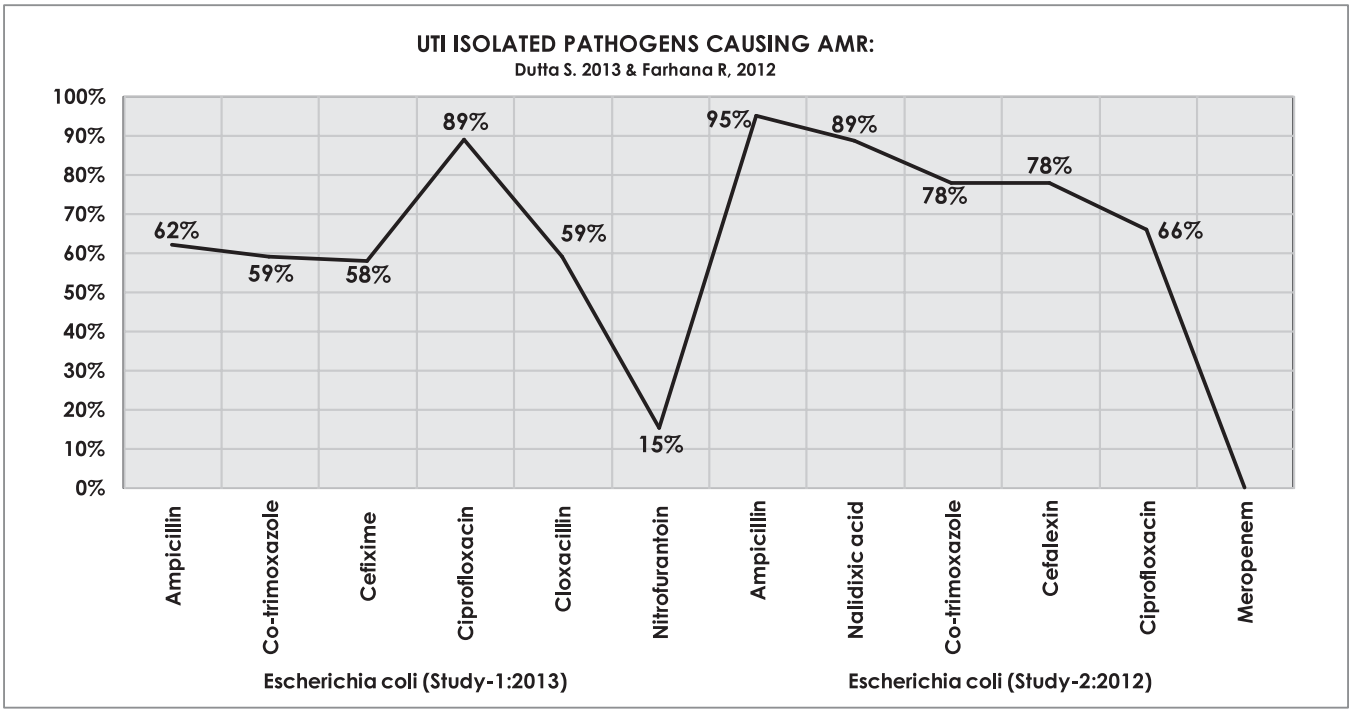
Farhana et al, (2012) in retrospective analysis of data from a pediatric urine sample (n=518) collected from the Institute of Child Health Foundation, Dhaka found 213 (45%) culture-positive cases, among which E. coli (97.9%) was found to be the most common causative organism followed by *Klebsiella* spp. (10.8%) and others (1.3%). The *E. coli* isolates were found to be highly resistant against ampicillin (95.1%), nalidixic acid (88.7%), cotrimoxazole (77.8%), Cefalexin (77.8%), ciprofloxacin (66%) and meropenem (0%). A high level of resistance was also found for *E. coli* against third generation cephalosporins, such as cefotaxime (63.1%), ceftriaxone (60.6%) and ceftazidime (50.2%). A large number of the *E. coli* isolates were sensitive to each of meropenem (94.8%), imipenem (93.6%), netilmicin (75.9%), gentamicin (65%) and nitrofurantoin (59.1%). Similar findings were observed in--- *Klebsiella* spp. Urine culture and sensitivity should be performed routinely to evaluate the antibiotic susceptibility of the urinary pathogens before therapy is initiated. The resistance pattern also emphasizes the necessity to redefine treatment strategy, optimize the best utilization of the available antibiotics, and prevent the AMR in best possible ways.[64]

## 5. Neonatal Infection (Sepsis) and Aetiology of Bacteraemia:

A study at Khulna Medical College Hospital, Khulna, Bangladesh found that neonatal sepsis constituted nearly one-third of the disease burden in the neonatal ward, the majority of them had early onset infections.[66] The predominant bacterial species causing neonatal sepsis changes with time and place. In terms of

**Table 8: Summary of AMR from UTIs caused by *E coli***

| Author, n= Sample size | Study Site | Study Population | Major Pathogens | Antimicrobials & Resistance Patterns (%) | | Comments |
|---|---|---|---|---|---|---|
| | | | | Resistance | % | |
| Dutta et at 2013 N=475/1,044 (46%) | National Healthcare Network (NHN), Microbiology Laboratory, Dhaka City | Women | *E. coli* | Ampicillin<br>Co-trimoxazole<br>Cefixime<br>Ciprofloxacin<br>Cloxacillin<br>Nitrofurantoin | 62.0%<br>59.0%<br>58.0%<br>89.0%<br>59.0%<br>15.0% | Ref. [57] |
| Farhana et at., (2012);<br><br>N =213/518 (45%) | Institute of Child Health Foundation, Dhaka | Children | *E. coli* | Ampicillin<br>Nalidixic acid<br>Co-trimoxazole<br>Cefalexin<br>Ciprofloxacin<br>Meropenem | 95.1%<br>88.7%<br>77.8%<br>77.8%<br>66.0%<br>00.0% | Ref. [64] |
| | | | *E. coli* | Cefotaxime<br>Ceftriaxone<br>Ceftazidime | 63.1%<br>60.6%<br>50.2% | |




treatment, previously sensitive pathogens are rapidly becoming resistant to commonly used antimicrobials due to indiscriminate use, making treatment increasingly challenging and costly. In a tertiary care hospital in Dhaka from January to December 2008, almost all organisms were resistant to ampicillin, gentamicin and third-generation cephalosporins.[67]

Though there is regional variation in pathogen type and difference in AMR patterns in neonatal sepsis, the most common bacterial pathogens responsible for sepsis are *Staphylococcus aureus, Klebsiella pneumoniae, E. coli, Pseudomonas* spp. and *Staphylococcus epidermidis* (Coagulase Negative *Staphylococcus* spp.).[68] A population based community-acquired neonatal bacteraemia study at Mirzapur, Dhaka, Bangladesh conducted between 2004 and 2006 showed resistance rates of gram negative pathogens against ampicillin (87%), gentamicin (63%), cephalosporins (47%), cotrimoxazole (43%), ciprofloxacin (20%), and imepenem (7%).[69]

Data also suggest that many neonates in hospitals in South Asia are now treated with carbapenems as a first-line therapy for sepsis or presumed sepsis.[70] The results of the recently concluded study on Aetiology of Neonatal Infection in South-Asia study; 2011-2015 are expected to produce more data on the profile of neonatal sepsis.[71] Table-9 below shows the summary of AMR patterns caused by the pathogens responsible for neonatal sepsis.

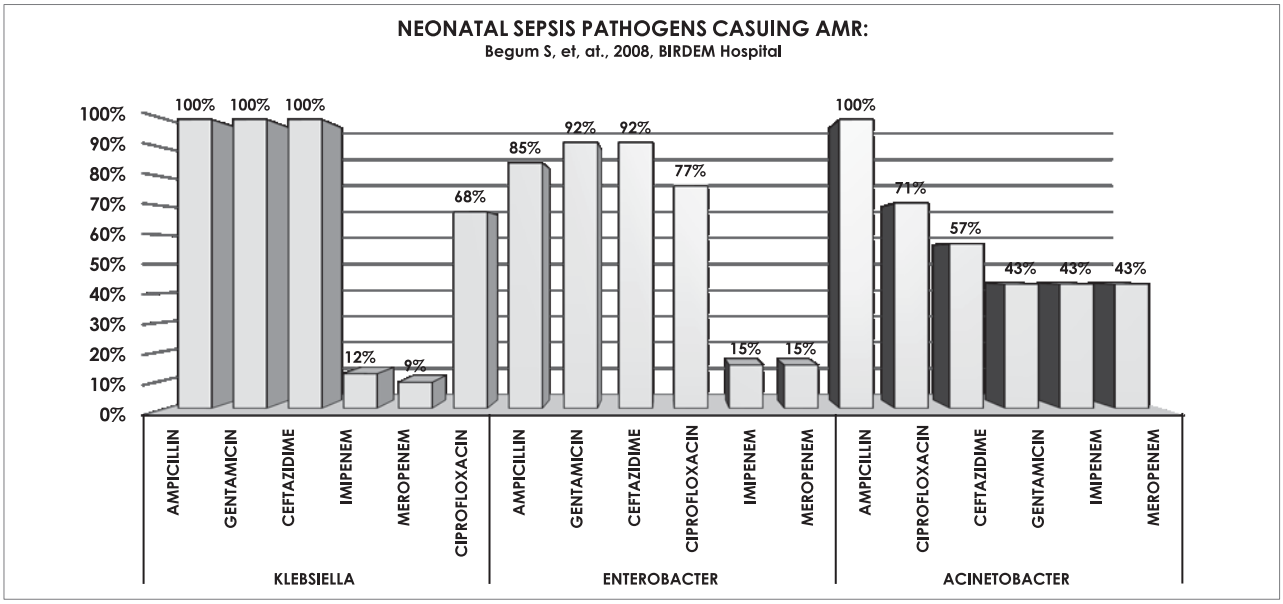
A retrospective study conducted on neonates (n=1,400) Chittagong, Bangladesh, found 104 (7.4%) had positive blood culture for neonatal sepsis. Among the infected children, 40 were born in hospital and 64 were born at home. The early-onset of neonatal sepsis accounted for 68 (65.4%) and late-onset neonatal sepsis accounted for 36 (34.6%). Among the isolated organism *Klebsiella pneumoniae* accounted for 76%), *Serratia marcescens* 18.3%, *Pseudomonas aeruginosa* 3.9% and *Staphylococcus aureus* accounted for 1.9%. Among the isolated species, 102 were attributed to gram negative bacteria and 2 were attributed to gram positive bacteria.

Most of the gram negative bacteria showed resistance to commonly used antibiotics such as ampicillin, ceftriaxone and gentamicin. In this study all isolates showed sensitivity to the imipenem. The study concluded that the collection of up-to-date data should be done to choose the appropriate antibiotics for treating neonatal sepsis.[72,73,74]

**6. Ear Infection (Otitis Media):** Ear infection is a common disease among young children and is an important cause of impaired hearing. Ear infection represents almost 10 percent of all infection-associated disease in Bangladesh for all age groups. A study from July to December 2010 found that about 11 percent of outpatients in four tertiary teaching hospitals of

**Table 9: Summary of AMR Patterns of Neonatal Sepsis Causing Pathogens**

| Author, n=sample size | Study Period | Study Site | Study Population | Major Pathogen(s), number of isolated pathogens | Name of Antimicrobials & Resistance patterns (%) | |
|---|---|---|---|---|---|---|
| | | | | | Antimicrobials | % |
| Begum S, et al. (2012), n=65 | 2008 | BIRDEM Hospital, Dhaka | Neonates | *Klebsiella* (34) | Ampicillin<br>Gentamicin<br>Ceftazidime<br>Imipenem<br>Meropenem<br>Ciprofloxacin | 100%<br>100%<br>100%<br>12%<br>09%<br>68% |
| | | | | *Enterobacter* (13) | Ampicillin<br>Gentamicin<br>Ceftazidime<br>Ciprofloxacin<br>Imipenem<br>Meropenem | 85%<br>92%<br>92%<br>77%<br>15%<br>15% |
| | | | | *Acinetobacter* (7) | Ampicillin<br>Ciprofloxacin<br>Ceftazidime<br>Gentamicin<br>Imipenem<br>Meropenem | 100%<br>71%<br>57%<br>43%<br>43%<br>43% |
| Darmstadt et al. (2009), n=500 | 2004-2006 | Kumudini Hospital, Mirzapur | Neonates | *Staphylococcus aureus* (10) | Ampicillin<br>Gentamicin<br>Cotrimoxazole<br>Ceftriaxone<br>Ciprofloxacin<br>Ceftazidime<br>Imipenem | 100%<br>10%<br>50%<br>10%<br>20%<br>50%<br>10% |
| | | | | *Streptococcus pneumoniae* (3) | Gentamicin<br>Cotrimoxazole<br>Ampicillin<br>Ceftriaxone | 67%<br>33%<br>00%<br>00% |
| | | | | *Pseudomonas spp.* (5) | Ampicillin<br>Gentamicin<br>Cotrimoxazole<br>Ceftriaxone | 80%<br>20%<br>60%<br>00% |
| | | | | *Acinetobacter spp.* (3) | Ampicillin<br>Gentamicin<br>Cotrimoxazole<br>Ceftriaxone<br>Ceftazidime | 100%<br>100%<br>33%<br>67%<br>33% |




Bangladesh were prescribed antimicrobials by graduate physicians to treat varying forms of otitis media, a common type of ear infection.[75] A prospective study carried out from 2000 to 2003 in Dhaka City and adjacent areas found that 19 percent of school children

age 4 to 9 years had otitis media effusion[76], with a higher burden of disease in the rural versus the urban communities.[77]

Otitis media is caused mainly by *S. pneumoniae, H. influenzae,* and *S. aureus,* in addition to viruses. Culture and sensitivity testing are not routinely performed for otitis media; so information on the resistance patterns of these pathogens is not available. An ongoing study at Dhaka Children (Shishu) Hospital documented that these pathogens *(S. pneumoniae, H. influenzae)* have been found to 60 percent more resistance against erythromycin and cotrimoxazole, though resistance to ciprofloxacin was less than 10 percent (Hakka Naziat, personal communication).

**7. Typhoid Fever:** *Salmonella Typhi* is the most frequently isolated blood-borne bacterial pathogen responsible for typhoidal fever, accounting for 37 percent of the total isolates recovered using automated blood culture technique in a study from 2005 to 2014[78] Table 10 below shows the Isolates of typhoidal Salmonella and non-typhoidal Salmonella spp. from icddr,b.

All these studies suggest that ceftriaxone is still effective for treating typhoid patients. Table-11 below shows a summary of AMR in typhoidal agents.

**8. Skin and Soft Tissue Infections (SSTIs):** SSTIs may be caused by any of a formidable number of pathogenic microorganisms, and they may be caused by one or multiple different bacterial species at the same time. The following are the important pathogens: *Staphylococcus aureus* (common pathogen); *Streptococcus pyogenes*; Site-specific infections-Indigenous organisms (e.g., gram-negative bacilli in perianal abscesses); Immunocompromised hosts and complicated SSTIs – these are multiple organisms or uncommon organisms (e.g., *Pseudomonas aeruginosa,* beta-hemolytic streptococci, Enterococcus); Polymicrobial necrotizing fasciitis – these are mixed infection with both aerobes (e.g., streptococci, staphylococci, or aerobic gram-negative bacilli); and Anaerobes (e.g., *Peptostreptococcus*, Bacteroides, or *Clostridium*), and Monomicrobial necrotizing fasciitis: *S pyogenes*.

**Table 10: Isolation of typhoidal Salmonella and non-typhoidal Salmonella spp. from icddr,b,**

| Organisms | Year | | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | |
| Names (N) | (1126) | (1132) | (1266) | (1566) | (1522) | (2003) | (1418) | (1391) | (1077) | (1514) | (14,015) |
| *Salmonella* (n) | 566 | 747 | 707 | 755 | 593 | 828 | 592 | 663 | 474 | 623 | 6548 |
| Percentage (%) | (50.3%) | (66.0%) | (55.8%) | (48.2%) | (39.0%) | (41.3%) | (41.7%) | (47.7%) | (44.0%) | (41.1%) | (46.7%) |
| *Salmonella typhi* (n) | 457 | 595 | 571 | 600 | 483 | 643 | 451 | 527 | 355 | 509 | 5191 |
| Percentage (%) | (40.6%) | (52.6%) | (45.1%) | (38.3%) | (31.7%) | (32.1%) | (31.8%) | (37.9%) | (33.0%) | (33.6%) | (37.0%) |
| *Salmonella paratyphi* A, B | 85 | 133 | 127 | 146 | 102 | 179 | 135 | 129 | 107 | 110 | 1253 |
| Percentage (%) | (7.5%) | (11.7%) | (10.0%) | (9.3%) | (6.7%) | (8.9%) | (9.5%) | (9.3%) | (9.9%) | (7.3%) | (8.9%) |
| *Salmonella* species | 24 | 19 | 9 | 9 | 8 | 6 | 6 | 7 | 12 | 4 | 104 |
| Non-typhoidal (%) | (2.1%) | (1.7%) | (0.7%) | (0.6%) | (0.5%) | (0.3%) | (0.4%) | (0.5%) | (1.1%) | (0.3%) | (0.7%) |

A study conducted between 2003 and 2004 found more than 40 percent resistance to all three first-line drugs against typhoid pathogens.[79] A decreasing trend of antimicrobial resistance against cotrimoxazole and ampicillin over a period of 10 years (from 2005 to 2014) has been observed.[78] In a hospital-based study of febrile illness of adults and children (n=300) in 2012, 18 isolates of S. typhi were detected with intermediate susceptibility to ciprofloxacin, and six were multidrug-resistant, exhibiting resistance to chloramphenicol, ampicillin, and cotrimoxazole, but all were susceptible to ceftriaxone and azithromycin.[80]

SSTIs may be divided into the following categories: Uncomplicated SSTI, Nonnecrotizing complicated SSTI and Necrotizing fasciitis. Uncomplicated SSTIs include superficial cellulitis, folliculitis, furunculosis, simple abscesses, and minor wound infections. These infections respond well to either source control management (i.e., drainage or debridement) or a simple course of antibiotics. These infections pose little risk to life and limb. Complicated SSTIs, on the other hand, involve the invasion of deeper tissues and typically require significant surgical intervention. The response to therapy is often complicated by underlying disease states.

**Table 11: Summary of AMR of Typhoidal Agents**

| Author, n=sample size | Study Period | Study Site | Study Population | Major Pathogen(s), number of isolated pathogens | Name of Antimicrobials and resistance patterns (%) | | Remarks (If any) |
|---|---|---|---|---|---|---|---|
| | | | | | Antibiotics | % | |
| Naheed et al. (2010), n=961 | 2003-2004 | Kamlapur-Dhaka | All age group | *Salmonella Typhi*(40) | Cotrimoxazole<br>Chloramphenicol<br>Ampicillin<br>Nalidixic acid<br>Ceftriaxone | 43%<br>43%<br>40%<br>40%<br>0% | Multi-Drug Resistance *S. Typhi* (MDR)- 16 (40%) observed in this study |
| | | Salmonella Paratyphi(8). Susceptible to all drugs tested (Ampicillin, Chloramphenicol, Cotrimoxazole, Nalidixic acid, Ciprofloxacin, Ceftriaxone) | | | | | |
| Maude et al. (2016), n=300 | 2012 | Chittagong Medical College & H Chittagong | Hospital Admitted patients (>6 months) | Salmonella Typhi(18). All were susceptible to Ceftriaxone and Azithromycin. All were intermediately resistant to ciprofloxacin. Multi-Drug Resistance *S. typhi* (MDR)- 6 (33%) observed in this study | | | |
| Ahmed et al. (2017), n=103,679 | 2005-2014 | Dhaka Hospital-Dhaka | Hospital attending patients | *Salmonella Typhi* (509) | Ampicillin<br>Cotrimoxazole<br>Ciprofloxacin<br>Ceftriaxone<br>Cefixime | 26%<br>24%<br>4%<br>0%<br>0% | |
| | | | | *Salmonella Paratyphi* A, B (110) | Ampicillin<br>Cotrimoxazole<br>Ciprofloxacin<br>Ceftriaxone<br>Cefixime | 0%<br>2%<br>1%<br>0%<br>0% | |
| Data presented for the year of 2014 only, 94% of the S. typhi pathogens; 99% of S. Paratyphi were intermediately resistant to ciprofloxacin | | | | | | | |

Aktar et, al., (2015) cultured specimens (n=300) of patients from Dhaka, Bangladesh, using blood agar and documented that 97 (32.4%) of the patients had skin and soft tissue infections of bacterial origin, with E. coli (52.0%), S. aureus (27%), Pseudomonas (18%), Acinetobacter (3%), and others (4%) being the common pathogens. Men within age group of 40-60 years had the highest number (42.0%) of infections, with E coli (21.6%) being the most common pathogen. Women within the reproductive age (18-45 years) were infected by E. coli, S. aureus and Pseudomonas (16.7%), while E coli (23.3%) was the predominant cause of infections in post-menopausal women. The rate of post-surgical nosocomial infection was 6.9% while 9.8% contracted nosocomial infections from non-surgical sources. The infections were recurrent in 25.5% cases. Wide-spread resistance against amoxicillin and β-lactams, azithromycin and second generation cephalosporins was found.[81]

## 3.2. PARASITIC DISEASE BURDEN AND ANTIMICROBIAL RESISTANCE

**3.2.1 Malaria:** Malaria is a serious life-threatening mosquito-borne blood disease, which can be fatal, and is caused by a Plasmodium parasite. When an infected mosquito bites a human, the parasites reach the host's liver and multiply; the parasites gradually infect red blood cells and destroy them. People who get malaria are usually very sick with symptoms such as high fevers, sweating, nausea, fatigue, vomiting, shaking chills (rigors), and flu-like illness. It is transmitted to humans through the bite of the Anopheles mosquito. Five types of malaria parasites infect humans: Plasmodium falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi. They are found in different parts of the world. Some cause a more severe type of malaria than others. P. falciparum is the type of malaria that is most likely to result in severe infections and if not promptly treated, may lead to death. In some places, malaria can be treated and controlled with early diagnosis.

According to World Malaria Report (WHO 2016), substantial progress has been made in fighting malaria since 2000. The latest estimates show that between 2000 and 2015, malaria case incidence was reduced by 41% and malaria mortality rates by 62% globally. At the beginning of 2016, malaria was considered to be endemic in 91 countries and territories, down from 108 in 2000. Much of the change can be attributed to the wide-scale deployment of malaria control interventions.

Despite this remarkable progress, malaria continues to have a devastating impact on people's health and livelihoods. Updated estimates indicate that 212 million cases occurred globally in 2015, leading to 429,000 deaths, most of which were in children aged under 5 years in Africa. Because malaria causes so much illness and death, the disease is a great drain on many national economies. Since many countries with malaria are already among the poorer nations, the disease maintains a vicious cycle of disease and poverty.[82]

Table-12 below shows the summary results of malarial prevalence in Bangladesh.

**Table 12: Summary of Malarial Prevalence in Bangladesh**

| Author, n=sample size | Study Period | Study Site | Study Population | Major Parasite(s), prevalence of isolated parasites | |
|---|---|---|---|---|---|
| | | | | Major Parasite(s) | Prevalence (%) |
| 1. Alam et al. (2016), n=9750 | 2013 | 13 Malaria endemic districts of Bangladesh | >1 year of age | 1. Plasmodium falciparum (mono-infection)<br>2. Plasmodium vivax (mono-infection)<br>3. Plasmodium falciparum, Plasmodium vivax (Mixed infection) | 77.8%<br>11.1%<br>11.1% |
| 2. Ley et al. (2016) n=181 | 2014 - 2015 | Alikadam Upazila Health Complex (UHC), Bandarban, Bangladesh | Patients with slide-confirmed malaria who were presented in Alikadam UHC | 1. Plasmodium falciparum (mono-infection)<br>2. Plasmodium vivax (mono-infection)<br>3. Plasmodium falciparum, Plasmodium vivax (Mixed infection) | 64%<br>30%<br>06% |
| 3. Rahman et al. (2011), Review article | Plasmodium falciparum is the most prevalent parasite and Plasmodium vivax is the second most common parasite species in the South-East Asia Region | | | 1. Plasmodium falciparum<br>2. Plasmodium vivax | |

1. Alam, et al. (2016): Major Findings: Reduction in malaria prevalence and increase in malaria awareness in endemic districts of Bangladesh has been observed. This was possible because of malaria eradication program of National Malaria Control Programme (NMCP) of Govt. of Bangladesh and a BRAC-led NGO consortium.

2. Ley, et al. (2016): Major Findings: Current treatment policy for uncomplicated malaria remains effective.

3. Rahman, et al. (2011): Major Finding: Emergence of artemisinin resistance at the Thai-Cambodia border has been reported recently. Malaria endemic areas in Bangladesh are close to this border. Plasmodium vivax is sensitive to chloroquine in Bangladesh.

In Bangladesh, estimating the disease burden on a scale of Years of Life Lost (YLLs), the rank of malaria has been moving from top 18 in 1990 down to 44 in 2010 indicating that the incidence, prevalence, morbidity, mortality and number of YLLs has been improved.[8] In 2000, the number of suspected case of malaria was identified as 742,529 cases in Bangladesh; of them *Plasmodium falciparum* cases were 39,475 and *Plasmodium vivax* cases 16,124 (reported cases of malaria by species). However, in 2015, the number of Plasmodium falciparum malaria cases has come down to only 6,120, which was 84.5% lower than in 2000 and the number of P. vivax cases reported was only 488, which was 96.9% lower than in 2000. The deaths due to malaria recorded in 2000 were 484 and deaths have come down to only 9 in 2015, a remarkable decline in deaths observed over the years.[82]

Malaria is regarded as one of the public health problems in Bangladesh. Out of 64 districts in the country, malaria is endemic in 13 districts, mostly situated in the north-east and the south-east part of Bangladesh, where a total of 13.3% of people are at risk of the disease. Three districts of Chittagong Hill Tracts and Cox's Bazar District reported 92% of the malaria cases in 2016. Bangladesh has both *Plasmodium falciparum* and *P. vivax* malaria, with *P. falciparum* making up about 96% of the burden, with a recent reduction in the prevalence of all malaria.[83,84] In a baseline survey done in 2007, the prevalence of malaria was reported to be about 40 cases per 1,000 populations in endemic areas, and by 2013, the prevalence declined to approximately 1.4 cases per 1,000 population in the same endemic area with the same survey protocol.[84]

In 2007, BRAC and icddr,b carried out a malaria prevalence survey in thirteen malaria endemic districts of Bangladesh. A multi-stage cluster sampling technique was used and 9,750 blood samples were collected. Rapid Diagnostic Tests (RDT) were used for the diagnosis of malaria. The weighted average malaria prevalence in the thirteen endemic districts was 4.0%. In five south-eastern districts weighted average malaria prevalence rate was 6.0% and in the eight north-eastern districts weighted average malaria prevalence rate was (0.4%). The highest malaria prevalence was observed in Khagrachari hill district.

The majority of the cases (90.2%) were P. falciparum infections. Malaria morbidity rates in five south-eastern districts were 2.9%. In eight north-eastern districts, morbidity was 0.07%.[85]

Globally, Artemisinin Combination Treatment (ACT) is used for the treatment of uncomplicated falciparum malaria. For uncomplicated malaria, the current antimalarial policy remains valid.[86] Artemisinin resistance has not been detected in Bangladesh, although it has emerged in some countries in Southeast Asia, including Cambodia.[87} Vivax malaria in Bangladesh is still sensitive to chloroquine.[88]

**3.2.2 Kala-azar:** Kala-azar, also known as Visceral leishmaniasis, is highly endemic in the Indian subcontinent (Bangladesh, India and Nepal), and in East Africa (North Sudan, Kenya and Ethiopia). Over 90% of new cases of Kala-azar occur in six countries; these are Bangladesh, Brazil, Ethiopia, India, Sudan and South Sudan. The National Kala-azar Elimination Program (NKEP), of Communicable Diseases Control (CDC) Unit, Directorate General of Health Services (DGHS), MoHFW of Bangladesh has been implementing kala-azar elimination activities since 2005 to reduce the incidence of kala-azar less to than 1 case per 10,000 population. Due to program activities, the number of kala-azar cases of 8,505 in 2005 has come down to 278 in September 2017 and hence the NKEP achieved the target of Kala-azar incidence less than 1 new case per 10 000 population.[124,125,126,127]

Amphotericin B deoxycholate was introduced in mid 1990s for the treatment of kala-azar with a distinct advantage over Sodium Stibogluconate (SSG). In 1998 onwards, the introduction of Liposomal Amphotericin B (AmBisome) in the treatment of Kala-azar has been found with much better efficacy with higher drug toleration and fewer adverse events compared to Amphotericin B deoxycholate. Clinical trial in 2007 with injectable Paromomycin for Kala-azar treatment in India was shown to be equally effective compared to Amphotericin B deoxycholate. Miltefosine, an oral tablet, for the treatment of Kala-azar also appeared to be effective compared to other injectable drugs. Over the last decade, the researchers had conducted several clinical trials within the Kala-azar endemic areas and identified four most important drugs to be superior to others such as L.AmB, Miltefosine, Paromomycin and SSG. These drugs are used either in single doses (AmBisome) or in combination for the treatment of new Kala-azar, Post Kala-azar Dermal Leishmaniasis (PKDL) and Cutaneous Leishmaniasis.[128,129,130]

Over 60% of patients with Kala-azar in Bihar State, India, did not respond to treatment with pentavalent antimonials. This is now considered to be due to acquired resistance. Although this class of drugs has been used for over 60 years for Kala-azar, it is only in the past 2 years that the mechanisms of action and resistance have been identified, related to drug metabolism, thiol metabolism, and drug efflux. With the introduction of new therapies, including miltefosine in 2002 and paromomycin in 2005-2006, it is essential that there should be a strategy to prevent the emergence of resistance to new drugs; combination therapy, monitoring of therapy, and improved diagnostics could play an essential role in this strategy. [150, 151]

## 3.3 STI DISEASE BURDEN AND ANTIMICROBIAL RESISTANCE

**3.3.1 Sexually Transmitted Infections (STIs):** An estimated 357 million new cases of curable STIs (gonorrhea, chlamydia, syphilis and trichomoniasis) occurred among 15-49 years-olds worldwide, including 131 million cases of chlamydial infection in 2012. People aged 15-24 acquire half of all new STDs, and 1 in 4 sexually active adolescent females has an STD, such as human papillomavirus or chlamydia. Compared with older adults, individuals aged 15-24 have a higher risk of getting STDs. [89]

STIs, also known as sexually transmitted diseases (STDs) or venereal diseases (VD) are diseases that are passed on from one person to another through unprotected sexual contact - the infection can be passed on through vaginal intercourse, oral sex, and anal sex. Examples of sexually transmitted diseases include: chlamydia; gonorrhoea; syphilis; trichomoniasis (trich); chancroid; crabs (pubic lice); genital herpes; genital warts; human papilloma virus (HPV); human immunodeficiency virus and acquired immunodeficiency syndrome (HIV and AIDS); trichomoniasis (parasitic infection); and molluscum contagiosum pelvic inflammatory disease (PID).

**1. Chlamydia:** Chlamydia is a STI caused by Chlamydia trachomatis, a gram-negative bacterium that infects humans exclusively. Chlamydia is the most common

cause of infection of genital and eye diseases. According to the CDC-Atlanta (Centers for Disease Control and Prevention), in 2015, nearly 3% of girls aged 15-19 had chlamydia. Untreated chlamydial infection in men can cause epididymitis and proctitis, and in women it may cause severe complications in the upper reproductive tract, primarily in young women, including ectopic pregnancy, salpingitis and infertility.

The drugs used for treatment vary with the different forms of chlamydia. The most common drugs used to treat chlamydia are azithromycin, doxycycline, tetracycline, erythromycin, ofloxacin, levofloxacin and amoxicillin. Antibiotic resistance of C. trachomatis has not been shown and is not currently a clinical problem. Persistent forms are also slightly antibiotic-sensitive which seems to be associated with reduced monoclonal antibodies directed against major outer membrane protein count and thus decreased transport of antibiotics to the cell. Therefore, in the case of chronic infections, therapy frequently results in failure. [90,91]

A cross sectional study was conducted to find out the seroprevalence of C. trachomatis genital infection in women of reproductive age at Mymensingh Medical College Hospital, Bangladesh over a period one year in 2009. A total of 108 serum samples from symptomatic and asymptomatic pregnant and non-pregnant women were tested for C. trachomatis specific IgG antibody by Enzyme Linked Immunosorbent Assay (ELISA). A total of 31 (28.7%) patients were found to have antibody of which 44% (26/59) were from pregnant group and 10.2% (5/49) from non-pregnant group. The seropositivity was 21.6% (16/74) in symptomatic cases and 44.1% (15/34) in asymptomatic cases. The study shows high prevalence of Chlamydial antibody which is common in pregnant and non-pregnant, symptomatic and asymptomatic adult women in Bangladesh. This implies screening for chlamydial infection should be done routinely by suitable tests in sexually active symptomatic and asymptomatic women including pregnant women to prevent serious complications.[91]

**2. Gonorrhea:** Gonorrhea is a sexually transmitted infection (STI) caused by the gram-negative bacterium called Neisseria gonorrheae that can infect both men and women. [92] *N. gonorrheae* can be diagnosed by culture or nucleic acid amplification tests (NAATs), and by gram stain in men with urethritis. In settings without available laboratory diagnostic support, diagnosis is often made clinically, based on the presence of symptoms such as vaginal and urethral discharge. The treatment of gonococcal infections is complicated by the rapidly changing antimicrobial susceptibility patterns of *N. gonorrheae,* raising concerns about the eventual development of untreatable gonococcal infections with serious sexual and reproductive health consequences.

The most common drugs used to treat gonorrhea are ceftriaxone, cefixime, spectinomycin, gentamicin, kanamycin, tetracycline hydrochloride, erythromycin, and chloramphenicol. Because of the emerging resistance data for gonococcal infections and reduced effectiveness of some antibiotics, good practice dictates that the choice of treatment should depend on reliable local data on antimicrobial susceptibility. Pregnant women should be closely monitored for complications. Treatment failures have been observed after single therapy for gonococcal oropharyngeal infections and therefore dual therapy (ceftriaxone and Cefixime in combination) is suggested over single therapy (ceftriaxone). Due to the large net benefit with treatment, good practice dictates that neonates should be treated for gonococcal conjunctivitis. The choice of treatment may depend on the cost and quality of the medicine in different settings and on equity considerations. Side-effects should be monitored in neonates. [93]

In a study conducted between 1997 and 2006 (n=1,767), an increasing trend of resistance of gonorrhea against penicillin and tetracycline was observed in Bangladesh. The prevalence of plasmid-mediated penicillinase-producing *N. gonorrheae* (PPNG) and plasmid-mediated tetracycline-resistant *N. gonorrheae* (TRNG) were also determined. Nine percent of the isolates were resistant to ciprofloxacin in 1997 compared to 87 percent in 2006. Multidrug-resistant *N. gonorrheae* emerged in 1997, and 44 percent of the strains (n=66) isolated during 2006 were multidrug-resistant. Forty-two percent of the isolates in 2006 were both PPNG- and TRNG-positive compared to none in 1997. [94]

The rapidly-changing pattern of gonococcal antimicrobial susceptibility supports the need for an antimicrobial susceptibility monitoring program and periodic analysis and dissemination of susceptibility data to guide clinicians and for successful STI/HIV

intervention programs in Bangladesh. Despite this, a syndromic approach is used for managing STIs. For example, 71 drop-in-centers or sub-drop-in-centers administered by the National AIDS/STD Programme (NASP), DGHS, of the Ministry of Health and Family Welfare use guidelines from 2006, based on empirical therapy. [95]

The Global Antibiotic Research and Development Partnership (GARDP), a joint DNDi/WHO initiative documented that the spread and incidence of gonococcal antimicrobial resistance is rapidly outpacing the development of new medicines. Without action, untreatable gonorrhoea will soon become a reality, bringing with it a host of clinical manifestations and complications (increased risk of HIV infection, pelvic inflammatory disease, ectopic pregnancies, infertility, neonatal conjunctivitis and blindness). N. gonorrheae threatens soon becoming untreatable due to its resistance to all available classes of antimicrobials. This programme will accelerate the entry of new antibiotics and explore the use of combinations. With the support of gonorrhoea experts, GARDP has devised short- and long-term Target Product Profiles (TPPs) to guide the development of an R&D strategy for STIs. [96]

**3. Syphilis:** Syphilis is a sexually transmitted infection (STI) caused by the bacterium Treponema pallidum. In 2015, about 45.4 million people were infected with syphilis,[137] with 6 million new cases.[138] During 2015, it caused about 107,000 deaths, down from 202,000 in 1990.[139] After decreasing dramatically with the availability of penicillin in the 1940s, rates of infection have increased since the turn of the millennium in many countries, often in combination with human immunodeficiency virus (HIV). This is believed to be partly due to increased promiscuity, prostitution, decreasing use of condoms, and unsafe sexual practices among men who have sex with men. In 2015, Cuba became the first country in the world to eliminate mother-to-child transmission of syphilis.[140]

In Bangladesh, estimating the disease burden on a scale of Years of Life Lost (YLLs), the rank of Syphilis has been moving from top 13 in 1990 down to 29 in 2010 indicating that the incidence, prevalence, morbidity, mortality and number of YLLs has been improved.[8] The annual mortality rate of syphilis is 3.1 per 100,000 population; the annual years of healthy life lost are 243 per 100,000 populations and changes in annual years of healthy life lost -74.8% in Bangladesh.

Farah et, at., (2013) conducted a study among (n=300) gonorrhoea and Syphilis patients in two Medical College Hospital (OPD) and two private chambers in Bangladesh to find out their socio demographic characteristics. The patients were between 10 to 60 years of age and among them 250 were male and 50 were female. The study found that the prevalence of gonorrhoea and syphilis are higher among younger age group and unmarried persons. Regarding occupation, service holders are affected more, and both the low and high income group population are affected irrespective of their socioeconomic condition,[144] and in another study done in 1997 (n=198), the seroprevalence of syphilis was 4.5% found among the heterosexual males adults attending two dermatology and sexually transmitted disease (STD) clinics, Chittagong, Bangladesh.[146]

Injecting drug users (IDU) were enrolled from two detoxification clinics and two needle/syringe exchange programmes (NEP) in central and northwest Bangladesh. Syphilis (23%), hepatitis C (66.5%) and HIV (1.4%) rates were highest in IDU from the NEP of central Bangladesh respectively, whereas current hepatitis B infection rates were highest in IDU from the NEP of northwest Bangladesh (12%).[145]

**4. HIV/AIDS:** In 2016, there were 36.7 million people living with HIV and 1.8 million people became newly infected with HIV in 2016 worldwide. 19.5 million people were accessing to antiretroviral therapy in 2016. 1 million people died from AIDS-related illnesses in 2016. Since 2010, new HIV infections among adults declined by an estimated 11%, from 1.9 million to 1.7 million in 2016. New HIV infections among children declined by 47% since 2010 and AIDS-related deaths have fallen by 48% since the peak in 2005.[147]

In Bangladesh, the incidence of HIV is less than 0.01 per 1,000 population; the total number people living with HIV who know their HIV status was 3,900; the total number of new HIV infection was 1,500 in 2016. The number of AIDS related deaths was 1,000. The numbers of people living with HIV who are on Anti-retroviral therapy (ART) are 1,800. The numbers of people living with HIV who are virally suppressed are not known. The numbers of new HIV infections in children are less than

100. 39% of children living with HIV are on treatment. The coverage of pregnant women, living with HIV accessing antiretroviral drugs is 17%. [148]

The HIV prevalence among the sex workers is 0.2%, however, the percentage of sex workers who are living with HIV and know their HIV status is only 31.2%. Condom use rate among the sex workers is 66.7%. The coverage of HIV prevention programs among the sex workers is 15.2%. The number of needles and syringes was 157 per drug injecting person distributed in 2016. Coverage of drugs users under the HIV prevention program was 27.8%. The clean needle use at last injection is 83.9%. The prevalence of men who have sex with men (MSM) and the transgender people is 0.2% and 1.4% respectively. The condom use rate among MSM is 45.8% and that among transgender people is 41.1%.[148]

### 3.4 PROPHYLACTIC USE OF ANTIMICROBIALS AND ANTIMICROBIAL RESISTANCE

Antibiotic prophylaxis is described as the use of antibiotics before surgery or a dental procedure to prevent a bacterial infection. This practice of using antibiotics as prophylaxis is not as widespread as it was even 10 years ago. This is due to the increase in the resistance of bacteria against the antibiotics. However, antibiotic prophylaxis is still used in people who have certain risk factors for bacterial infection. Professional guidelines recommend using antibiotics before procedures that have a high risk of bacterial infection. These include surgeries for head and neck cancer; gastrointestinal surgeries; cesarean delivery; surgeries for implanting a device, such as a pacemaker, stents or defibrillator; cardiac procedures such as coronary artery bypass grafts; valve replacements; and heart replacements.[100]

Prophylactic use of antimicrobials benefits the patients in many ways. Prophylactic uses of antimicrobials in colorectal surgery, dental surgery, and abdominal hysterectomy have been documented in Bangladesh.[97,99] Ciprofloxacin is the most common prophylactic antimicrobial used, followed by metronidazole (always given in combination with another antimicrobial) and cefuroxime.[98] The study suggests that patients who took ciprofloxacin (n=50) as prophylaxis, separately or in combination with other antimicrobials, had a higher success rates (92% patients did not suffer from post-operative infections) while some (8%) developed surgical site infections (SSIs), which might be a result of microbial resistance or other high-risk factors. [98]

Reports by The Global Antibiotic Research and Development Partnership (GARDP) estimated that, at present, almost half of surgical site infections and over a quarter of infections associated with anticancer chemotherapy involve antimicrobial-resistant bacteria. This trend indicates an increasing proportion of infections that cannot be treated. Procedures that benefit most from risk reduction due to prophylactic antimicrobial treatment (i.e., colorectal surgery 30%, and cancer chemotherapy 10%) will be the first to suffer from increasing AMR rates. Similarly, for organ recipients who routinely undergo immune suppression, infection by multidrug-resistant pathogens will pose a serious threat.[96]

### 3.5 HOSPITAL ACQUIRED INFECTIONS AND ANTIMICROBIAL RESISTANCE:

Hospital-acquired infections (HAIs) are caused by bacterial, viral, and fungal pathogens; the most common types of HAIs are bloodstream infections, pneumonia (e.g., ventilator-associated pneumonia), urinary tract infections (UTI), surgical site infections (SSI), gastroenteritis and puerperal fever. The most common organisms causing HAIs are Staphylococcus aureus, Methicillin Resistant Staphylococcus aureus (MRSA), Candida albicans, Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia, and Clostridium difficile, E. coli, Tuberculosis, and Legionnaires disease.

The most important and frequent mode of transmission of nosocomial infections is by direct contact, Transmission may occur when droplets containing microbes from the infected person are propelled a short distance through the air and deposited on the patient's body; droplets are generated from the source person mainly by coughing, sneezing, and talking, and during the performance of certain procedures, such as bronchoscopy. The HAIs occur worldwide and affect both developed and developing countries. By definition, these are infections that occur at least 72 hours after admission into the hospital. Data from lower-income countries suggest that 6.5 to 33

percent of patients get hospital-acquired infections, with pneumonia being the most frequent.[101]

During April 2007 to April 2010, the incidence of hospital-acquired diarrhoea was reported at 4.8 cases per 1,000 patient-days in three tertiary care public hospitals in Bangladesh.[102] Another study conducted between April 2007 and March 2008 at three public tertiary care hospitals in Bangladesh found a prevalence of 1.7 percent of hospital-acquired respiratory disease.[101] The WHO has declared preventing hospital-acquired infections in lower-income countries to be a global priority.[103] Table-13 in the next page shows the summary of hospital acquired infections in Bangladesh.

stewardship program must be implemented in hospitals and especially in Intensive Care Unit (ICU) to combat high drug resistance problem which causes high morbidity and mortality in ICU patients. [106]

In Bangladesh, one study published in 2012, the organism most commonly responsible for HAIs was *E. coli* (55.9%). Other organisms identified were *Pseudomonas* sp. (33.3%), *Proteus* sp. (12.7%), *S. aureus* (5.9%), *Klebsiella* sp. (4.9%) and *Acinetobacter* sp. (3.9%).[104] The organisms were resistant to commonly used antimicrobials, and resistance markedly increased with the length of hospital stay. Prolonged stays in the hospital, the need for isolation, and the use of additional laboratory and diagnostic tests make HAIs expensive to treat.

**Table 13: Summary of Hospital Acquired Infections in Bangladesh**

| Author, n=sample size | Study Site: Bangladesh | Study Population | Major Pathogens(s) responsible for nosocomial infection with major findings | |
|---|---|---|---|---|
| | | | Pathogens(s) | % |
| 1. Mohiuddin et al. (2010), n=152 | Dhaka Medical College Hospital; BIRDEM Hospital-Dhaka, Bangladesh | 1. Patients with post-operative infections;<br>2. Post catheterized UTIs;<br>3. Diabetic patients with wound and<br>4. Post-operative patients without wound. | 1. *E. coli*<br>2. *Pseudomonas* sp.<br>3. *Proteus* sp.<br>4. *Staphylococcus aureus*<br>5. *Klebsiella* sp. and<br>6. *Acinetobacter* sp. | 56%<br>33%<br>13%<br>6%<br>5%<br>4% |
| 2. Bhuiyan et al. (2014), n=23,004 | Three Medical College Hospitals such as Faridpur, Rajshahi , Khulna of Bangladesh | Hospital based surveillance on new onset of diarrhoea of all aged patients of pediatric and medicine wards.<br>Study Period: 2007- 2010 | | |
| 3. Gurley et al. (2010), n=22,652 | Three Medical College Hospitals such as Suhrawardy-Dhaka, Rajshahi and Faridpur of Bangladesh | Hospital based surveillance on hospital-acquired respiratory infections in patients hospitalized for >72 hours in one male ward and one pediatric ward in each of 3 public tertiary care hospitals in Bangladesh.<br>Study Period: 2007-2008 | | |
| 4. Fatema, et al. (2016) | Intensive Care Unit (ICU) of BIRDEM Hospital, Dhaka<br>2004-2016 | ICU admitted patients: Pseudomonasspp was most common bacteria in ICU from 2004-2008. After 2008 this trend changed. Acinetobacterspp. became the most common bacteria in ICU settings. | *Pseudomonas* spp<br>*Acinetobacter*spp | |

1. Mohiuddin et al., (2010): It was evident that E. coli, Pseudomonas sp, Proteus sp, Klebsiella sp. Isolated from the different objects of hospital environment might be a potential source of nosocomial infection. The isolated organisms showed high level of resistance to commonly used antibiotics. The resistance of the organisms markedly increased with the hospital stay. [104]

2. Bhuiyan et al., (2014): The incidence of hospital-acquired diarrhoea was 4.8 cases/1000 patient-day. Children less than 1 year of age were more likely to develop hospital acquired-diarrhoea than older children. [102]

3. Gurley et al., (2010): Patients have frequently experienced hospital-acquired respiratory infections, including 1 in every 20 patients hospitalized for 172 hours in 1 ward. [101]

4. Fatema, et al., (2016): Strict infection control policies and antibiotic

In Bangladesh, the ICU-related drug-resistant pathogens similar to those in high-income countries have also been reported.[105] Trend analysis in ICU patients in a tertiary care hospital reveals Pseudomonas spp. as the most prevalent pathogens identified from 2004 to 2008, while after 2008, Acinetobacter spp. became more frequent. The resistance rate of Pseudomonas spp. was 33% in 2004, rising to 80% in 2016. The most resistant organisms are Acinetobacter spp., with sensitivity only to the last resort antimicrobial Colistin. The frequency of Extended Spectrum β lactamases (ESBL) producing Enterobacteriaceae spp. varied from 11% to 81% between 2004 and 2016.[106]

### 3.6 MANAGEMENT OF HEALTHCARE WASTE AND ANTIMICROBIAL RESISTANCE

Healthcare waste is generated from biological and medical sources and activities, such as the diagnosis, prevention, or treatment of diseases. Between 75% and 90% of the waste produced by healthcare providers is comparable to domestic waste and usually called "non-hazardous" or "general healthcare waste". The remaining 10–25% of health-care waste is regarded as "hazardous" and may pose a variety of environmental and health risks. The hazardous healthcare waste could be categorized as sharps, infectious, pathological, pharmaceutical, cytotoxic, chemical, and radioactive waste. [107] The infectious waste contains pathogens and poses a risk of disease transmission (e.g. waste contaminated with blood and body fluids; laboratory cultures and microbiological stocks; waste including excreta and other materials from patients infected with highly infectious diseases). [107]

The total healthcare waste including infectious waste generated in hospitals (kg per occupied bed per day or kg per patient per day in developing countries) varies from 1.28 kilogram to as high as 3.47 kilogram per patient per day. However, the health-care waste including infectious waste in the high-income country such in USA may be as high as 10.7 kg/occupied bed/day and infectious waste may be as high as 2.8kg/occupied bed/day. [107]

All health providers and individuals coming into close proximity with hazardous healthcare waste are potentially at risk from exposure to a hazard, including those working within health-care facilities who generate hazardous waste, and those who either handle such waste or are exposed to it as a consequence of careless actions. The general public could also be at risk whenever hazardous healthcare waste is abandoned or disposed of improperly. Infectious waste should always be assumed to potentially contain a variety of pathogenic microorganisms. Pathogens in infectious waste that is not well managed may enter the human body through a puncture, abrasion or cut in the skin; mucous membranes; by inhalation; and by ingestion. Figure-3 right side shows the typical waste compositions in health-care facilities. [107]

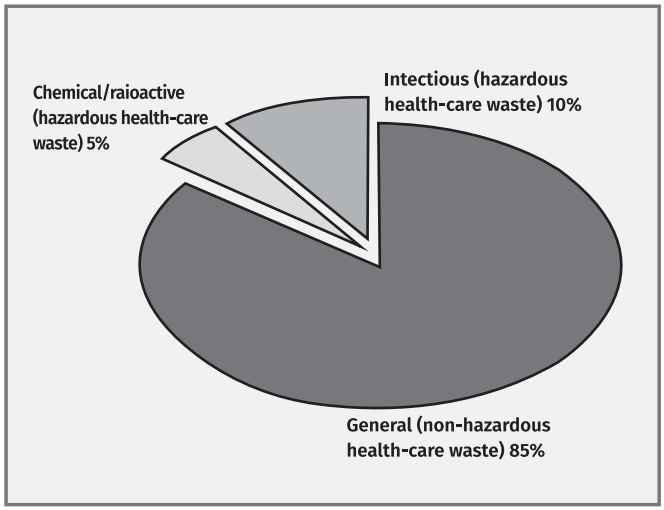



**Figure-3: Typical waste compositions in health-care facilities**

The public health impacts of infectious waste and sharps have been estimated and in the year 2000, sharps injuries to health-care workers were found to have caused about 66,000 hepatitis B virus (HBV), 16,000 hepatitis C virus (HCV) and 1,000 HIV infections among health-care workers. For health-care workers, the fractions of these infections that are due to percutaneous occupational exposure to HBV, HCV and HIV are 37%, 39% and 4.4%, respectively. It is estimated that more than two million health-care workers are exposed to percutaneous injuries with infected sharps every year.[108]

Disposal of this waste is a big environmental concern in Bangladesh especially in big city like Dhaka City Corporation (DCC). Management of hospital waste poses a major health problem in Dhaka, Bangladesh. A quantitative assessment done in 2006 showed that an estimated 37 ± 5 tonnes of waste was produced in DCC per day.[109] The proportion of this waste that would be classified as hazardous according to WHO guidelines was found to be approximately 21%. The amount of waste, and the proportion of hazardous waste, was found to vary significantly with the size and type of Health Care Establishments (HCE). At least 1,012 HCEs were documented by the DCC in 2012 by PRISM-Bangladesh, a non-government organization working in the field of waste management in Dhaka. [110]

The assessment found that there were rarely any procedures for dealing with hazardous wastes separately. [110] HCEs disposed waste into open bins of DCC without any system. Waste is often collected by scavengers and waste collectors for recycling. During this process, waste was repacked and resold, and finally

underwent secondary recycling. In each case, the recycling process involved, at most, simple washing. Disinfection or sterilisation was not observed. Internal storage facilities are poorly managed and are also used for other activities. Most of the waste workers experienced accidental injury, itching, eye burns, skin rash and coughs. PRISM-Bangladesh has been trying to improve management practices since 2005 to minimize the risks to workers and the environment with the collaboration of DCC authorities. This attempt has been partially successful, but more effort is still needed.[110]

Only about 9% of the Bangladeshi hospitals were found to be following waste disposal guidelines, of which 4% followed their own guidelines and about 5% followed government guidelines (manual).[111] Though some manuals and training handbooks have been developed for waste disposal, due to lack of government initiatives they have yet to be implemented in healthcare facilities. Some non-governmental hospitals claimed to have their own guidelines but could not provide documentation.

There is no specific legislation directly related to the handling, transportation or disposal of medical waste in Bangladesh. In the Environmental Conservation Act (1995), wastes are classified under Section 2 (1) as "any liquid, solid and radioactive substance that is discharged, disposed, or dumped which may cause adverse/negative change to the environment". All documented procedures were very general and not specific for management of medical waste.[111]

However, this shortcoming has been addressed by the Government of Bangladesh through 'the Medical Waste Management and Administration Act 2010' and 'the Medical Waste Management Rules 2010' to improve the management of waste disposals by government and private hospitals and clinics.[112] The MoHFW has begun to address medical waste management as a priority in the Health, Nutrition and Population Sector Program (HNPSP). The medical waste management program is one of the performance indicators under MoHFW though there is insufficient monitoring. [113]

### 3.7 MEDICAL EDUCATION AND UNDERSTANDING OF AMR

Professional medical community and healthcare providers should move forward the activities to contain he antimicrobial resistance and share the knowledge of AMR among the general population. A study conducted in March 2011 among 5th-year medical students of different medical colleges reported that about 71% had accurate knowledge on antimicrobials for use in clinical settings; while 67% had accurate knowledge about the "theory of antibiotic resistance" and 58% of the "antimicrobial spectrum".[75] Additional data were collected in this study to understand the antimicrobial use behavior of medical students, of which 76% of students took antimicrobials according to the prescription of qualified physicians, while 16% received antimicrobials without prescription and the remaining 6% were unsure. Of the students who took antimicrobials prescribed by qualified doctors, 80% completed antimicrobial course and the remaining 20% stopped taking them before completion of the course. [75]

The same study evaluated the emphasis of antimicrobial resistance in written questions of pharmacology and microbiology MBBS examinations. In pharmacology, 16% and 1% of questions covered antimicrobials and resistance, respectively; whereas it was only 2% and 1% in microbiology. The emphasis on "antimicrobial" in written issues of pharmacology of Master of Surgery (MS) and Doctor of Medicine (MD) examinations was 18% and 13%, whereas it was 1% and 1% regarding "resistance." In various MS and MD examinations of the Department of Microbiology, 1% and 1% of the questions were on "antimicrobials" and 2% and 1% were about resistance respectively. [75]

Prescribing inappropriate or unnecessary antibiotics is professionally unethical. A hospital-based, cross-sectional, randomized, and questionnaire-based survey conducted in March 2015 among intern doctors (n=50) reveals a knowledge gap on antimicrobial resistance.[114] Among the respondents, 58% of participants said that their hospital had antibiotic guidelines, while 32% indicated no such guideline existed; 64% of intern doctors never got a copy of antibiotic guidelines from their hospital, neither saw any antibiotic guideline on the Internet. On the other hand, 32% said that they never personally used or consulted antibiotic guidelines when considering an antibiotic needed for a patient; 98% of participants thought that antimicrobial resistance was a national problem and 64% thought that the same problem also existed in other hospitals. However, 58% of students thought that antimicrobial resistance (AMR) would be a greater problem in the future.[114]

The knowledge level on "antibiotic and resistance" of 3rd to 5th Year MBBS students (n=164) of a medical college in Malaysia revealed that majority (88%) of the study participants stated that they would like to have more training and educational interventions on antibiotic selection to avoid gaps between theoretical inputs and clinical practices, and to overcome the threat of antimicrobial resistance.[149]

### 3.8 SOCIETAL FACTORS INFLUENCING ANTIMICROBIAL USE AND AMR

Overstatement and misinformation about antibiotics are very common in Bangladesh, which significantly influences doctors' prescribing behaviors. Currently, pharmaceutical companies are the only organizations in Bangladesh providing medicine information to health professionals, and in some cases, the information provided is not consistent with recommendations from public health bodies.[115] A large number of physicians are reported to accept economic incentives from the pharmaceutical companies, in the form of cash and/or kinds of gift item, such as computers, mobile phones, land phones, towels, air conditioners, refrigerators, table lights, calendars, paperweights, pen, penholder and other items for personal and family uses. These gifts are usually printed with the company's insignia and the trade names of medicines for promotional purposes.

The economic incentives also include free air tickets and free lodgings for foreign trips, in the name of attending foreign medical seminars and workshops; and as a result, the physicians receiving economic incentives feel obliged to prescribe company's branded medicines including antimicrobials irrespective of quality consideration. The ultimate effect is high costs incurred to unfortunate patients for inappropriate and/or unnecessary expensive antimicrobials, leading to the development of antimicrobial resistance.[116,117]

Low-income patients may forgo the cost of a physician consultation and chose self-medication. Many patients are guided by self-preference demanding antimicrobial treatment even when it is not indicated.[105] Patients are used to buying antibiotics over-the-counter from the retail pharmacies. In one survey from the Rajbari District of Bangladesh, 100,000 doses of antibiotics had been dispensed in one month without a prescription.[118] In another study, it was found that 92% of medications were dispensed by pharmacies without a doctor's prescription.[119]

In 2015, a questionnaire-based survey was conducted in Maternal & Child Health Hospital, Chittagong, Bangladesh and found that the physicians provided too much of their attention to pharmaceutical representatives/advertising without consideration of the quality of antibiotics. The consequence is the production of antimicrobial resistance.[114] Antimicrobials are available over the counter, and antimicrobials can be prescribed by any healthcare provider. Most drugs are prescribed or sold in Bangladesh by non-qualified or relatively under qualified health workers.[105,120]

In national disease control programs, antimicrobials may be allowed to be prescribed by the trained health workers, in particular cases such as Acute Respiratory Infection (ARI). Antimicrobials are often prescribed unnecessarily for viral fevers and post-operation as prophylaxis.[14] Patients, especially the poor, prefer to seek health care from informal health care providers only to compromise physician consultation fees.[105] These informal health care providers are deeply embedded in the local community and culture, readily available and provide inexpensive services to rural populations with deferred payments and payment in-kind accepted instead of cash.[105]

Informal healthcare providers include traditional practitioners and unqualified allopathic practitioners with varying durations of training in diagnosing and treating common ailments, mostly from unregulated private institutions of dubious quality. These categories of providers, of greatest importance to the poor and disadvantaged populations in rural areas, have largely been ignored by the public sector/government, as well as by NGOs.[105 The untrained and self-prophetic homeopathy practitioners also prescribe antibiotics and other allopathic medicines in addition to homeopathy. This is more common in rural Bangladesh where modern healthcare facilities and doctors are not readily available. These healthcare practices with unnecessary use of antibiotics result in an increase antibiotic resistance.

However, the government recently opened about 13,500 Community Clinics (CC) throughout the country, to serve the poorer communities of rural Bangladesh. The CCs have been developed by the public sector to extend the access to primary healthcare services to the doorsteps of rural people all over Bangladesh. Thousands of people now receive health services from CCs and they have become an integral part of the national health system. The CCs are a unique example of public-private partnership, since most of the CCs have been constructed on the private land donated by the community people, while the cost of the construction of CCs buildings, medicines, salary of the Community Health Care Providers (CHCP), logistics and all other inputs are born by the government. The community people and the government manage the CCs through formation of community groups.

What is concerning for antimicrobial resistance is that CCs are not run by registered physicians, rather by the CHCP, who have received only 3 to 6 months of basic training on management and treatment of common diseases based on a training manual developed by the MoHFW in cooperation with other stakeholders. The CHCPs are allowed to prescribe a list of antibiotics based on clinical signs and symptoms of the patient. With this limited knowledge, the CHCPs may over or under prescribe antibiotics and this may produce antimicrobial resistance in the future.

Infectious diseases are a major health problem in Bangladesh, which require the proper use of antimicrobials.[105] Diagnosis and treatment of the disease is mostly empirical rather than evidence based. The sensitivity patterns of pathogens causing diarrhoeal disease, respiratory tract infections, urinary tract infections, enteric fever, ear infections and soft tissue infections are not routinely available for decision making in drug selection. Many infectious diseases do not respond to conventional antimicrobial agents as the causative agents are becoming resistant due to frequent and widespread inappropriate use.[75,105] In light of this, implementation of the national action plan to mitigate antimicrobial resistance is urgently needed.

### 3.9 FORCEFULLY DISPLACED MYANMAR NATIONALS IN BANGLADESH, ANTIMICROBIAL DISEASES AND AMR:

Forcefully Displaced Myanmar Nationals (FDMN) in Bangladesh is the fastest growing crisis of migrants in the world and is one of the biggest man-made disasters in the South-East Asian region for decades. The most of the FDMNs have been identified as Rohingya, who have fled to Bangladesh to escape violence in Myanmar's Rakhaine State. Nearly 800,000 people are currently fleeing conflict and oppression due to their race and religion, and their homes are no longer safe places to live and their government no longer provide them with protection. They have crossed into the Cox's Bazar area of South-Eastern Bangladesh since conflict broke out in Rakhine State in western Myanmar in late August 2017. This is in addition to more than 200,000 refugees from Myanmar already sheltering in the area before the latest outbreak of violence that took place in 1990. Children and families were in desperate need of food, shelter and medical care. Without immediate access to water and sanitation facilities there is a high risk of disease outbreaks. [152, 153] Infectious diseases and conflicts are strongly correlated. Diarrhoeal diseases, acute respiratory infections (ARI), malaria, typhoid fever, tuberculosis (TB), STIs and skin diseases are some of the major infectious diseases commonly occur in refugee camps. Multi-drug resistance organisms (MDRO) have been found significantly high among refugee populations due to poor medical care leading to incomplete treatment. An increase of MDROs in the near future increases the possibility of MDROs spreading to Bangladesh and Myanmar. [154] A systematic review and meta-analysis was conducted to identify and synthesize data on antibiotic resistance in migrants to Europe to examine rates of AMR, the distribution of AMR among refugees and asylum seekers compared to other migrant groups, and patterns of antibiotic resistance in migrants in high migrant community settings (e.g. camps, transit centres). [155]

The results above review and meta-analysis show that the prevalence to any antibiotic resistance is 33.0% in refugees and asylum seekers and is very similar with that in high-migrants community setting. The prevalence of methicillin-resistant Staphylococcus aureus (MRSA) is 8.2% in refugees and asylum seekers, whereas the prevalence MRSA (9.8%) is little high in high-migrants community setting. The prevalence of gram-negative bacteria is 27.2% in refugees and asylum seekers, whereas the prevalence (32.1%) is high in high-migrants community setting. [155] The study concluded that increased rates of AMR among refugees and asylum seekers may be attributed to exposure in

high-migrant community settings like camps and transit centres in host countries, in which high rates of AMR were detected. There was a lack of evidence migrants are significantly increasing the burden of antibiotic resistance in host countries through the importation of antibiotic resistance, or onward transmission to host populations. [155]

Emerging infectious diseases (EIDs) could infect the refugee populations currently displaced in south-eastern part of Bangladesh. The common new and re-emerging infectious diseases are severe acute respiratory syndrome, pneumonia, influenza, swine flu (H1N1), tuberculosis (TB), hepatitis, malaria, cholera, chikungunya, meningitis, food-borne gastroenteritis, salmonellosis, and campylobacteriosis, which continue to threaten national public health. A large population of these refugees remaining in poor conditions would provide a source of people susceptible to contracting EIDs where the diseases could then spread to nearby populations of Chittagong hill districts. Through repeated, everyday travel between infected districts, EIDs could feasibly spread to farther parts of the country.

Health care in Rakhaine state of Myanmar is poor, especially in areas where conflict and poverty have delayed medical development. The conditions in the refugee camp could lead to the appearance of infectious diseases like cholera, measles, rubella and diphtheria. More than 200 mobile vaccination teams have given about 900,000 doses of oral cholera vaccine to the Myanmar refugees. (5) [156] However, another contagious bacterial infection, diphtheria, has appeared. As of February 2018, a total of 2637 suspected cases diphtheria were reported in among the Rohingya refugees, of which 53 were positive on PCR. [153] Contact tracing is ongoing, and includes post-exposure prophylaxis of close contacts with antibiotics and vaccination, regardless of age. The majority of patients are between 5 and 14 years old. The emergence and the spread of diphtheria show how vulnerable Rohingya refugees are. The majority of them are not vaccinated against any diseases, as they had very limited access to routine healthcare, including vaccinations, back in Myanmar. The second round of vaccination campaign against diphtheria concluded on 10 February, 2018 with 391 678 children immunized. [156, 157]

A total of 150 national and international health sector partners have responded to the needs through health service delivery in more than 270 static and mobile health facilities in the refugee camp, and have been actively engaged in emergency preparedness and mitigation efforts ahead of the expected rainy season. The total number of doctor's consultations reaches to about 2 millions. The most common diseases treated were Acute Respiratory Infection (n = 75,080), Acute Watery Diarrhoea (n = 36,527), bloody diarrhoea (n = 14,739), and suspected malaria (n = 5121) of which 27 cases were confirmed as Malaria. However, acute watery diarrhoea, measles and diphtheria are currently being monitored on the basis of early warning alert and response system. As of end of February 2018, there are an estimated 53 266 pregnant women among the Rohingya refugees with 16 513 expectant deliveries over the next 3 months. As per the Sexual Health and Reproductive Task Force, about 2 477 pregnancies are expected with obstetrical complications. [153,158]

Health care services are currently concentrated in the more accessible areas of the camps. As a result, some areas are over-served while in other areas have no or very limited access to health care. Communicable disease risks, crowded living conditions, inadequate water and sanitation facilities and low vaccination coverage present significant risks of communicable disease outbreaks. As of February 2018, a total of 738 suspected cases of measles were reported. Essential reproductive health/maternal, child and newborn health services, particularly obstetric services, are inadequate either due to insufficient bed space or lack of facilities in hard-to-reach hilly areas Teknaf and Ukhia. Home deliveries are anecdotally reported to be high. Many Rohingya are reported to have been physically and mentally traumatized by the violence, including sexual and gender-based violence. [152,153]

In conclusion, the Forcefully Displaced Myanmar Nationals (FDMN) in Bangladesh refugee crisis should be addressed from both humanitarian and health aspects and the victims should be provided with proper relief, health services, utility and shelter to reduce the occurrence and spread of infectious diseases, allowing for a more stable preventive supports and protecting long-term public health threats like multi-drug resistance organisms (MDRO) and emerging infectious diseases (EIDs) on a priority basis.

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# CHAPTER-4

# DRUG REGULATIONS, SUPPLY CHAIN MANAGEMENT & ACCESS TO ANTIBIOTICS

## CHAPTER-4: DRUG REGULATIONS, SUPPLY CHAIN MANAGEMENT & ACCESS TO ANTIBIOTICS

### 4.1 BANGLADESH DRUG POLICY, REGULATIONS, ORDINANCE AND STRATEGIES

**4.1.1 Drug Regulation and its requirement:** Drugs are regarded as specialized consumer products and the patient is considered as an exceptional customer, who needs professional advices during any ailment from the physicians to procure drugs from the pharmacy, indicating type, its doses, route of administration, and duration in a particular disease condition, and to know the side effects of drugs against the potential benefits. Medical professionals, pharmacists, dispensers, nurses and other health staff should have the capacity to make informed decisions about all aspects of drug use for patients in their respective responsibilities. Therefore, they need special training and access to necessary medical and therapeutic information. The production, distribution, storage, and dispensing of drugs also require special knowledge, understanding, skill and expertise. The basic medical training should include the drug safety, efficacy, and quality along with other aspects of pharmacology, its pharmacodynamics and pharmacokinetics as a whole.

The physician may encounter therapeutic failure, the disease condition of the patients may worsen, resistance to drug may develop, and the patient may die, if inappropriate, unsafe and low quality drugs are used. Quality control tests on different drugs show a high failure rate, treating patients with poor quality medicines results in low bioavailability promoting the development of antibiotic resistance. Reports on counterfeit medicines by therapeutic class, show the highest percentage are antibiotics. Healthcare facilities, medical professionals, manufacturing companies and distributors may also lose their confidence because of the therapeutic failure. This furthermore causes patients to perceive that the money spent on ineffective, unsafe and poor quality medicines is wasted.[1,2]

**4.1.2 Health Rights Protection:** In order to protect the health rights of the population, the government has a responsibility to establish a strong national regulatory authority to ensure that the manufacture, trade and use of medicines are regulated effectively in order to be able to protect and promote public health in the country. Drug regulation demands the application of sound medical, scientific and technical knowledge and specific technical skills, and operates within a legal framework. Regulatory functions involve interactions with various stakeholders such as manufacturers, traders, consumers, health professionals, researchers and governments.

**4.1.3 Factors for Strong Drug Regulation:** The fundamental objective of having effective drug regulation is to ensure safe, effective and good quality drugs for the citizens of the country. There are several aspects to form strong drug regulation, which include strong political will and commitment; strong public support; necessary qualified and experienced pharmaceutical, medical and other professionals; and effective cooperation between the regulatory authority and other government institutions including law enforcement agencies (e.g. customs and police); and international cooperation. Moreover, the national drug regulatory authority should have appropriate organizational structure and facilities; clearly defined roles and responsibilities; adequate and sustainable financial resources, including resources to retain and develop staff; and preparation of appropriate tools, such as standards, guidelines and procedures.

**4.1.4 Effective Regulatory Functions:** The drug regulatory authority must have the following important regulatory functions to ensure safe, effective and quality drugs, these are: (i) Licensing of the manufacture, import, export, distribution, promotion and advertising of medicines; (ii) Assessing the safety, efficacy and quality of medicines, and issuing marketing authorization for individual products; (iii) Inspecting and surveillance of manufacturers, importers, wholesalers and dispensers of medicines; (iv) Controlling and monitoring the quality of medicines on the market; (v) Controlling promotion and advertising of medicines; (vi) Monitoring safety of marketed medicines including, collecting and analysing adverse reaction reports; and (vii) Providing independent information on medicines to professionals and the public (Source: WHO Policy Perspectives on Medicines no 7, 2003).[1,2]

### 4.2 BANGLADESH REGULATORY NETWORK AND DRUG REGULATION

**4.2.1 The National Regulatory Authority (NRA):** The Ministry of Health and Family Welfare (MoHFW) of the

Government of the People's Republic of Bangladesh established the "Directorate of Drug Administration (DDA)" to act as the national regulatory authority (NRA) in 1976. The DDA was upgraded in January 2010 and became the Directorate General of Drug Administration (DGDA). DGDA is entrusted with the responsibility to ensure the safety, efficacy, and the quality pharmaceutical products through the implementation of the relevant drug legislation. The directorate is trying its best to fulfill the requirements of the pharmaceutical sector together with the need for ensuring medicines remain safe, effective and of high quality.

The DGDA supervises and implements all prevailing pharmaceutical regulations in the country and regulates all activities related to procurement and import (raw materials, packing materials, and finished medicines), production, and distribution of finished medicines. Furthermore, DGDA regulates export, sales and pricing of Active Pharmaceuticals Ingredients (API) and finished medicines. DGDA supervises and implements all prevailing pharmaceutical regulations in the country and regulates all activities related to Ayurvedic, Unani, Herbal, Homeopathic products medicines and medical devices. The DGDA is empowered to regulate 852 manufacturers of allopathic, Unani, Ayurvedic, Herbal, and Homeopathic and Biochemical products.

**4.2.2 Different Drugs Acts, Rules, Policies, Ordinances and Strategies:** The Drugs Act 1940 was promulgated by the Government of British India on 17th October 1940. [3] The Drugs Rules 1945 was developed under the Drugs Act 1940 with an explanatory memorandum and was reprinted in 1953 under the Drugs Act 1940 (XXlll of 1940). [4] The Bengal Drugs Rules 1946 was amended by the Government of East Bengal in December 1952, in exercise of the power conferred by the Drugs Act 1940 (Act, XXIII of 1940). [6]

The Drugs Act 1940 has been criticized as grossly inadequate for the control of prices of pharmaceutical raw materials and processed pharmaceuticals. It also largely failed to prevent the appearance of substandard and counterfeit pharmaceuticals on the market, unethical promotion, and the proliferation of harmful and useless pharmaceuticals. [5] In order to overcome these limitations, the Government of Bangladesh reorganized the Directorate of Drug Administration (DDA) and reviewed the Drug Act 1940, the Drug Rules 1945 and the Bengal Drug Rules 1946 to provide further regulation relating to labelling, packing, biologicals, and other special products in 1982. [5,7]

In 1982, the government introduced new "National Drug Policy 1982", gave priority to the production of selected essential drugs, and removed all harmful, useless and undesirable products from the market. In June 1982, the government also approved and enacted the Drug (Control) Ordinance 1982 as a first step in implementing the new National Drug Policy 1982, which helped to increase local production of drugs. Moreover, the NDP 1982 ensured the procurement, local production, quality control, distribution and utilization of all drugs under unified legislative and administrative control. The Drugs (Control) Ordinance, 1982, (Ordinance No. VIII of 1982), was published on 11th June, 1982. The DCO 1982 was enacted to meet the objectives of the NDP 1982. The DCO 1982 regulates the manufacture, import, distribution and sale of pharmaceuticals in Bangladesh; promotes the local pharmaceutical industry; and discourages imports of medicines. [5,7,8]

The NDP 1982 and DCO 1982 resulted in substantial benefits for Bangladesh, in particular, they facilitated the increase in local production of essential drugs from 30% to 90%; furthermore, they helped local companies to increase their market share of 30% in 1970 to more than 80% in 2002 of local needs, and as a result reduced the prices of medicines substantially in the local market. The DCO 1982 has also contributed markedly to the improvement in quality of medicines and resulted in the reduction of substandard drugs from 36% in 1970 to 2% in 2002, a remarkable improvement of drug standard achieved over the period. Overall, the NDP 1982 and DCO 1982 were found to be pro-people and anti-poverty, an attempt to give people access to essential drugs. [5,9]

In 2001, MoHFW of Bangladesh constituted a "National Drug Review Committee" to review the NDP 1982 and DCO 1982 and formulated an updated policy "National Drug Policy 2005", which met the requirements of "Trade-related Aspects of Intellectual Property Rights (TRIPS) compliance and the current local needs to preserve the pharmaceutical industry and improve the public health goals of the country. The NDP 2005 included the policy areas such as laws and regulations relating to drugs; the mandate for Drug Regulation

Authority (DRA); rules and procedures and criteria related to drug registration; drug production; drug procurement; drug distribution, sales and storage; drug pricing; quality assurance of drugs and pharmaceuticals; technical manpower in the manufacturing unite; drug information and monitoring; and essential drugs. [5,9]

The MoHFW formulated the National Drug Policy 2016 on December 2016 to keep compliance with the National Health Policy 2011 and the National Population Policy 2012, and (i) to ensure that the people can have easy access to safe, effective and good quality drugs at affordable prices; (ii) to ensure rational and safe use of drugs and proper dispensing; (iii) to achieve self-sufficiency in the manufacture of drugs and raw materials by providing services and facilities on a priority basis to all local drug manufacturing industries; (iv) to expand the export of drugs that are manufactured in the country; and (v) to establish effective surveillance system of medicines. [10]

The important elements and areas of NDP 2016 have been explicitly mentioned including the support to develop the pharmaceutical sector in Bangladesh in light of the WTO/TRIPS agreement and to transform the DGDA to "Directorate General of Food and Drug Administration (DGFDA)" for assurance of quality and safety of different types of food and cosmetics in addition to drugs and rearrange the jurisdiction and organizational structure to establish legal control over these products. The NDP 2016 includes further areas to modernize the National Control Laboratory (NCL) for drug testing and analysis with WHO accreditation and standards. [10]

National Drug Policy 2016 has been formulated upon review of National Drug Policy 2005. This National Drug Policy 2016 articulates well-defined directives for drug safety, efficacy, rational use, effective drug control management, production, marketing, distribution, storage and import-export. This drug policy will facilitate further growth and expansion of the pharmaceutical sector, enhance capabilities of production of better quality drugs, and also augment the scope and opportunities for drug export in many areas.[10]

Table-1 below shows the milestones that marked the gradual development of the pharmaceutical regulatory framework in Bangladesh.

**4.2.3 The National Drug Strategic Plan 2017-2021:**[11] The purpose of the five-year strategic plan is to serve as a roadmap to strengthen the regulatory systems and build the capacity of the DGDA (also country's NRA) to implement regulatory functions effectively and efficiently, and at the same time, cover the regulatory functions captured in the fourth sector wide approach national "Health, Nutrition and Population Sector

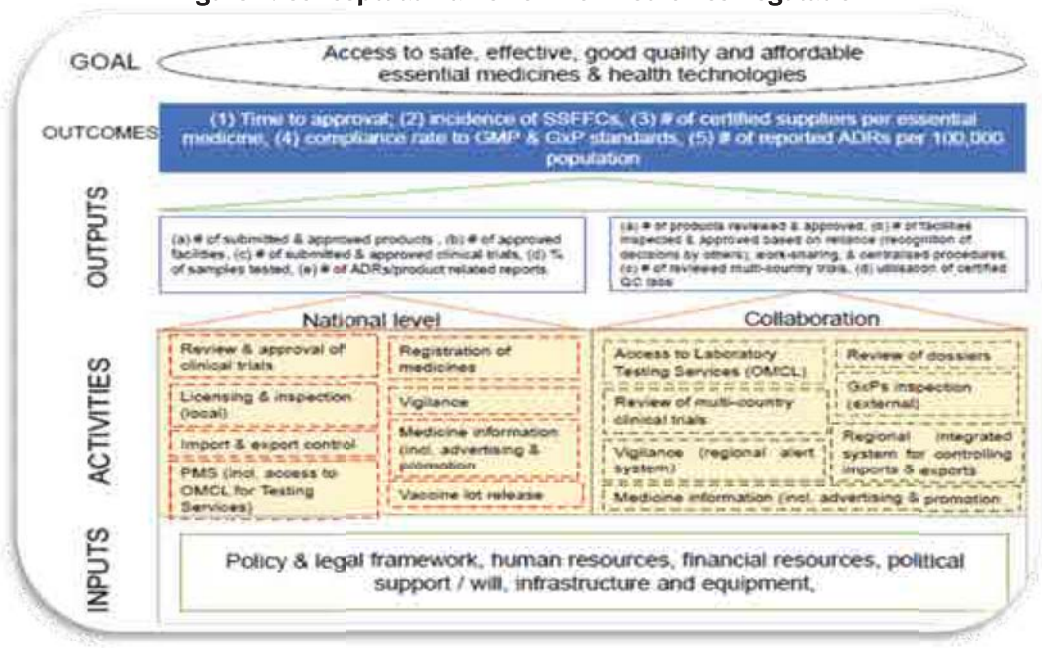
**Table-1: Milestones of development of the pharmaceutical regulatory framework in Bangladesh** [5]

| | YEARS | Different Acts, Rules, Regulation, Policies and Strategy |
|---|---|---|
| 1. | 1940 | The Drugs Act 1940, (XXIII of 1940) |
| 2. | 1945 | The Drug Rules, 1945, under the Drugs Act, 1940 |
| 3. | 1946 | The Bengal Drugs Rules, 1946 |
| 4. | 1976 | Directorate of Drug Administration(DDA) was created as a National Regulatory Authority (NRA) for drug |
| 5. | 1982 | Drugs (Control) Ordinance, 1982, Drugs (Control) (Amendment) Ordinance, 1982 |
| 6. | 1982 | National Drug Policy, 1982 |
| 7. | 1984 | Drugs (Control) (Amendment) Ordinance, 1984 |
| 8. | 1992 | Bangladesh National Formulary, First Edition, published |
| 9. | 2003 | Bangladesh National Formulary, Second Edition, published |
| 10. | 2005 | National Drug Policy, 2005 |
| 11. | 2006 | Drug (Control) Ordinance Amendment Act, 2006 |
| 12. | 2006 | Bangladesh National Formulary, Third Edition, published |
| 13. | 2009 | DDA Capacity: WHO-SEARO Mission discussed to build DDA Capacity |
| 14. | 2010 | DGDA Created: DDA was upgraded to the Directorate General of Drug Administration (DGDA) |
| 15. | 2010 | WHO Mission: Reviewed Pharmaceuticals in Healthcare Delivery in Bangladesh |
| 16. | 2016 | National Drug Policy, 2016 approved |
| 17. | 2017 | National Drug Strategic Plan: 2017-2021 |

Program (4th HNP SP: 2017-2022)". The five-year Drug Strategic Plan: 2017-2021 focuses on the following strategic areas. These areas are grouped into seven key result areas: Figure-1 below shows the conceptual framework for drug regulation.[11,12]

tool in all identified regulatory functions applicable to DGDA for full functional NRA, and to achieve regulatory compliance to the Pharmaceutical Inspection Co-operation Scheme (PIC/S) guidelines for accession to the forum.

**Figure-1: Conceptual Framework for Medicines Regulation**

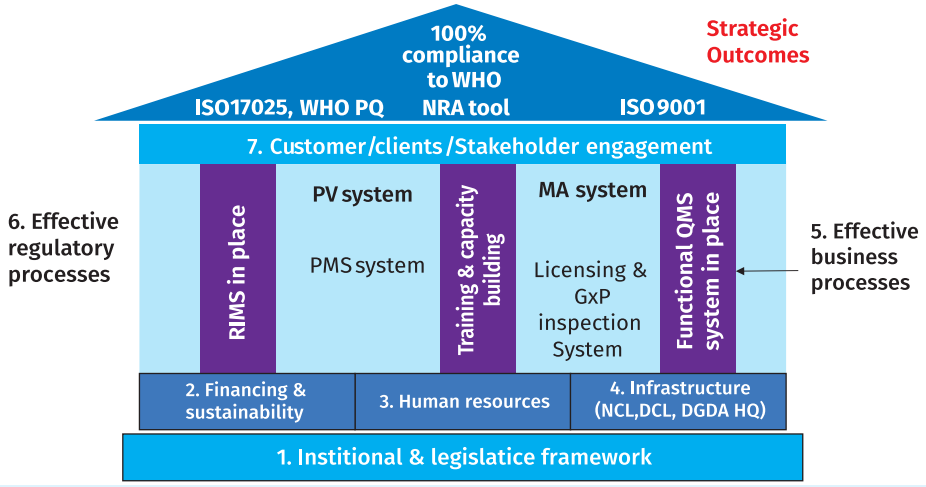



**Conceptual Framework for Medicine Regulation**
**Source:** L Gwaza and G.N. Mahlangu. Business Plan for the African Medicines Agency 2016

The strategic plan outlines critical issues, strategies, objectives, broad activities, timelines, and provides an indicative budget to achieve the DGDA's overall goals and aspirations. The objective of the drug regulatory framework is to update the regulations and institutional framework in line with WHO recommendations for NRA, to improve regulatory compliance to relevant levels of the WHO assessment

Figure-2 below illustrates the interplay between the input factors, with the institutional and legislative framework forming the foundation on which other input factors (financing, human resources and infrastructure) rely. The strength of the regulatory and business processes are the key pillars, which ensure that the strategic outcomes are achieved. The key strategic outcomes for this strategy are summarized at

**Figure-2: Interplay of the key result areas and the regulatory system.[11]**

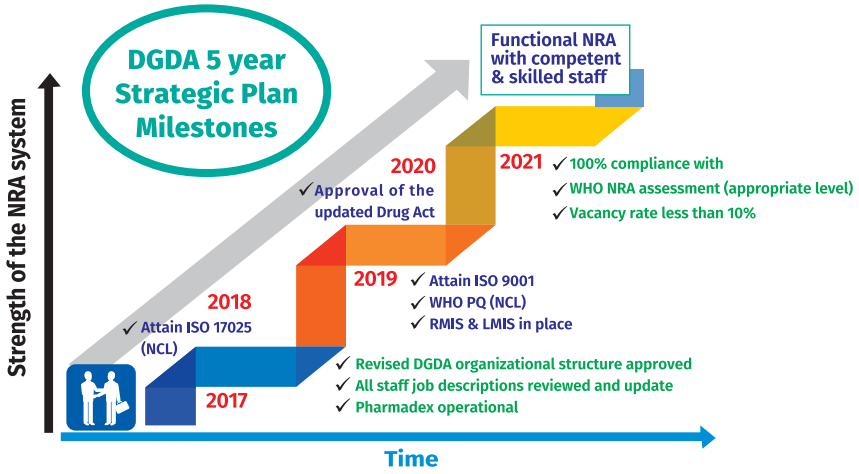



QMS – Quality Management System; PMS – Post Marketing Surveillance, PV – Vigilance System, RIMS – Regulatory Information Management System; WHO PQ – WHO Prequalification, NRA – National Regulatory Authority, NCL – **National Quality Control Laboratory**

the top in figure-2. Achieving these will ensure that the key regulatory outcomes and goals, as shown in figure-1 above, are achieved. The M&E plan includes a log frame for the DGDA, which incorporates the conceptual framework for medicines regulation and this strategic plan.

The foundation for drug regulation is an appropriate legal framework supported by an appropriate institutional framework. The drug regulatory activities have been consolidated under DGDA, however, the legislation is undergoing revision in-line with international norms and WHO recommendations. The updated legislation should be approved within this strategic period. The institutional framework requires alignment with the key regulatory functions. The key milestones for this five-year strategy necessary to reach the strategic outcomes are reflected in figure-3.[11]

**Figure-3: The Milestones of 5-Year National Drug Strategic Plan of DGDA**




**Strategic directions:** The strategic directions for this plan are guided by the existing gap analysis reports, and the strategic planning workshops. In this respect, the proposed objectives, outcomes, strategies, outputs, and targets have been analysed in accordance with the seven key results areas (KRAs). This strategic plan takes note of the existing situation and trends, and proposes objectives and strategies that would help address the existing weaknesses and threats, and ensure adequate strengthening of medicines regulatory system in Bangladesh.

## 4.3 PHARMACEUTICALS (DRUGS/MEDICINES) IN HEALTH CARE DELIVERY

Bangladesh has an extensive health care system, with substantial infrastructure and trained health care personnel, but there are a number of issues in the pharmaceutical sector concerning drug supply, selection, use, regulation, policy, information and coordination.

**4.3.1 Drug Supply and Selection:** Essential Drugs Company Limited (EDCL), a state owned pharmaceutical company based in Dhaka, functions under the MoHFW and supplies about 70% of drugs to all public health facilities including tertiary hospitals; the other 30% drugs are supplied by the Central Medical Store Depot (CMSD). This arrangement is based on the ratio of bed versus patients and consumption of medicines in the previous year. However, the inappropriate ratio of 1 bed per 1,670 population causes hospital beds to be overloaded with patients, the supply of drugs are usually insufficient, and there is a large shortfall of drugs with many complaints about stock-outs from all public health facilities. Half of or more of patients must buy their drugs from private pharmacies, paying for them out-of-pocket.

Good quantification and forecasting of drugs is needed but currently it is not possible to forecast properly due to poor inventory control and management, and the absence of an electronic inventory control system in public health facilities. It is recommended to establish an electronic medicine inventory system within the DGHS, tertiary hospitals, district hospitals, and Upazila Health Complexes to better estimate the need and to monitor adherence to the Essential Drug List (EDL), which was prepared in 2008, focusing mainly on drugs from primary healthcare. The DGDA has updated the EDL in 2016 under the National Drug Policy 2016, which includes a total of 285 essential drugs. [10,14]

**4.3.2 Information on Drug Use:** The "WHO Pharmaceuticals in Health Care Delivery (2010)" report shows that there was a shortage of official published information on medicine use in hospitals in

Bangladesh, but much information was published from the pharmacology departments of local universities. Overall this information showed that there is much poly-pharmacy, high vitamin use, and high use of antibiotics, particularly in hospitals, where there is very low prescribing of generic named drugs to be purchased in the private pharmacies. Moreover, there is no comprehensive national standard treatment guideline, but there is a Bangladesh National Formulary prepared in 1992 (1st Edition) and subsequently revised in 2003 (2nd Edition) and 2006 (3rd Edition). Unfortunately few practitioners were found to prescribe using the Bangladesh National Formulary or any clinical guidelines or other source of independent drug information. However, most practitioners from the public sector received drug information from pharmaceutical representatives on a daily basis in the evening when practicing in their private clinics usually after official working hours.

In order to improve and monitor medicine use, a vigilant health promotion unit should be developed within DGDA, MoHFW. Other recommendations for the improvement of medicine use include: strengthening Drug and Therapeutic Committees (DTC) in all hospitals; developing and distributing updated clinical guidelines and incorporating them into Continuing Professional Development (CPD) curricula; and developing public education programs on medicines use to be delivered through the existing medical education system.

**4.3.3. Implementation of Drug Regulation:** The DGDA "Strategic Plan for Drug: 2017-2021" in it SWOT analysis validates a severe manpower shortage in the National Regulatory Authority of the DGDA, making it extremely difficult to carry forward regulatory functions. This manpower shortage is regarded as an extremely serious problem in a country with a very large pharmaceutical sector, there being more than 852 allopathic and alternative medicine manufacturers, with 1,23,542 registered retail pharmacy shops and 26,910 allopathic branded products in the market.

Adequate inspection and supervision of manufacturers and drug outlets is not possible due to a lack of Drug Inspectors (each district has only one Drug Inspector supervising a total of 2,236 registered pharmacy shops). As a consequence, it was reported that pharmacists were not often available in pharmacy shops to supervise dispensing of drugs. However, in NDP 2016, the list of 39 OTC drugs has been finalized, and as a result, there is a drug schedule available in the pharmacy distinguishing between those drugs that should be sold only with a prescription and those drugs that can be sold without a prescription.

**4.3.4 Human and Financial Resources:** The DGDA had a total of 370 staffs in 2016. At present, DGDA has 55 district offices in the country. Each district has one "Drug Inspector". All 55 Officers in the district level function in pursuant to the drug laws and regulations, and assist in the implementation of drug regulations all over the country; and are expected to supervise and monitor all retail pharmacies and all registered medicines manufactured by 852 pharmaceutical companies in the country. There are inadequate numbers of qualified and skilled personnel within DGDA to cover the regulatory workload. More than 25% of positions are vacant in DGDA and initiatives have taken to recruit the right number of staff supervise and monitor regulatory activities throughout the country.[10,11]

The DGDA has developed a new organogram under the present National Drug Strategic Plan: 2017 - 2021, proposed to increase the number of skilled staff, and submitted to MoHFW for approval. However, one year has passed and it is not yet approved. Moreover, lengthy recruitment process by the government's Public Service Commission (PSC) that is beyond DGDA's control; high vacancy rate; lack of qualified and skilled manpower to cover the regulatory requirements and work load; lack of autonomy in hiring own staff by DGDA; inadequate financial resources and lack of autonomy to use the revenue collected from fees to augment government support; inability to recover all costs; inadequate IT systems; and limited career growth are some of the most important issues that need to be addressed to overcome the challenges.

The threats have been identified by situation and SWOT analysis. These are: frequent changes in top management could lead to changes in priorities and focus; change in government may change the policy direction; direct involvement of the pharmaceutical industry in decision making; reliance on external partner support for key regulatory functions with no sustainability plan in place threatens continuation of key regulatory activities beyond funding phase; bureaucratic corruption; political instability; general

lack of skilled workers in the country; and lack of strong regional harmonization and cooperation in regulation may jeopardize the implementation of drug regulation in the country.

There was no adequate monitoring of drug promotional activities or vetting of adverts aimed at prescribers or the public. There were insufficient laboratory testing facilities to ensure medicine quality. Some activities such as drug evaluation for registration (which was manual) were criticized for being biased by over-representation of the pharmaceutical industry in the Drug Control Committee.

**4.3.5 Governance Issues in DGDA:** The challenges and limitations of the existing drug laws, rules, acts, policy, regulations and ordinances have been identified. For example, some sensitive products for the human body like medical devices, food supplements and cosmetics were not included in the past drug laws and regulations before 2016.[18,22] However, there were no clear guidelines to regulate such items and they were not included in the functions of DGDA. As a result, if anybody produced, imported or marketed unsafe, ineffective, low quality and risky medical devices, food supplements or cosmetics, the DGDA failed to take any legal measures in the past. However, the government, realizing the importance of the health rights of the population, has included medical devices, food supplements and cosmetic products under NDP 2016, and brought these products under the regulatory control of NRA of DGDA.[10]

There are ten different types of drug committees to guide and help implement the drug policy, laws, regulations and ordinances of the DGDA but the laws do not provide clear criteria and guidelines for the formation of committees, operation processes, number of members in the committee, technical expertise of the members, terms of reference (TOR), etc. The DGDA has formed such committees based mostly on directives as provided by the MoHFW through official circulation. This process of forming committees has created and increased the risk of appointing members based on political considerations and creating conflict of interest. While making an in-depth review of the list of the committees it was found that the representatives of the Bangladesh Association of Pharmaceutical Industry (BAPI) have been included in all the drug committees except the ADR Advisory Committee and district drug committee. Furthermore, many of the same people sat on the various different committees, which could result in conflicts of interest and impact decision-making.

The pharmacovigilance activities were so little that the concerned ADR Advisory Committee had not met. The Standard Operating Procedures had not been updated for a long time and were often not being followed. In addition, the DGDA was responsible for many activities that were not strictly regulatory ones such as developing and updating the EDL and the Bangladesh National Formulary. It is recommended that the manpower shortage be rectified as a matter of urgency; Standard Operating Procedures (SOPs) be revised for the various committees; and a committee to monitor drug promotion be established. The DGDA has taken initiatives to develop software and smart phone applications (IOS & Android base) to allow for online reporting of ADR, identification of fake medicines, over pricing of drugs and to lodge complaints. The DGDA received funding for this project as a compliment for submitting the innovative idea from the access to information program of Prime Minister's Office.

In NDP 2016 under Article 4.22: Clinical Trial and Bio-equivalence Studies of Drugs, it is mandatory to conduct bioequivalence studies to ensure the quality and effectiveness of drugs. The DGDA is expected to quickly establish a globally accredited Bioequivalence Study Centre and Clinical Trial Centre in Dhaka and formulate guidelines in conducting the activities of bioequivalence studies and clinical trials. The initiative has not yet been taken by the DGDA. This increases the risk of importing drugs with adverse health effects. The existing laws/policies do not promote rational use of drugs by making prohibitive/punitive measures against the prescription of irrational, unjustified drugs by physicians. They also mention nothing about prescriptions as prerequisite for selling drugs. Therefore, Drug Authority is unable to take legal measures with this respect.[10]

Various other important limitations of the existing laws include: the absence of guidelines on the increasing number of quality testing facilities in accordance with changing demand and need; according to law establishing only one such central laboratory has been made mandatory, no provisions for local level testing labs or branches; absence of timeframe of gazette

notification on maximum price of a drug for which DGDA is unable to take legal actions if a company is selling medicine at higher prices (last gazette notification made in 2000).[22]

Capacity Constraints: The DGDA has capacity constraints such as infrastructural, logistical, institutional, and other limitations and challenges in face of huge growth in the pharmaceutical sector; its own head quarter premise is yet to be completed, present office lacks adequate space; it is challenged by the inadequate logistic support; collecting samples, preserving samples and transporting samples are hampered because of lack of transportation; shortage of manpower having 55 Drug Inspectors instead of 64, with 4 Supers instead of 64, a total 25% of positions remain vacant, directors are not appointed; lack of professional knowledge and regular training provision for relevant field staff (e.g. inspectors and supervisors); lack of inadequate skilled manpower at testing labs; limited communication and collaboration between central and field offices; absence of unified reporting format (reporting by the field offices to HQ); inadequate number of district offices (47 out of 64); and lack of own legal staff for conducting litigations (dependence on PP).[22]

There have been a number of influential pharmaceutical companies, which form syndicates to influence the DGDA to secure approval for importing low quality raw materials and fixing drug prices. In addition they start marketing drugs well before they get permission. One study reported the DGDA has some legal shortcomings as well. For example, the Drug Act 1940 and Drug (control) Ordinance 1982 do not specify the standards of medical devices, food supplements and cosmetics. As a result, it cannot take action against those importing and marketing risky and low-quality products.

The DGDA fails to check corruption and irregularities because punishments under the laws are light. Only 0.18% of the country's health budget is spent for regulatory activities compared to 5.3% in India and 0.8% in Pakistan. At least 38% of the approved posts of the DGDA are vacant. For this, officials fail to inspect two-thirds of the drug stores (retail pharmacies) and test the quality of many drugs. Furthermore, it has no office in 11 districts.[22] Table-2 below describes the Cause-Effect-Impact Analysis of Lack of Governance in the DGDA.

**Table-2: Cause-Effect-Impact Analysis of Lack of Governance in the DGDA** [18,22]

| | Causes | Effect | Impact |
|---|---|---|---|
| 1. | Weak implementation of drug policy, legal framework, and enforcement | No penalty/legal action; risk of increasing corruption in pharmaceutical industry | Disregard to human health rights affecting public health of the country |
| 2. | Lack of political commitment and willingness to build capacity | Inadequate ability to supervise, monitor and control drug market | Irregularities & corruption institutionalized |
| 3. | Shortage of skilled manpower and necessary logistics | Weak inspection creates scopes of corruption | Progress in drug export runs risk of being affected |
| 4. | Lack of laboratory and capacity | Drug quality control hampered | |
| 5. | Lack of transparency and accountability in strategies implementation and control | Internal grouping and indiscipline in distribution of tasks and weak accountability mechanism | |
| 6. | Influence of politicians and business enterprise in policy decision making | Influentials get priorities in decisions resulting conflicts of interest | |

The institutional capacity of the DGDA is not adequate considering the scope, geographic coverage and expansion of the drug market. There are institutional limitations in terms of human resource, infrastructure, logistics and skills for operating its activities properly. Moreover, the present legal structure is not sufficiently strong for supervising, monitoring and controlling the drug market and for facing contemporary challenges.[18]

The lack of proper implementation of the laws and regulations have been also identified. There is a lack of transparency and accountability in terms of operating the mandate of the DGDA resulting in-house incapacitation and weakness in management and creating corruption in the pharmaceutical sector resulting in unsafe, ineffective and low quality drugs. The in-house challenges include disproportionate distribution of tasks following the organogram, lack of transparency in distribution of work, and lack of

monitoring and accountability of the officials in delivery. As a result, corruption is somewhat institutionalized at every point of pharmaceutical value and supply chain of drugs and especially small pharmaceutical companies resort to such practices more than the rest.[18]

Moreover, the influence of the representatives of the large pharmaceutical companies reinforces the collusive nature of corruption through their inclusion in different committees. Finally, it can be said that there is lack of political will in strengthening the capacity of the DGDA at the policymaking level. This is reflected in various aspects such as not increasing human resources over the years, not improving the logistics and other facilities, not increasing the allocation, and not taking measures for legal reforms to face contemporary challenges in monitoring and controlling drugs.

**4.3.6 Development of Guidelines and Coordination:** Many functions such as the monitoring of medicine use, adherence to the EDL, coordinating continuing professional development (CPD), supporting the drug and therapeutic committee (DTC), developing and updating clinical guidelines, distributing clinical guidelines, incorporating into CPD and undergraduate curricula, and public education on medicine use, are not undertaken by any of the MoHFW department. Furthermore, it was found that there is a National Drug Policy 2016 document, in it there were many aspects which are not implemented, particularly with regard to use of medicines. This problem had already been recognized in 2008 when there was a consultation on establishing a "Core Committee for Rational Use of Drugs" that has never been instituted.

It is recommended that (1) the "Core Committee for Rational Use of Drugs" should be revived and endorsed by government as a multidisciplinary statutory committee, and (2) that a fully resourced executive unit dedicated to monitoring medicines use and coordinating the implementation of the current strategic plan to improve medicine use as recommended by the Core Committee, be set up in the DGDA/MoHFW.[14]

Bangladesh, being a member state of South Asian Association for Regional Cooperation (SAARC) with seven other countries having cooperation in many development areas, does not have relationships with other drug regulatory bodies. The DGDA does not have a formal relationship with any other medicines regulatory authorities in the SAARC region, other than collaborating with Thailand National Laboratory to send product samples for quality testing. Pharmaceutical-related issues have never been addressed and could be a potential area to bring the members together to set standards on medicines regulatory harmonization and can help with building capacity, knowledge exchange, and information sharing.[13]

## 4.4 DRUG QUALITY AND CONTROL MECHANISM

**4.4.1 Types of Drug Committees:** The DGDA has formed ten different committees to uphold the regulatory activities within the country and make recommendations improving qualities on drugs, vaccines, biological products and other medicines for human, veterinary and aquaculture use. The names of different committees are given follows (Table-3):

**Table-3: Names of types of different Drug Committees operating under DGDA** [24]

| | Names and Types of the Drug Committees at DGDA | Year of Review |
|---|---|---|
| 1. | ADR Advisory Committee | Apr. 2013 |
| 2. | Drug Control Committee (DCC) | Sep. 2014 |
| 3. | Drug Control Committee (DCC) for Technical Sub Committee | Jul. 2013 |
| 4. | Drug Pricing Committee (DPC) | Jul. 2011 |
| 5. | Drug Pricing Committee (DPC) for Technical Sub-committee | Nov. 2008 |
| 6. | Herbal Drug Advisory Committee | Nov. 2010 |
| 7. | Manufacturing Project Evaluation Committee | Jul. 2011 |
| 8. | Standing Committee for Imports Pharmaceuticals | Nov. 2008 |
| 9. | Technical Sub Committee for Medical Devices | Dec. 2015 |
| 10. | District Drug Licensing Committee | |

**4.4.2 Lack of Effectiveness of Drug Committees:** There are ten different committees to facilitate the functions of DGDA to uphold the drug safety, efficacy and quality. However, there are limitations in the functions of these committees. They include no specific timeframe for the conduction of meeting for all committees, formation of committees without giving attention to WHO guidelines, dominance of manufactures' association in committees and political influence in the decision-making of committees, absence of technical persons in some committees and lack of transparency in the operations of committees. As a result, conflict of interest arises in the operations of committees particularly in setting drug prices and approving new manufacturing units.[22]

**4.4.3 The Role of National Control Laboratory (NCL):** In 2010, the MoHFW named the Drug Testing Laboratory (DTL) as the National Control Laboratory (NCL). The NCL has two major wings: the first one is for vaccine testing and second one is for drug testing under supervision of National Regulatory Authority (NRA). The main aim of the NCL is to ensure safe, potent and efficacious vaccines, drugs and biological in the country. To achieve this goal, the NCL performs tests and assays to ensure products comply with the requirements and specifications established and approved by NRA during the registration and licensing process. It is important to have reliable, reproducible test results at the NCL. Accreditation of the laboratory by WHO and through the ISO 17025 accreditation process is underway. This laboratory was established under the Drugs Act, 1940. The NCL has been functioning independently under the supervision of the DGDA since June 2010 at Dhaka, Bangladesh.

In NDP 2016 under Article 4.16 National Control Laboratory: The terms of reference NCL has been enhanced and will play the role of central laboratory for drug testing and analysis. Branches of NCL will be established in all divisions of the country phase wise. Specialized, modern laboratories for unani, ayurvedic, herbal, and homeopathic and biochemical drugs will be established. A separate cell will be set up in the drug testing laboratory for the testing of Unani, Ayurvedic, Herbal, Homeopathic and Biochemical system of drugs. The National Control Laboratory will be given responsibility to prepare working standards importing reference standards in order to make the reference standard/working standard easily available and cost-effective. These standards could be sold to drug manufacturers as per requirement.

In addition, the current practices of granting permission to drug manufacturers to import reference and working standards will be continued. For the test and analysis of modern and traditional system of medicines, capable public, private and autonomous research organizations will be recognized as reference laboratories of NCL. BCSIR (Bangladesh Council of Scientific and Industrial Research), as a capable research organization, will be endorsed for testing and analysis of modern and traditional medicines and as a reference laboratory.

**4.4.4 Model Pharmacy Initiative:** Recently, the DGDA has begun implementing the "Bangladesh Model Pharmacy Initiatives (BPMI)" program to upgrade retail drugstores to Model Pharmacies in two tiers: (i) Level-1 Pharmacy & (ii) Level-2 Drug stores. The MoHFW has already approved the criteria and standards set by the DGDA for accreditation as a Model Pharmacy which include: (i) Sales of antibiotics should be prohibited without prescription, (ii) The Model Pharmacy should have the ability to preserve medicines at a proper temperature, (iii) Zero tolerance for the sales of fake and counterfeited medicines, (iv) Drugs must be administered by a Graduate Pharmacist, and (v) Drug counselling facility should be available on-site.

## 4.5 THE ANTIBIOTIC SUPPLY CHAIN AND ACCESS TO ANTIBIOTICS

The antibiotic supply chain is the process of fulfilling the patient's need for antibiotics in the treatment of bacterial infections. The antibiotic value chain, on the other hand, is a set of interrelated activities a pharmaceutical company uses to create a competitive advantage for a particular antibiotic. For the purpose of antibiotic resistance, we would limit our focus on the antibiotic supply chain which include the flow of information related to antibiotic, its production, other necessary products and materials, and funds between the different stages of production and selling of antibiotics.

The supply of antibiotics begins with the supply chain management process and goes through procurement of raw material as inputs (APIs); production of antibiotics as outputs from the pharmaceutical company; storage

at central warehouses and different zonal office; distribution of antibiotic at different levels including health facilities, retail pharmacies; and the use of antibiotics by the end users, the patients (human and animal).

The supply chain includes all functions involved in receiving and satisfying patients' need. These functions include inbound logistics, operations (product development and production of antibiotics as outputs), marketing and sales, distribution, finance, and customer service.

**4.5.1 Types of Drug Manufacturing Companies:** There are five types of different drug manufacturing companies totalling of 852 exists in Bangladesh (March 2017). These are as follows (Table-4) [11,15]

**Table-4: Types of Drug Manufacturing Companies**

| | Types of Drug Manufacturing Companies | (n) |
|---|---|---|
| 1. | Allopathic Pharmaceutical Drug Manufacturing Company | 267 |
| 2. | Ayurvedic Drug Manufacturing Company | 207 |
| 3. | Unani Drug Manufacturing Company | 267 |
| 4. | Herbal Drug Manufacturer Company | 32 |
| 5. | Homoeopathic & Biochemical | 79 |
| | **Total Manufac turing Companies** | **852** |

There are 1,200 veterinary drugs manufactured under the same license of allopathic drug manufacture with different product registration numbers. There are ten medical devices produced under the same license of allopathic pharmaceutical industry.

**4.5.2 Pharmaceutical Sector Manufacturing of Antibiotics**: In Bangladesh, the pharmaceutical industry develops, produces and markets all most all medicines including antibiotics, insulin, hormones, anticancer drugs and other essential drugs. The pharmaceutical industry provides 97% of the total medicinal requirement of the local market in the country. The industry also exports medicines to global markets, to about 133 countries. The industry are allowed to deal with both generic and brand medications and medical devices. They are subject to a variety of laws and regulations regarding patenting, testing, ensuring safety and efficacy, quality and marketing of drugs. The majority of leading pharmaceutical companies also work in consumer health, animal health, nutritional products, medical devices & diagnostics business segments.

A total of 267 allopathic pharmaceutical companies have been registered in Bangladesh, however, 207 pharmaceutical companies are functioning and producing drugs maintaining value and supply chain. While 33 companies have been suspended from the production of medicines due to the failure of compliance with good manufacturing practices (GMP), and the licenses of 26 companies have been cancelled due to non-compliance of GMP and other drug regulations. The production and marketing of one company has been temporarily held-up. [10,15,17,18]

**4.5.3 Achievement of Pharmaceutical Industry:** About 90% of market share is dominated by local manufacturers while multinational companies hold 10% share. Bangladesh pharmaceutical industry satisfies 97% of domestic demands and the remaining 3% of drugs are imported. The import policy is to restrict those drugs that are locally manufactured and available. Pharmaceutical industry mostly produces generic drugs, in fact, Bangladesh is now a hub for affordable and high-quality generic medicines. About 85% of the drugs sold in Bangladesh are generic and 15% are patented drugs. As of December 2017, the DGDA has approved a total of 1,404 generic drugs and the number of registered branded drugs reaches to about 26,910 different forms of dosages and strengths.[15,16]

The top 20 pharmaceutical companies in most cases generate 85 percent of the total revenue, of which 10 top companies produce 68.2% of the total revenue (Table-5) A total of 30 pharmaceutical companies in Bangladesh export drugs to about 133 countries in the world, which comprise not only tablets, capsules and syrups but also specialized products like Hydrofluoroalkane (HFA) inhalers, Chlorofluorocarbons (CFC) inhalers, suppositories, nasal sprays, injectable and intravenous infusions. The pharmaceutical industry is free from obligations to implement patents and data protection for pharmaceutical until 2033.

According to the Export Processing Bureau (EPB) of Bangladesh, the pharmaceutical industry exported USD 37.9 million (BDT 3.0 billion) worth of drugs, during the fiscal year 2015 -2016. The Bangladesh government has approved the establishment of a pharmaceutical industrial park situated near Dhaka (Baushia, Gajaria, Munshiganj), the cost of which has been estimated to about USD 55.5 million (4.39 billion BDT) with 42 APIs manufacturing industrial units to be set up there.[15] According to the government export processing Bureau (EPB), the top ten manufacturers share 68.2% of the market revenue. Table-5 below shows the revenue earning by the top 10 pharmaceutical companies in Bangladesh as follows:

Although several hundred registered companies are producing complementary and alternative medicine in Bangladesh, none of them have appropriate R&D activities to standardize the ayurvedic, unani, herbal, and homeopathy medicines to ensure their safety, efficacy and quality. For example, there is little evidence to support homeopathy as an effective treatment for any specific condition, moreover, several key concepts of homeopathy are inconsistent with fundamental concepts of chemistry and physics. Some of these products may contain plant extracts, minerals, metals or chemicals, which may be harmful, particularly if used improperly or without the direction of a trained practitioner.

**Table-5: The revenue earning of the top 10 pharmaceutical companies**

| | Top Ten Pharmaceutical Companies | % |
|---|---|---|
| 1. | Square Pharmaceutical Company Ltd | 19.0 |
| 2. | Incepta Pharmaceutical Ltd | 9.5 |
| 3. | Beximco Pharmaceutical | 9.0 |
| 4. | Opsonin Pharmaceutical Company Ltd | 5.0 |
| 5. | Renata Pharmaceutical Company Ltd | 4.9 |
| 6. | Eskayef Pharmaceutical Ltd | 4.7 |
| 7. | ACI PharmaceuticalLtd | 4.3 |
| 8. | ACME Pharmaceutical Ltd | 4.1 |
| 9. | Aristopharma Ltd | 4.0 |
| 10. | Drug International Ltd | 3.7 |
| | **Total Percentage (%)** | **68.2** |

**4.5.4 Alternative and Complementary Drug Manufacturers (Total No. 585):** The manufacture of alternative medicines including Ayurvedic (total production unit is 207 with 441 generic and 3,700 brand medicines); Unani (total production unit is 267 with 437 generic and 5,166 brand medicines), Herbal (total production unit is 32 with 68 generic and 370 brand medicines) and Homeopathy (total production unit is 79 with 483 generic and 2,327 brand medicines) have been regulated by the National Regulatory Authority (NRA) of DGDA. The NRA has suspended 23 Ayurvedic, 6 Unani and 15 homeopathic production units for making substandard drugs in March 2017. [10,15,17,18]

Table-6 below shows different types of Alternative medicines practiced in Bangladesh.

Quality control and methods of preparation of these medicines are done by primitive methods. Since there is lack of enough well-designed and well-controlled clinical trials and absence of systematic research reviews as done in the case of modern medicine, the scientific evidence to claim for the effectiveness for these conventional alternative medicines is subjective and inconclusive, and therefore, it is difficult to scientifically prove that these conventional alternative approaches are beneficial to patients. [19]

**Table-6: Types of Alternative Medicines Practiced in Bangladesh**

| | Types of Alternative Medicines | Production Units | No. of Generic Drugs | No. of Branded Drugs |
|---|---|---|---|---|
| 1. | Ayurvedic retails pharmacy | 207 | 441 | 3,700 |
| 2. | Unani retails pharmacy | 267 | 437 | 5,166 |
| 3. | Herbal retail pharmacy | 32 | 68 | 370 |
| 4. | Homoeopathic & biochemical retail pharmacy | 79 | 483 | 2,327 |
| | **Total** | **585** | **1,429** | **11,563** |

**4.5.5 Regulatory and Legal Actions Taken:** In 2016, drug mobile courts realised a fine of Tk. 6.66 Crore (USD 0.83 million) in relation to 2169 cases filed for producing and selling substandard medicine from the accused manufacturers. Moreover, the mobile courts have awarded imprisonment to 58 offenders in different terms and sealed off 37 establishments. A total of 41 cases were filed with drug tribunals and 64 cases with magistrate courts for producing and selling of substandard, fake and adulterated medicines during the same period. Moreover, the NRA under the drug rules and ordinance seized and destroyed substandard, fake and adulterated medicines worth USD 2.13 million. [11]

**4.5.6 Types and Number of Retail Pharmacy:** In Bangladesh, medicines and medical devises are directly sold to patients for their use from retail pharmacies. There are different categories of retail pharmacy operating in the pharmaceutical business including whole sale (26) and model pharmacies (82). Table-7 below shows the different types with numbers of retail pharmacies in Bangladesh.

**Table-7: Types of different medicines categories with number of retail pharmacy**

| | Types of Retail Pharmacies | (n) |
|---|---|---|
| 1. | Allopathic retail pharmacy | 119,751 |
| 2. | Ayurvedic retail pharmacy | 504 |
| 3. | Unani retail pharmacy | 750 |
| 4. | Herbal retail pharmacy | 19 |
| 5. | Homoeopathic & biochemical retail pharmacy | 2,518 |
| | **Total number of Retail Pharmacy** | **123, 542** |

Both pharmaceutical industry and retail pharmacy sellers are subjected to operate under the drug regulations as enforced by the DGDA. [11]

**4.5.7 Drug Distribution Channels:** There are two primary antibiotic distribution channels in Bangladesh: (i) the public sector channel and (ii) the private sector channel. The public sector source antibiotics mainly from the state-owned Essential Drugs Company Limited (EDCL); whereas the private sector, including whole sale and retail pharmacies, sources from the private pharmaceutical companies. Public hospitals can also source from private pharmaceutical companies through tender bids.

In the private sector, there is a network of wholesalers comprising around 1,200 wholesale medicine shops. Small- and medium-scale pharmaceutical companies sell to wholesalers directly from the factory. Large pharmaceutical companies typically have a complementary distribution network of their own maintaining central whole sales deport and zonal sales deports. They carry drugs from their factories to a central depot, then to the zonal depots located in the divisional and district towns, and from there, the drugs are sold to wholesalers and to retail pharmacy through representatives and/or assistants.

Bangladesh's drug distribution marketplace is composed of small independent retail pharmacies. Pharmaceutical companies sell their products to retail pharmacies, public hospitals, international organizations, and NGOs. Pharmaceutical companies also target government healthcare facilities because government doctors are acquainted with the company's drugs and prescribe the drugs in their private clinics. Moreover, the drugs are not readily available at public facilities because of the frequent stock-outs. The patients receiving treatment at public healthcare facilities may sometime go to a private pharmacy to procure the required drugs.

**4.5.8 Retail Pharmacy as Distribution Channel:** Retail sales of drugs in Bangladesh are allowed only under the direct supervision of a pharmacist registered with the Pharmacy Council of Bangladesh. Licenses for retail pharmacies and wholesalers are regulated by the NRA of DGDA. There are 123,542 licensed retail pharmacies in the country. Drugs like antibiotics can also be found in village grocery shops available without proper supervision. While many drugs are meant to be dispensed only with a prescription by laws, but in reality some medicines are available without any prescription. Table-8 below shows the pharmaceutical drug production units, number of generic and registered branded drug products (Trade Names) and distribution outlets. Table-8 shows the production units, number of registered products and distribution outlets.

**Table-8: Pharmaceutical Production Units, Registered Drug Products and Distribution Outlets**

| Categories of Medicines | Number of Pharmaceutical Drug Production Units | | | | | Number of Generic & Registration Brand | | Distribution Outlets |
|---|---|---|---|---|---|---|---|---|
| | Functional Product Units | Non-Functional Product Units | Production Held-up | Number of Production Units Suspended | Total Production Units | Generic Drugs | Number of Registration Brand | Number of Retail Pharmacy |
| Allopathic | 207 | 26 | 1 | 33 | 267 | 1,404 | 26,910 | 119,751 |
| Unani | 251 | - | - | 16 | 267 | 437 | 5,166 | 750 |
| Ayurvedic | 183 | 1 | - | 23 | 207 | 441 | 3,700 | 504 |
| Homoeopathic | 63 | - | 1 | 15 | 79 | 483 | 2,327 | 2,518 |
| Herbal | 32 | - | - | - | 32 | 68 | 370 | 19 |
| Total | 736 | 27 | 2 | 87 | 852 | 2,833 | 38,473 | 123,542 |

There are 119,751 registered allopathic private pharmacies in Bangladesh, 9,000 or more identified non-registered and unauthorized pharmacies are also selling drugs. These non-registered pharmacies are illegal and operate without a license. Pharmacists working in these non-registered pharmacies have varying education levels, and many lack adequate pharmacy training. However, 9,000 or more unregistered retail pharmacies have also been identified and legal actions against them are in process.

Most pharmacies are individual shops, though some chains are starting to develop, especially in urban areas. Large pharmacies buy medicines according to sales trends, while medium and small pharmacies typically have an affiliation with a medical doctor. Their sales are therefore usually skewed towards the medical professional's preferences. People residing in areas more distant from the city centre consume more indigenous medicines such as Ayurvedic and Herbal medicines than urban populations. Indigenous medicine has a reasonable market size of an estimated BDT 10 billion (about 15 percent of the total medicine market share).[14,15]

The top 20 pharmaceutical manufacturing companies have established extensive sales and distribution networks. Most retail pharmacies have been receiving the drug supply from the large and medium sized pharmaceutical companies on a regular basis. Hundreds of Medical Promotion Officers (MPOs) from top pharmaceutical companies visit retail pharmacies on a daily basis to take drug orders. Pharmaceutical company's sales have become extremely market-oriented.

Companies can boost their sales by giving incentives to retail pharmacies and doctors in the form of higher commissions, so that they recommend their products to patients. On an average, a company incurs 10 to 15 percent of their total costs in this process. Each retail pharmacy may receive approximately 12 to 15 shipments per month from a particular company. The small pharmacies keep medicine for a maximum of six months.[15]

## 4.6 Essential Drugs Company Limited (EDCL)

### Essential Drugs Company Limited (EDCL)

Essential Drugs Company Limited (EDCL) is a 100% state owned Pharmaceuticals Company in Bangladesh. In the year 1962 it was functioning under the then Central Government of Pakistan in the name and style of Government Pharmaceuticals Laboratory (GPL). In 1979, Government of Bangladesh subsequently renamed it as Pharmaceuticals Production Unit (PPU). In the interest of public health and smooth running of the organization, it was registered as a Public Limited Company as Essential Drugs Company Limited (EDCL) under the Company's Act-1994, the MoHFW being its controlling authority, with the main objective to manufacture quality drugs at an affordable price and supply to the public hospitals and other health institutions.

EDCL has developed a strong position in Bangladesh in the government sector and is well positioned to sustain its growth and have a sound platform to serve export markets. Since the inception of its production, the company has been supplying essential drugs to the Government Hospitals, Civil Surgeon's Offices, Health Institutions of Government, Non-Government and International (Non-profit makings) Organizations like UNICEF, WHO, ICDDRB, etc. At present the company has been producing various drugs and contraceptive products with a sales target of Taka 400.00 Crore in the Financial Year 2013-14, its present manpower is 2,500. In the year 1985 another unit by name Essential Drugs Company Limited, Bogra was established through Japanese Grant. It has also been supplying Essential Drugs to Government Hospitals, Civil Surgeon's Offices in Northern and Southern Districts of the Country This Company has been expanding very rapidly to serve the Health Sector. The Cephalosporin Project is another unit in Bogra and will commence commercial production soon. Its production capacity will be 18,000 vials per hour.

With a view to controlling population, the Bangladesh Government has established a condom factory in Khulna, named the Khulna Essential Latex Plant (KELP), as another unit of the Essential Drugs Company Limited. Production capacity of this project has been primarily installed at 150 Million pcs per annum. Now it increase to 250 million per annum. The major part of the production will be consumed by the Directorate General, Family Planning, Government of Bangladesh. In shortest time it will also to export after meeting domestic demand. EDCL has also established a Latex Processing Plant to use locally developed raw materials at Modhupur in the Tangail District under Khulna Essential Latex Plant. EDCL has taken another project "EDCL (3rd Plant)" for producing contraceptives from pill to birth control injections, I-V Fluid, penicillin products at Gopalganj. The estimated project cost is Tk. 597.28 Crore by GOB Fund and will go for production by 2015.

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# CHAPTER-5

# ANTIMICROBIAL RESISTANCE IN LIVESTOCK, FISHERIES AND AGRICULTURE IN BANGLADESH

## ANTIMICROBIAL RESISTANCE IN LIVESTOCK, FISHERIES AND AGRICULTURE IN BANGLADESH

The availability and use of antimicrobial drugs commonly used in the treatment of disease in farm animals, fish farms, plants and in crop production are essential to both human and animal health and productivity. They contribute to food security, food safety, and human well-being and animal welfare, and in turn, to the protection of livelihoods and the sustainability of animal and crop production.[1] However, the misuse, overuse and widespread use of antibiotics lead to the development of antibiotic resistant and foster the emergence and spread of resistant pathogens within the community and environment. Resistant microbes and microbial genes can circulate within humans, livestock animals, aquatic animals, food, water and the environment, and pose a serious threat to public health outcomes with direct negative impacts on the productive lives of the people.

In food-producing animals (livestock, poultry and fish farms), antimicrobials are typically used for three purposes: (i) therapeutic reasons (for treatment of diseases), (ii) prophylactic reasons (prevention of diseases) and (iii) growth promotion (sub-therapeutic quantities of antimicrobials increase animal growth rates and improve feed efficiency). In Bangladesh, according to the Fish Feed and Animal Feed Act 2010, Fish Feed Rule 2011 and Animal Feed Rule 2013, the use of antimicrobials for a sub-therapeutic purpose (growth promotion) has been completely prohibited to avoid the development of antimicrobial resistance and its effects. All the antimicrobials used in food-producing animals in Bangladesh are solely for therapeutic purposes that is, only for the treatment of the disease conditions.[5,10]

### 5.1 INTRODUCTION TO MINISTRY OF FISHERIES AND LIVESTOCK:

**5.1.1 Ministry of Fisheries & Livestock (MoFL):** The Ministry of Fisheries and Livestock (MoFL) is a ministry of the government of the People's Republic of Bangladesh, the role of which is to ensure the sustainable utilization of fisheries and livestock. MoFL has been working to improve the productivity of this sector to meet the demand for animal protein for the population by increasing the production of fish, meat, milk and eggs. This labor intensive and rapidly income-generating sector contributes significantly to poverty reduction and foreign currency earnings through employment generation for poor and marginal people. MoFL contributes about 5-6 percent of the total GDP, of which approximately 3.7% comes from the fisheries sub-sector and 1.8% from the livestock sub-sector. In addition, more than 90% of animal protein comes from the fisheries and livestock sectors. The primary objective of the MoFL is to ensure people's demand is met for animal protein through enhancement of production and productivity of fish, meat, milk and eggs, and to improve the nutritional status and health condition of the citizens of Bangladesh.

**5.1.2 Major Functions of the Ministry of Fisheries and Livestock (MoFL):** The role of the MoFL is to formulate, update and implement laws and policies relating to fisheries and livestock sector; develop different varieties of fish, livestock and poultry products; prevent and control diseases; conduct research and training programs relating to fisheries and livestock; and improve fisheries and animal nutrition and artificial insemination; survey of fisheries and livestock and matters related to zoos; and development, extraction, conservation and management of marine fisheries including the management of dairy, cattle and poultry farms; conduct quality control and export of fisheries and livestock products; and increase production of fish, meat, milk and eggs to achieve self-sufficiency in protein.

**5.1.3 Department of Livestock Services (DLS):** The Department of Livestock Services (DLS), one of the two organizations of the MoFL, is headed by a Director General (DG) with four broad units led by four directors. These are: (i) Administration and Animal Health Unit has number of sub-units called Livestock Resources Economics, Planning and Evaluation, Central Veterinary Hospital, District Livestock Hospitals and Zoo and Parks. This unit conduct livestock surveys in the country; (ii) Productions of Livestock Unit is responsible for milk, meat and eggs production including cattle reproduction, poultry & animal feed production, and rearing livestock farms such as district milk farms, central poultry farm, regional poultry farms, district & upazila poultry farms, buffalo reproduction, goat reproduction and pig production; (iii) Research, Training & Evaluation (RTE) Unit is responsible for production of different types of livestock vaccines

against the prevention of common animal diseases; and (iv) Director Extension Unit is responsible for proving support to five divisional livestock offices and extending livestock services at district and upazila level. This unit is also responsible for artificial insemination and production of grass and grassing land for the cattle animal in the country. There is one Officers Training Institute headed by a Principal conducting livestock training for the in-house officers and other livestock staffs.

The Annual Report (July 2016-June 2017) of DLS reported that there have been a total of 8,385 sanctioned staff positions to cover the country wide livestock activities, however, the number of occupied positions as of June 2017 is 6,418 indicating that a total of 1,967 (23.5%) positions remain vacant. There are 18 strategic positions vacant at the district and upazila headquarter level which need to be filled-up on a priority basis. The main reason for this bottle neck is the lack of proper policy guidelines for upgrading the position. No new policy, rules or any ordinance has been promulgated during the last fiscal year. However, the amendment of the Animal Feed Act 2013 has been in progress. The amendment of the Animals Slaughter (Restriction) and Meat Control Act 2011 is also in progress. The DLS has developed "Animal Separation Prevention Rules 2015" and is waiting for ministry approval. The "Animal Welfare Rules 2016" has also been developed and is waiting for ministry vetting.[9]

**5.1.4 Importance of Livestock Sector in Bangladesh:** Livestock is a key component of the agricultural economy of Bangladesh performing multifarious roles. The contribution of the livestock sector to overall GDP has been provisionally estimated at 1.78% for 2013-14. In 2012-13, it was 1.84% (Bangladesh Economic Review-2014) and in 2011-12 it was 2.5%.[21] Its share of agricultural GDP in 2013-14 was 14.1% (provisionally estimated). Despite its modest share of overall GDP, livestock serves an essential role as a source of protein, employment generation, export earning, and provision of food security. Livestock resources play an important role in the sustenance of landless people, livelihood options for rural poor families and are potentially important for poverty reduction. In the livestock sub-sector, backyard poultry, goat and sheep rearing are the key activities, which are mainly performed by rural women, whose contributions are recognized and incorporated in all the future national policies accordingly. Table-1 below shows the contribution of livestock and poultry in the national economy of Bangladesh.

**Table-1: Contribution of Livestock and Poultry in the National Economy of Bangladesh, FY 2016-2017**

| SL | Contribution of Livestock and Poultry in the National Economy | (%) |
|---|---|---|
| 1. | Contribution of Livestock in Gross Domestic Product (GDP), % | 1.6 0 % |
| 2. | GDP growth rate of Livestock, % | 3.32 % |
| 3. | GDP volume in current price in BDT in Crore | 35,576 |
| 4. | Share of Livestock in Agricultural GDP, % | 14. 31 % |
| 5. | Employment (Directly), % | 20 % |
| 6. | Employment (Partly), % | 50 % |
| 7. | Cultivation of land by livestock, % | 50 % |
| 8. | Fuel supply from livestock and poultry, % | 25 % |

The contribution and the importance of livestock and poultry in the national economy is enormous indeed. Most rural households rear livestock, including poultry, for a ready source of cash and to provide them with employment. It is estimated that approximately 20% of employment is directly associated with livestock sub-sector and 50% of employment is partly associated. Approximately 50% of land is cultivated using. In Bangladesh, 47.6% of the total labour force is engaged in the agricultural sector for their livelihood and they are predominantly poor.[10]

## 5.2 LIVESTOCK PRODUCTION IN BANGLADESH:

In Bangladesh, highly domesticated food animals are cattles, buffaloes, goats, sheep and poultry. Pig farming in Bangladesh is very little and is confined mainly within a particular tribal group. Estimate of the Department of Livestock Services (DLS) shows that the population of livestock and poultry rose to 54.74 million and 329.20 million, respectively in FY 2016 – 2017.

Livestock production, during the last few years, particularly after the formulation of National Livestock

Development Policy in Bangladesh, has progressed well in terms of milk, meat and egg production. The milk, meat and egg production were 6.97 million metric tons, 5.86 million metric tons and 1,099.52 million (in number) respectively in FY 2015 which were 2.65 million metric tons, 1.04 million metric tons and 565.32 million (in number) respectively in FY 2007-08. This data indicates that the size of the livestock sub sector increased 3-4% between FY 2007 and FY 2015. The following table-2 and table-3 show the growth of livestock and poultry and production of milk, meat and eggs in Bangladesh over the past few years.[10]

(HFSNA) 2009 found that the rates of acute malnutrition is 13.5%, underweight is 37.4%, and stunting is 48.6% in the country.[10]

Livestock is considered as the most important protein source providing about 44% of the protein demand of the country, a ready cash source for poor families and the sustenance of landless people, livelihood options for the rural poor families particularly women and is potentially important for poverty reduction. According to the estimation of the Department of Livestock (DLS), the country's existing production against demand for milk, meat and egg is 43.4%, 67.2% and 63.7%

**Table-2: Livestock Population in Bangladesh (in million)**

| SL | Livestock Species | 2008-09 | 2009-10 | 2010-11 | 2011-12 | 2012-13 | 2013-14 | 2014-15 | 2015-16 | 2016-2017 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
| 1. | Cattle | 22.98 | 230.51 | 23.12 | 23.20 | 23.34 | 23.49 | 23.64 | 23.79 | 23.94 |
| 2. | Buffalo | 1.30 | 13.49 | 1.39 | 1.44 | 1.45 | 1.46 | 1.46 | 1.47 | 1.48 |
| 3. | Sheep | 2.88 | 29.77 | 3.00 | 3.10 | 3.14 | 3.21 | 3.27 | 3.34 | 3.40 |
| 4. | Goat | 22.40 | 232.75 | 24.15 | 25.12 | 25.28 | 25.44 | 25.60 | 25.77 | 25.93 |
| 5. | Total Animals | 49.56 | 506.52 | 51.68 | 52.84 | 53.21 | 53.59 | 53.97 | 54.36 | 54.75 |
| 6. | Chicken | 221.39 | 2280.35 | 234.69 | 242.87 | 249.01 | 255.31 | 261.77 | 268.39 | 275.18 |
| 7. | Duck | 41.23 | 426.77 | 44.12 | 45.70 | 47.25 | 48.86 | 50.52 | 52.24 | 54.02 |
| 8. | Total Poultry | 262.63 | 2707.12 | 278.81 | 288.57 | 296.26 | 304.17 | 312.29 | 320.63 | 329.20 |
| 9. | **Total Livestock** | **312.19** | **3213.64** | **330.49** | **341.40** | **349.48** | **357.76** | **366.27** | **374.99** | **383.95** |

**Table-3: Production of Milk, Meat and Eggs**[10]

| SL | Products | Units | 2008-09 | 2009-10 | 2010-11 | 2011-12 | 2012-13 | 2013-14 | 2014-15 | 2015-16 | 2016-17 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| 1. | Milk | Million (MT) | 2.29 | 2.37 | 2.95 | 3.46 | 5.07 | 6.09 | 6.97 | 7.28 | 9.28 |
| 2. | Meat | Million (MT) | 1.08 | 1.26 | 1.99 | 2.33 | 3.62 | 4.52 | 5.86 | 6.15 | 7.15 |
| 3. | Egg | Crore (n) | 469.61 | 574.24 | 607.85 | 730.38 | 761.74 | 1016.80 | 1099.52 | 1191.24 | 1493.31 |

The nutritional status of the people, particularly children and lactating mothers is far below from the WHO threshold. A study published by the WFP/UNICEF/ Institute of Public Health Nutrition (IPHN) on household food security and nutrition assessment

respectively. Deficit for milk, meat and egg against demand is 56.6%, 32.8% and 36.4%, respectively. So, there is great scope to explore this sub-sector to meet the above mentioned gaps in fulfilling requirements. Table-4 below shows the demand, production, availability and deficiency of milk, meat and eggs during the financial year 2016-17.

**Table-4: Demand, Production and Deficiency of Milk, Meat and Eggs in FY 2016-17**

| SL | Variable | Milk (Million Metric Tons) | Meat (Million Metric Tons) | Eggs (Crore, n) |
|---|---|---|---|---|
| 1. | Demand | 14.87 | 7.14 | 1694.16 |
| 2. | Production | 9.28 | 7.15 | 1493.31 |
| 3. | Deficiency | 5.59 | -(0.19) | 200.85 |
| 4. | % Deficiency | 37.77 % | ** | 11.86% |
| **SL** | **Variable** | **Milk** (ml/day/head) | **Meat** (gm/day/head) | **Eggs** (no/day/head) |
| 1. | Daily Demand | 250 | 120 | 104 |
| 2. | Availability | 158 | 122 | 93 |
| 3. | Deficiency | 92 | -(2) | 11 |
| 4. | % Deficiency | 36.8 % | ** | 10.58 % |

Estimated population of the country: 16.25 Crore (As on December, 2017); ** indicating surplus[22]

The demand and production gap in national requirement for milk is 37.77%, meat is however surplus and the gaps in eggs are 11.86% respectively. The demand and production gaps should be overcome by producing these essential food substances on a priority basis to improve the national health status. The deficiency in daily requirement of milk (ml/day/head) is 36.8% and eggs (no/day/head) is 10.58%, which should be overcome by producing these food products on a priority basis to avoid malnutrition especially among the children, adolescent and child bearing mothers. The production of meat (gm/day/head) is surplus.

## 5.3 STATUS OF LIVESTOCK HEALTH AND DISEASE BURDEN:

**5.3.1 Animal Disease Situation:** The outbreak of different infectious diseases pose a huge threat to livestock production. The impacts of diseases are multifaceted including loss to the farmers through mortality, loss of productivity, cost for disease management including treatment and sanitation, low quality of livestock products, disruption in the production cycle, market effects, discarding, rejecting and others. These affect seriously the livelihood of the poor farmers. The climatic condition of Bangladesh is conducive and favourable to animal diseases. The high density of animals and their seasonal aggregation particularly in the monsoon period aggravate these hazards. The Table-5 below shows the main animal diseases.

**Table-5: Types of Livestock and Major Livestock Diseases**

| SL | Major Livestock | Major Livestock Diseases |
|---|---|---|
| A. | **Cattle and Buffaloes** | Anthrax, Black-quarter (BQ), Hemorrhagic septicaemia (HS), Tetanus, Tuberculosis, Mastitis, Foot and Mouth Disease (FMD), Rabies, Babesiosis, Theileriosis, Anaplasmosis, enteric infections, Internal and External Parasites and metabolic diseases. |
| B. | **Goats and Sheep** | Peste des Petits Ruminants (PPR), Contagious ecthyma, Pox, Contagious Caprine Pleuropneumonia (CCPP), Anthrax, Enterotoxaemia, Protozoal diseases, Internal and External Parasites. |
| C. | **Poultry (Chicken, Duck & Birds)** | Newcastle Disease (ND), Gumboro Disease (IBD), Avian Influenza, Infectious bronchitis, Egg drop syndrome, Mareks Disease, Mycoplasmosis, Colibacillosis, Infectious Coryza, Salmonella infections, Necrotic enteritis, Fowl Pox, Fowl Cholera, Fowl Coccidiosis, Duck Plague, Duck cholera, Internal Parasites and deficiency diseases. |

Unofficial cross border trade of livestock and poultry (live and in product form) happens frequently in the country. Live animals and birds enter through illegal trade by-passing the quarantine stations, established by the government to enforce the 'Animal and Animal Product Quarantine Act 2005'. They are a potential threat for the transmission of diseases. Cattle, eggs, day-old chicks, and poultry feed ingredients are the main livestock items entering the country through unofficial cross border trade. About 40% of total slaughtered cattle come through cross border trade. Government and institutional support in reducing the production gap may reduce unofficial cross border trade.

**5.3.2 Livestock Disease Burden:** Some estimates suggest that the losses due to internal parasites by far exceed the losses caused by other livestock diseases. But the total disease complex is not clear, owing to the general lack of diagnostic and disease recording services in the DLS. Analysis of the economic impacts of diseases in Bangladesh is rather limited. An estimates were available for Foot and Mouth Disease (FMD), Peste des Petitis Ruminants (PPR), Hemorrhagic septicaemia (HS) and Avian influenza by Islam et al., 2014. The report stated that "The predicted annual direct loss stands at BDT 819 million (US$ 10.92 million) for FMD, BDT 1,842 million (US$ 24.56 million) for PPR and BDT 1,105 million (US$ 14.74 million) for HS.[23]

Indirect loss from diseases and overhead cost of the state veterinary services were not considered for this analysis. A study on the economic impact of Highly Pathogenic Avian Influenza (HPAI) outbreaks in 2007 and 2008 was conducted at Bangladesh Livestock Research Institute (BLRI).

The study estimated a total loss of Tk. 38,583 million (US$ 551 million) due to HPAI outbreaks in the first two years. The estimate included direct loss of Tk. 86 million, indirect loss of Tk. 2,497 million and the loss due to production downtime effect Tk. 36,000 million. If the figure were to be adjusted to the outbreak data of total five years, 2007 – 2011, the total loss would stand at Tk. 51,720 million (US$ 690 million)". [10]

**5.3.3 Brief Description of the Common Livestock Diseases in Bangladesh:** Livestock diseases cost millions of dollars in losses every year. In addition to death, they cause loss of production and frequently a loss of body condition. Unhealthy animals require more food and take a longer time for growth than healthy ones. One should be vigilant against cattle diseases as dairy cattle are affected by a variety of diseases. In Bangladesh, Ullah S.M., et al (2015) recorded livestock clinical cases and classified these cases into major diagnostic groups of which the highest prevalence was recorded in digestive disorders (47.1%), followed by parasitic infection (26.8%), infectious diseases (7.8%), respiratory disorders (6.2%) and surgical affection (5.2%).[13] The percentage occurrence of major diagnostic groups of diseases in cow constituted digestive disorders (41.7%), infectious diseases (41.7%), parasitic diseases (37.8%), respiratory disorders (21.1%) and ectoparasitic infection (16.7%). Though each of the diagnostic groups of diseases is significant, digestive disorder, parasitic and infectious diseases were the most pressing constraint for improvement of cattle in Bangladesh.[13] Some of the common and important livestock diseases are described below:

**Anthrax:** Anthrax is caused by Bacillus anthracis. It is a large Gram-positive aerobic, rod shaped, bacillus bacterium and is the only obligate pathogen within the genus bacillus. In Bangladesh, there are three main types of Anthrax found that affect the skin, lungs and the digestive system. Cattle infected with anthrax will progress from a normal, healthy state to death in a matter of hours. Symptoms and signs are weakness in herd cattle include difficulty in breathing, convulsions, bloody discharges from natural openings of the body, mild fever, muscle aches and stomach pain. Anthrax typically causes an unusual rise in body temperature followed by depression, cardiac distress, staggering and death. Antibiotics such as ciprofloxacin and doxycycline are the choice of treatment. Prophylactic vaccination is extensively used in preventing anthrax in livestock.[16]

In Bangladesh, Be-Nazir, et al., (2010) reported that 62 cattles infected with anthrax were recorded with 69% mortality at Pabna Milk Shed, in the western part of country, during 1980-84; and 333 anthrax animal cases recorded during 1989-96 in Bangladesh.[14] A number of outbreaks of animal anthrax were also reported during 2009-10 infecting 140 cattle and goat in different districts of Bangladesh. To prevent anthrax disease, vaccination is practiced in the country since long. In 2009-2010, the total vaccine production was 38.29 million doses. Various reports indicate that the disease is more prevalent in Pabna, Sirajganj and Tangail districts where the cattle populations are large. [14]

**Black Quarter:** Black quarter (BQ) is an acute, infectious disease caused by Clostridium chauvoei - a Gram-positive, anaerobic organism usually affecting cattle, sheep, and goats. This disease is characterized by inflammation with gaseous oedema of skeletal muscle and severe toxaemia. The disease usually occurs in an acute form, affected animals dying within 24 to 48 hours of the onset of symptoms. Symptoms include a high fever with a hot, tense, painful swelling usually in one of the quarters, more often a hind-quarter, although such swelling may also occur in other parts of the body before death, the swelling becomes cold and painless and crepitates on pressure due to the presence of gas in it. Administration of penicillin in repeated doses may be effective if injected before muscle damage has occured. Use of black-quarter vaccine protects animals against the disease for about a year. Animals should be vaccinated with this about three to one month before the onset of rains.[16]

Mahmuda et al., (2008) conducted a study in Upazila Veterinary Hospital at Raozan in Chittagong, Bangladesh from June to August 2006.[15] During the study period, 25 cases of BQ in cattle were found in eight Unions. Death was observed in 18 (72%) cases. In the case of animals that suffered from BQ, septicaemia developed after 12 hours of onset of clinical signs and symptoms. Treatment was ineffective in the advanced septicaemic stage. Antibiotic therapy was found to be effective when administered within 12 hours of the clinical symptoms. [15]

**Hemorrhagic Septicaemia (HS):** Hemorrhagic Septicaemia (HS) is an acute septicaemic disease of cattle and is widely prevalent in Bangladesh. It occurs generally in low-lying areas periodically inundated by rainwater and in areas where irrigation facilities have been developed. The causal organism, Pasteurella multocida, is a small gram-negative cocco-bacillus. The symptoms and signs are redness of eye and lancination along with fever, severe dyspnea and hot painful swelling of head, jowl region or brisket region. In severe cases sudden death may occur due to high fever and severe dyspnea. The disease generally runs an acute course. Cattle and buffaloes often develop a highly septicaemic condition and die within the course of about 24 hours of infection. Affected animals show a high rise in body temperature.

The lesions comprise haemorrhagic spots in the lymph nodes, on the serous membranes and in other organs,

including the inner lining of the heart. The entire gut is highly inflamed and intensely red with bloody contents. Early cases of the disease are responsive to treatment with sulphonamides, notably sulphadimidine coupled with antibiotics, such as penicillin. The disease may turn into a serious condition within a short course of time, and may cause sudden death. Vaccination with the improved type of adjuvant vaccine, carried out about a month before the onset of rains, will protect animals against the attack of the disease for about one year. In endemic areas such vaccination should be carried out every year. [16]

**Foot-and-Mouth Disease (FMD):** Foot-and-mouth disease is a highly communicable disease affecting cloven-footed animals. It is characterized by fever, formation of vesicles and blisters in the mouth, udder teats and on the skin between the toes and above the hoofs. In Bangladesh and India, the disease is widespread and assumes a position of importance in the livestock industry. The disease spreads by direct contact or indirectly through infected water, manure, hay and pastures. It is also conveyed by cattle attendants. It is known to spread through recovered animals, field rats, porcupines and birds.

The common symptoms are high fever, profuse salivation ropes of stringy saliva hanging from the mouth, vesicles appear in the mouth and in the inter digital space, lameness is observed, cross bred cattle are highly susceptible to it. Quick spread and the occurrence of lesions in the mouth and feet of affected animals are characteristic symptoms. It can be cured by severe antibiotic therapy and topical application of ointments. The external application of antiseptics contributes to the healing of the ulcers and wards off attacks by flies. A common and inexpensive dressing for the lesions in the feet is a mixture of coal-tar and copper sulphate.

High yielding animals and exotic breeds of cattle bred for milk should be protected regularly. It is advisable to carry out two vaccinations at an interval of six months followed by an annual vaccination programme. Isolation and segregation of sick animals. It should be informed immediately to the veterinary doctor. Disinfection of animal sheds with bleaching powder or phenol should be done. Attendants and equipment for sick animals should be ideally separated. The equipment should be thoroughly sanitized, proper disposal of left over feed by the animal proper disposal of carcasses and control of flies should be done. [16]

Mondal SP, Yamage M (2014) conducted a retrospective study on the epidemiology of anthrax, foot and mouth disease (FMD), haemorrhagic septicaemia (HS), peste des petits ruminants (PPR) and rabies in Bangladesh during a period of three years 2010-2012. These diseases are considered to be endemic in Bangladesh. This retrospective study was conducted to understand the geographic and seasonal distribution of these major infectious diseases in livestock based on data collected through passive surveillance from 1 January 2010 to 31 December 2012. Data analysis for this period revealed 5,937 cases of anthrax, 300,333 of FMD, 13,436 of HS, 247,783 of PPR and 14,085 cases of dog bite/rabies. Significantly higher ($p<0.01$) numbers of anthrax (84.5%), FMD (88.3%), HS (84.9%) and dog bite/rabies (64.3%) cases were reported in cattle than any other species. PPR cases were reported mostly (94.8%) in goats with only isolated cases (5.2%) in sheep.

The diseases occur throughout the year with peak numbers reported during June through September and lowest during December through April, with significant differences ($p<0.01$) between the months. The annual usages of vaccines for anthrax, FMD, HS and PPR were only 7.3%, 0.6%, 0.8% and 11.6% of the susceptible livestock population, respectively. Prophylactic vaccination against rabies was 21.2% of cases. There were significant differences ($p<0.01$) in the administration of anthrax, FMD and HS vaccines between border and non-border districts, but not PPR or rabies vaccines. It has been recommended that surveillance and reporting of these diseases need to be improved throughout the country. Furthermore, all suspected clinical cases should be confirmed by laboratory examination. The findings of this study can be used in the formulation of more effective disease management and control strategies, including appropriate vaccination policies in Bangladesh. [17]

**5.3.4 Health Care and Disease Control in Livestock:** Inadequate health care and veterinary services are serious constraints to sustainable livestock development in the country. Health care and disease control are constrained by the following factors:

**i. Hospital-based Healthcare:** The DLS is the only department providing health care services to farmers from centre to the sub-district level in the country. Only 1-2 qualified veterinarian(s) along with 2-3 vet technicians are providing health care services at upazila level covering almost 0.7 million animals. In Bangladesh, veterinary services are hospital based and the farmers usually bring their animals to the hospitals for treatment. Since Bangladesh does not have any well-equipped ambulatory system for sick animal

transportation, the hospital services are mostly accessible by the population who are living within 1-2 km radius of the hospital. Thus the farmers at the periphery of upazila don't get timely advice for health care of the animal;

**ii. Absence of Preventive Healthcare:** The DLS has mostly engaged with treatment of sick animals, while preventive health care through vaccination program has been found to be inadequate. Consequently, the high mortality of the food animals as a result of epidemics like anthrax, haemorrhagic septicaemia, black quarter and foot and mouth diseases imposes huge losses to farmers. The quantity of vaccines produced and delivered by the DLS at present are not adequate. Commercial vaccines are available but these are costly and their efficacy and quality are not checked by DLS.

**iii. Lack of Laboratory Diagnostic Tools:** Unlike human diseases, currently the diagnosis of animal diseases is based on the clinical examination only. Laboratory diagnostic tools and services are almost absent; moreover, programs for the surveillance of new and emerging diseases are almost absent or not present. This leads to the emergence of trans-boundary diseases, such as avian influenza and bovine tuberculosis.

**v. Lack of Ambulatory Services:** Lack of ambulatory services leads to the limitation of veterinary services around the upazila headquarters; in the case of poultry farms, biosecurity is almost absent in small and medium sized farms which leads to the spread of diseases in the poultry farms; quarantine is visible in the ports with limited strengths and facilities in the country. These results in trans-boundary movement of diseases and spread within the country; unorganized animal slaughter and lack of veterinary inspection in slaughter houses and live animal markets leads to the spread of infection from one area to another area, and high prices with no quality control of veterinary and breeding inputs.

**5.3.5 Livestock Vaccines Demands, Production and Supply:** Vaccination is very effective in preventing different disease in animals (table-6). Vaccines are useful even after an outbreak has occurred, especially in the case of anthrax but the time for resistance to occur is approximately 14 days after vaccination. Antibiotics should not be used together with vaccines. Livestock Research Institute (LRI) is the responsible institution producing 17 different types of vaccines to prevent 17 types of livestock diseases in the country.

Table-6 below shows different types of livestock diseases and their corresponding vaccines indicating demands, production, supply and gaps in one particular month (From 21 October 2017 to 20 November 2017). This information is collected from the Department of Livestock Services (DLS) of the Ministry of Fisheries & Livestock of the Government of the People's Republic of Bangladesh.[12]

**Table-6: Livestock Vaccine Demands, Production and Supply in One Month (21 Oct 2017 to 20 Nov 2017)**

| Livestock Vaccine Demand, Production & Supply in One Month (From 21 October 2017 to 20 November 2017) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| SL | Livestock Diseases | Livestock Vaccines | Demands | Production | | | Supply | | |
| | | | | Production (n) | Production Gaps (n) | Production Gaps (%) | Supply (n) | Supply Gaps (n) | Supply Gaps (%) |
| 1 | 2 | 3 | 4 | 5 | 4-5=6 | 7 | 8 | 4-8=9 | 10 |
| 1 | Ranikhet (New Castle) | Ranikhet (NC) Vaccine (RDV) | 10,632,700 | 9,144,000 | 1,488,700 | 14.0 | 6,932,700 | 3,700,000 | 34.8 |
| 2 | Baby Chick Ranikhet (BCR) | BC Ranikhet Vaccine (BCRDV) | 14,706,000 | 5,282,400 | 9,423,600 | 64.1 | 10,466,000 | 4,240,000 | 28.8 |
| 3 | Fowl Pox | Fowl Pox Vaccine | 3,199,000 | - | 3,199,000 | 100.0 | 1,238,800 | 1,960,200 | 61.3 |
| 4 | Pigeon Pox | Pigeon Fox Vaccine | 585,000 | - | 585,000 | 100.0 | 209,400 | 375,600 | 64.2 |
| 5 | Fowl Cholera | Fowl Cholera Vaccine | 1,546,000 | 204,400 | 1,341,600 | 86.8 | 415,000 | 1,131,000 | 73.2 |
| 6 | Gumboro | Gumboro Disease Vaccine | 5,014,000 | 3,600,000 | 1,414,000 | 28.2 | 2,846,000 | 2,168,000 | 43.2 |
| 7 | Duck Plague | Duck Plague Vaccine | 5,382,100 | 200,000 | 5,182,100 | 96.3 | 2,609,600 | 2,772,500 | 51.5 |
| 8 | Mareks Disease | Mareks Disease Vaccine | 683,000 | 1,000,000 | -317,000 | -46.4 | 437,000 | 246,000 | 36.0 |
| 9 | Salmonella Disease | Salmonella Vaccine | 1,000,000 | 241,200 | 758,800 | 75.9 | 324,200 | 675,800 | 67.6 |
| 10 | Anthrax Disease | Anthrax Vaccine | 713,700 | 500,000 | 213,700 | 29.9 | 702,500 | 11,200 | 1.6 |
| 11 | Hemorrhagic Septicemia (HS) | HS Vaccine | 121,100 | 102,000 | 19,100 | 15.8 | 118,100 | 3,000 | 2.5 |
| 12 | Black Quarter (BQ) | Black Quarter Disease Vaccine | 97,200 | - | 97,200 | 100.0 | 71,400 | 25,800 | 26.5 |
| 13 | Foot & Mouth Disease (FMD) | Foot & Mouth Disease Vaccine | 102,640 | 16,000 | 86,640 | 84.4 | 49,472 | 53,168 | 51.8 |
| 14 | Peste des Petits Ruminants (PPR) | PPR Vaccine | 942,000 | 950,000 | -8,000 | -0.8 | 524,500 | 417,500 | 44.3 |
| 15 | Low Eggs Passage (LEP) | Low Eggs Passage Vaccine | 319 | - | 319 | 100.0 | 319 | 0 | 0.0 |
| 16 | High Eggs Passage (HLP) | High Eggs Passage Vaccine | 449 | - | 449 | 100.0 | 449 | 0 | 0.0 |
| 17 | Goat Pox | Goat Fox Vaccine | 47,100 | 0 | 47,100 | 100.0 | 47100 | 0 | 0.0 |

It is evident from the above the table that production has been reduced to zero in six vaccines, these are fowl pox, pigeon pox, black quarter, low & high eggs passage for rabies and goat pox. The production gaps remain comparatively high in BCR (64.1%), fowl cholera (86.8%), duck plague (96.3%), salmonella disease (75.9%) and FMD (84.4%). Although the stock of all these vaccines from previous months have been found satisfactory, there have been marked gaps in demand and supply for most of the vaccines except, anthrax, haemorrhagic septicaemia, LEP, HEP and goat vaccines indicating a critical failure in the supply chain vaccine countrywide. It is desirable to prevent livestock diseases through vaccination programs, which will in turn contribute to a decrease in morbidity and hence antibiotic use, in animal populations. The less the antibiotics are used the less is the risk of AMR in livestock. Therefore, the DLS should focus more on vaccinating the livestock population.

**5.3.6 Service Sectors:** Three major public sector institutions functioning for livestock related activities are: (i) Department of Livestock Services (DLS), responsible for all livestock related activities in the country including extension and regulatory functions; (ii) Bangladesh Livestock Research Institute (BLRI), functioning for research; and (iii) Bangladesh Agricultural University (BAU) and few other universities, also dedicated for livestock related education and research.

## 5.4 ANTIMICROBIAL SUPPLY CHAIN AND ANTIBIOTIC USE IN LIVESTOCK:

**5.4.1 Use of Antimicrobials and Resistance in Livestock Sector:** Antimicrobials are lifesaving drugs. In food-producing animals they are typically used for three purposes:

(i) Therapeutic reasons (treatment of disease): Antibiotics are used to treat the clinical diseases of livestock animals. Its uses are only recommended by the registered doctor to treat the diseases for therapeutic purpose only. Sometimes the uses of antibiotics in clinical setting are indistinct; definitions of each type of use vary, and the approaches are often applied concurrently in livestock populations. For example, 16% of all lactating dairy cows in the U.S.A receive antibiotic therapy for clinical mastitis each year. Similarly, 15% of beef calves that enter feedlots receive antibiotics for the treatment of clinical respiratory disease. [3] The antibiotic use such as fluoroquinones like ciprofloxacin, levofloxacin, or ofloxacin are preferred treatments for anthrax. Ciprofloxacin, Tetracycline and Doxycycline are to be used only as second-line of defence.

(ii) Prophylactic reasons (prevention and control of diseases): Nearly all dairy cows receive intra-mammary infusions of prophylactic doses of antibiotics following each lactation to prevent and control future mastitis—primarily with penicillin, cephalosporin, or other beta-lactam drugs. The prophylactic antibiotic doses are also administered to 10% of apparently healthy beef calves to mitigate anticipated outbreaks of respiratory disease. [3]

(iii) Growth promotion: Sub therapeutic quantities of antimicrobials increase animal growth rates and improve feed efficiency. Some antibiotics are not recommended for food animals.

Despite the widespread adoption of antibiotic use in food animals, reliable data about the quantity and patterns of use (e.g., dose, frequency and duration) are not available in Bangladesh. Quantifying antibiotic use in food animals is challenging due to variations in studies conducted in Bangladesh — investigators may measure only therapeutic uses, only nontherapeutic uses, or a combination thereof, depending on their outcome of interest—and lack of clarity surrounding the definitions of therapeutic vs. nontherapeutic uses.

Under Article 14 of the Bangladesh Fish Feed and Animal Feed Act 2010, the use of antibiotic as growth promoter, growth hormone, steroid, pesticides and other harmful chemicals in fish and animal feeds is banned. [5] But research has revealed residues of antibiotic are still present in poultry meat and eggs.[6] This may happen due to injudicious use of antibiotic during treatment or a preventive procedure or the addition of antibiotic to feed as a growth promoter. Vested interest, low veterinary regulation and low enforcement of the Act may be the root causes of this situation. Antibiotic resistant bacteria are being produced due to antibiotic abuse which is a big threat for man, animals and for the ecosystem.

It is documented in a review article that the accumulation of toxic and harmful residues in meat and eggs of poultry and birds treated with antibiotics, as sub-therapeutic purposes to ensure rapid growth and good health. However, inappropriate and non-judicious use of these drugs results in an

accumulation of toxic and harmful residues in the meat and eggs of the treated poultry and birds which affect consumer health by triggering allergic reactions and transmitting antibiotic-resistant microbial infections. Therefore, regulatory authorities must take rigorous steps to stop inappropriate use of drugs for animal use in order to ensure safe food for human consumption. [7,8]

There is no regular data to quantify different antimicrobial agents used in the livestock sector in Bangladesh. Primarily it has already been planned to collect data from local manufacture companies and the importers on their yearly sales volumes in the domestic market.

this situation, DLS is planning to adopt a public awareness program to educate people about the prudent use of antimicrobials. Furthermore, most commercial poultry farmers also use antimicrobials themselves directly from feed sellers or chemists or even directly from companies without consulting qualified veterinary practitioners. Due to this practice, it is challenging to monitor whether those poultry products, chicken meat and eggs are being sold in the wet market after maintaining the withdrawal period as well. To overcome this situation, DLS is planning to adopt public awareness program to educate people about the prudent use of antimicrobials.

### 5.4.3 Most common antimicrobials used in livestock proction:

**Table-7: The common antimicrobials used in livestock production**

| SL | Generic Names of the Drugs | Trade Names of the Drugs |
|---|---|---|
| **A.** | **Drug Used in Food Animals (Other than Poultry)** | |
| 1. | Tetracycline | Oxytetracycline |
| 2. | Penicillir | Procaine and Benzylpenicillin, Ampicillin, Amoxicillin |
| 3. | Sulphonamide | Cotrimoxazole, Sulfadimidine |
| 4. | Fluorquinolone | Ciprofloxacin |
| 5. | Cephalosporin | Ceftriaxone |
| **B.** | **Drugs Used in Poultry:** | |
| 1. | Tetracycline | Oxytetracycline |
| 2. | Penicillir | Amoxicillin |
| 3. | Sulphonamide | Cotrimoxazole |
| 4. | Fluorquinolone | Ciprofloxacin |
| 5. | Macrolides | Erythromycin, Gentamycin |

**5.4.2 Antimicrobial Supply Chain, Distribution and Use in Livestock Production:** In Bangladesh, most life-saving antimicrobial drugs are manufactured by a local pharmaceutical companies. It is assumed that around 70% of the total quantity of Antimicrobials that are used in food-producing animals are manufactured locally, and the rest are imported by trading companies to distribute in the local market. All the antimicrobials either locally manufactured or imported which are destined to be distributed in the domestic market must have registration from the Directorate General of Drug Administration (DGDA) of Bangladesh.

The present situation of the supply chain and distribution system of antimicrobials is that both domestic manufacturers and importers have been distributing antimicrobial products to the Wholesalers, Chemists, Retail Pharmacies and feed sellers and even to commercial poultry farmers to some extent. A major portion of antimicrobials are sold to customers, i.e., animal farm owners through OTC (over-the-counter) and also by the quacks. Only a very negligible amount of total sale volume of antimicrobials is sold through prescription. To overcome

**5.4.4 Antimicrobial Resistance Situation:** Only limited scientific information is available about the antimicrobial resistance properties of bacteria isolated from the livestock sector in Bangladesh. A small amount of data is published on the antimicrobial resistance properties of E. coli in Bangladesh, especially in poultry and poultry products. In a recent study conducted in the Chittagong area, in Bangladesh, on broiler birds, Hashem et al., (2012) observed that 54.55% samples were infected with E. coli and among these 100% were resistant to cotrimoxazole, 75% to gentamycin and 75% to penicillin as well.[18] According to Akond et al., (2009), they found that 58% of the samples isolated from poultry were positive for E. coli. 52-88 % were found to be resistant to Penicillin, Ciprofloxacin, Rifampicin, Kanamycin, Streptomycin, Cefixime, Erythromycin, Ampicillin and Tetracycline. Twenty percent of the strains showed resistance to both Chloramphenicol and Neomycin.[19]

**5.5.1 National Livestock Policies, Acts and Rules:** The Ministry of Fisheries and Livestock (MoFL), produced

a comprehensive "National Livestock Development Policy 2007 (NLDP 2007)" to promote sustainable improvements in livestock products; in income, nutrition and employment for the landless, small and marginal farmers; and to facilitate increased private sector participation and investments in livestock production, livestock services, market development and export of livestock products and by- products.[24] National Poultry Development Policy 2008 was formulated in the light of NLDP-2007 to encourage poultry industry and to control quality of inputs for sustainable poultry development with research and quality control. [25] For ensuring standard and quality control in poultry development and poultry feed, the policies refer to the Fish and Animal Feed Act 2010 and Animal Feed Rule 2013 for standard and quality control of poultry feeds.[28,29,30]

National Livestock Extension Policy 2013 was promulgated to reflect the increasing trend of livestock production related to service demands; increasing trend of investment; veterinary public health, food security and food safety issues; effective extension service; supply chain development; dissemination of models and technologies; strong linkage among research, extension, education and farmers; impediments of farmers access to services; increasing demand of organic products; and family level small scale farming. [26] Animal Slaughter and Quality of Meat Control Act 2013 was formulated to control animal and human diseases of animal origin. However, this act is very poorly implemented in the country. Animals are being slaughtered everywhere. None of the slaughter houses of the country follow a standard hygienic procedure. Veterinary inspection is either very poor or absent. [27]

Fish Feed and Animal Feed Act 2010, Fish Feed Rules 2011 and Animal Feed Rules 2013 have been promulgated to ensure quality of feed used in fisheries and livestock sub-sectors and came into effect in 2010. The main objective of these Act and Rules are to monitor the quality of feed of both local and import origin; and have implication for the production, processing, marketing, selling, distribution and also adulteration and quality control of animal feeds. Use of Antimicrobials in feed as growth promoter has been banned according to Fish Feed and Animal Act 2010. [28,29,30] Table-8 below shows the existing acts, policies, rules, regulation and strategies:

**5.5.2 Livestock Waste Management:** The livestock waste originates as manure, slaughtered by-products, live animal market waste, used poultry industry litter,

**Table-8: Types of Acts, Rules and Ordinances related to Livestock and Products** [B]

| SL | Year | Types of Acts, Rules and Ordinances |
|---|---|---|
| 1. | 1920 | The Bengal Cruelty to Animals Act 1920 |
| 2. | 1957 | Animals Slaughter (Restriction) and Meat Control Act 1957 |
| 3. | 1962 | Prevention of Cruelty to Animals Ordinance 1962 |
| 4. | 1982 | Bangladesh Veterinary Practitioners Ordinance 1982 |
| 5. | 2005 | Bangladesh Animal and Animal Product Quarantine Act 2005 |
| 6. | 2005 | Animal Disease Act 2005 |
| 7. | 2007 | National Livestock Development Policy 2007 |
| 8. | 2008 | National Poultry Development Policy 2008 |
| 9. | 2008 | Animal Disease Rule 2008 |
| 10. | 2008 | Avian Influenza Compensation Strategy and Guidelines 2008 |
| 11. | 2009 | Bangladesh Zoo Act 2009 (Draft) |
| 12. | 2010 | Fish Feed and Animal Feed Act 2010 |
| 13. | 2011 | Animals Slaughter and Meat Control Act 2011 |
| 14. | 2013 | National Livestock Extension Policy 2013 (Final Draft) |
| 15. | 2013 | Animal Feed Rules 2013 |
| 16. | 2015 | National Livestock Manure Management Policy 2015 |
| 17. | 2015 | Bangladesh National Conservancy Strategy (Livestock Resources) 2015 |
| 18. | 2015 | Livestock Milk Production Artificial Reproduction Policy 2015 |
| 19. | 2015 | Amendment of Animal Disease Rules 2015 |
| 20 | 2017 | Bangladesh Livestock Research Institute Act 2017 |

etc. A broiler (poultry) produces 2.5 pound waste in her life and 20 – 30 pound by a layer bird per cycle (Ritz and Merka, 2013). An estimate says that 0.2 million tons of litter (faces with bedding material) and 2.3 million tons of manure are produced from 42 million layer birds daily in Bangladesh (SA PPLPP, 2009). Most of these are valuable wastes if these are managed properly. These can be transformed into biogas, organic fertilizer and other forms of energy.

There is no such official study that can say how much waste is produced in the country. However the amount will be big as the size of the animal industry, particularly poultry industry is very big. Now a day injudicious management of animal waste, particularly used poultry litter and manure are causing environmental pollution. Harmful greenhouse gases, e.g. methane, nitrous oxide and carbon dioxide are being produced from these wastes and causing other foul public nuisance by smelling and spreading pathogens, e.g. Salmonella, enterpathogenic E. coli etc.

**5.5.3 Way Forward:** DLS prepared a National Action Plan on Antimicrobial Resistant Containment (ARC) with joint collaboration of Directorate General of Health Services (DGHS). An operational plan has also been developed on how to combat with Antimicrobial Resistance for Animal Health Sector. If the strategic activities of this operational plan are implemented, AMR situation will be mitigated up to the mark. In order to implement the strategic objective of ARC, DLS already submitted a project to the ministry on AMR surveillance system.

## 5.6 FISH PRODUCTION, FISH DISEASES, ANIBIOTICS USED AND AMR IN FISHERIES

Department of Fisheries (DoF) is under the administrative control of the Ministry of Fisheries and Livestock (MoFL) of the Government of the People's Republic of Bangladesh. It is headed by a Director General, who is assisted by four Directors (one reserve) and 2 Principal Scientific Officers (equivalent to Director). There are 1,553 technical officers of different stairs and supporting staff in the DoF. They render their services to achieve the mission and vision of the DoF. There are administrative set-ups at Division, District and Upazila (sub-district) levels headed by Deputy Director, District Fisheries Officer and Senior/Upazila Fisheries Officer respectively. Besides these, there are three fish inspection and quality control stations under DoF. Furthermore DoF also comprises of Marine Fisheries Station, Fisheries Training Academy, Fisheries Training and Extension Centres, and Fish Hatcheries. [20]

**5.6.1 Mandates of the Department of Fisheries (DoF):** There are number of mandates and obligations to be performed by the DoF as follows: to disseminate improved aquaculture technologies through training and demonstration and to extend extension advisory services to the focal stakeholders; to enhance fisheries resources through enacting conservation and management measures; to assist the administrative ministry to formulate policies, acts etc; to enforce quality control measures and issuance of health certificates for exportable fish and fish products; to conduct fisheries resources survey and assessment of stock to develop fisheries database for proper planning; to facilitate arrangement for institutional credit for fish and shrimp farmers, fishers and fish traders and entrepreneurs; to facilitate alternative income generating activities for rural poor and unemployed people towards poverty alleviation; to formulate and implement development projects/programs towards sustainable utilization of fisheries resources to ensure food security; and to disseminate improved aquaculture technologies through e-Extension service. [20]

The DoF has number of sister organisations, they are (i) Bangladesh Fisheries Research Institute (BFRI); (ii) Bangladesh Fisheries Development Corporation (BFDC); (iii) Marine Fisheries Academy (MFA); (iv) Fisheries and Livestock Information Department (FLID). The BFRI conduct basic and applied research on freshwater aquaculture, inland fisheries management, lake management, fish diseases, marine fisheries, brackish water aquaculture, fish breeding genetics etc. Some of the technologies innovated by this institute are being disseminated to the fields by DoF. The BFDC is mainly involved in harvesting fisheries resources and developing marketing facilities in the country. BFDC has established fish harbours, landing and distribution centres, ice plants and processing plants in several locations of Bangladesh. In the past, BFDC played a vital role in supplying safe and quality fish in the domestic market. [20]

The MFA is maintaining proper and optimum management of sea fishes through developing expertise on Marine Fisheries. MFA is entrusted to train cadets skilful through modern techniques and equipment, in order to meet the challenges of Sustainable Development Goals in shipping sectors. On completion of three years training in the academy, the qualified cadets are awarded with Bachelor of Science

in Marine Fisheries (BSc.MF) degree from the National University. FLID has prepared many booklets and leaflets to transfer latest technologies and update information regarding the development activities in the fisheries and livestock sectors. A monthly bulletin is also published from FLID which have many update news, technology and information about fisheries and livestock development activities. [20]

**5.6.2 Prospects and Potentials of Fisheries Sector:** (i) National Contribution: Fisheries sector contributed 4.43% to national GDP and 22.21% to the agricultural GDP and 2.73% to foreign exchange earnings by exporting fish products in 2010-11. Fish provides 60% of national animal protein consumption. Fisheries sector also plays an important role in rural employment generation and poverty alleviation. (ii) Source of Fish Production: There are three categories of major fisheries resources, these are- inland capture (34%), inland culture (48%), and marine capture (18%). The inland fisheries comprises rivers, ponds, estuaries, small lake (Beel), medium to large lakes (Haors & Baors) floodplains, brackish water, etc. There are 260 fish species and 24 prawn species in inland fresh water in the country. In the early sixties inland fisheries contributed about 90% of total fish production of the country. Fish production from aquaculture has increased to a great extent but open water fish production is in slow progress. Now only about 34% of total fish production comes from inland open water. [20]

**5.6.3 Fish Production in Bangladesh:** Table-9 below shows the sources wise fish production in the year 2007 to 2011 for a period of five years. The steady average annual growth rate of fish production in last 4 years was 5.84%. In financial year 2010-2011, the total fish production was 3.06 million metric ton. The production from inland culture (closed water body) has been increasing very sharply due to dissemination of adaptive technologies and need-based extension services rendered by DoF. There are more than 260 different freshwater fish species and 475 marine fish species in the country. About 12 exotic and colourful fish species are being cultured in the country.

Marine Fisheries: The Bay of Bengal is situated in the South of Bangladesh. There is a total of 166,000 sq. km. water area including Exclusive Economic Zone (EEZ). Fishing is only confined within 200-meter depth. About 158 trawlers, 45,377 mechanized and non-mechanized boats are engaged in fishing. Pelagic and deep-sea resources are still untapped. In the year 2010-11 total fish production from marine source was 0.55 million metric tons. [20]

Recently Bangladesh has got the right to access 1.00 lakh sq. kilometre water area in Bay of Bengal through International Tribunal for the Law of the Sea (ITLOS). The DoF has planned to assess the fisheries resources in the Bay of Bengal for maximum sustainable yield. A research vessel is under process of procurement to conduct appropriate stock assessment. Vessel Tracking Monitoring System will also be developed.

**5.6.4 National Fisheries Policy:** A national fisheries policy has been adopted to make the aquaculture and fisheries management activities environment friendly and sustainable. The policy has been formulated aiming at the primary objective of increasing fish production through optimum utilization of the available resources. In this policy a separate chapter containing shrimp culture and export guideline has been incorporated. National shrimp policy rule is under consideration of the government employment generation and poverty alleviation have also been given importance in fisheries policy. National Fisheries Strategy has been developed and approved by the Ministry of Fisheries and Livestock in 2006 on the basis of National Fisheries Policy. The Fisheries strategy comprises of 8 sub-strategies and action plan.

**5.6.5 Development Activities in Fisheries Sector:** (i) Annual Development Program: In addition to the normal activities of the DoF, several development projects are being implemented aiming at boosting up fish production and conservation of fisheries resources.

**Table-9: Sources-wise Production of Fish in Yeas 2007-2011**

| SL | Financial Years | Source-wise Production (Metric Ton) | | | Total | Percentage (%) increased |
|---|---|---|---|---|---|---|
| | | Inland Capture | Inland Culture | Marine Capture | | |
| 1. | 2010 -2011 | 1,054,585 | 1,460,769 | 546,333 | 3,061,687 | 5.60 % |
| 2. | 2009-2010 | 1,029,937 | 1,351,979 | 517,282 | 2,899,198 | 7.32 % |
| 3. | 2008-2009 | 1,123,925 | 1,062,801 | 514,644 | 2,701,370 | 5.39 % |
| 4. | 2007 -2008 | 1,060,181 | 1,005,542 | 497,573 | 2,563,296 | 5.05 % |
| 5. | 2006-2007 | 996,761 | 955,812 | 487,438 | 2,440,011 | ---- |

In 2010-2011 a total of 25 investment projects, two programs and four technical assistance project have been in implementation. Through the development activities the habitat restoration, conservation of natural resources, community based resource management, human resource development, and alternate income generating activities etc have been implementing through this sector. (ii) Website for Fisheries: For quick and update information about DoF and aquaculture technologies, a fisheries website (www.fisheries.gov.bd) is running. To extend e-extension services up to field level e-extension program under Access to Information (A2I) is running in 10 upazilas. DoF has already developed a software by using of which fish farmers can get the advice about modern aquaculture.

**5.6.6 Aquaculture Practices:** (i) Freshwater Aquaculture: Indian major carps (type of high breeding fish) and exotic carps are largely cultured in the country. Culture practices are mainly improved-extensive and semi-intensive. Beside carp aquaculture, monoculture of Thi Pungus, Tilapia, Shorputi, Thai Koi are also practiced. Average fish production in the ponds is 3,285 kg/ha/year. Freshwater prawn (M.rosenbergii) is also cultured along with carps in some areas of the country.

(ii) Brackish Water Aquaculture: It is widespread in Satkhira, Khulna, Cox's Bazar and Bagerhat District. Tiger Shrimp P. monodon and giant prawn M. rosenbergii are the species of shellfish cultured in those areas. M. rosenbergii is largely cultured in southwest region of the country. The total production of shrimp and prawn in 2010-2011 was about 0.24 million metric ton.

(iii) Fish and Shrimp Hatchery: Fish hatchery especially carp hatchery started to come up in late seventies. At present there are 845 private fish nurseries, 76 public fish hatcheries and 124 public fish seed multiplication farms in the country.

A total of 629.2 metric tons of spawn was produced from public and private hatcheries in the year 2011. Collection of fish seed from natural grounds has increased to about 4.4 metric tons. In 2010-11 there were about 60 P. monodon (Bagda Shrimp) hatcheries and 80 M.rosenbergii (Galda Shrimp) hatcheries. About 5.95 million Bagda post larva and about 120 million Golda post larvae were produced in these hatcheries. Almost all Bagda hatcheries are located in Cox's Bazar region, but major culture grounds are situated in southwest region of Bangladesh. [20]

**5.6.7 Open Water Management:** (i) Hilsa Fishery Management: Hilsa is an important diadromous fish, which migrate between salt and fresh waters mostly found in the South and South-East Asia especially in Bangladesh. It is considered as the national fish of Bangladesh and contributes to the national economy, generates employment and earns foreign currency through export. Hilsa has the highest contribution in the country's fish production as the single fish species. More than 11% of the country's fish production comes from Hilsa. In 2010-11 Hilsa production was 0.34 million metric tons, which values around 10,000 Crore Taka.

Department of Fisheries (DoF) has taken some steps to strengthen the on-going hilsa management through Jatka (small hilsa) Conservation Project/Program like to establish five hilsa sanctuaries; to arrange need based training to involve the hilsa fishers for effective intervention of alternation income generating activities; and to support the hilsa fishers with 30 kg food grains/family/month during the ban periods for four months. A total of 20 thousand fishers in hilsa sanctuary areas are being directly benefited through alternate income generation activities.

(ii) Protection of Natural Breeding Ground Halda: DoF is restoring the natural breeding habitats of the Halda River to protect natural breeding ground of Indian Major Carps. In 2012 the total natural collected spawn/hatchling is 1.6 metric tons. (iii) Fishers ID card: Government has decided to issue identification (ID) card to the fisher's community of the country through a project under DoF. Through this development project database of genuine fishers will also be developed.

(iv) Integrated Natural Resource Management: Department of Fisheries (DoF) is implementing integrated natural resource management system by local user's contributors to conserving the biodiversity and livelihoods in the selected wetlands and floodplains in the Padma-Jumna rivers delta region through a development project. (v) Fish Habitat Restoration: In 2011-12 total 970 water bodies (areas about 2,123 hectare) have been developed by 7 development projects under DoF. As a result additional 3,000 metric tons of fish will be produced annually. In addition 450 hectare Modhumoti Baor has been excavated mechanically in this fiscal year. About 60 hectare Hurasagar River will be re-excavated in the coming years. [20]

**5.6.8 Export of Fish & Fish Products:** There are 162 fish processing plants in the country. Out of 162 plants European Commission has approved 74 plants. Hazard Analysis and Critical Control Points (HACCP) has already been introduced in fish processing establishments. Major importing countries are European countries, USA and Japan. About 98% of total fish products are exported to those countries. Remaining are exported to the countries in Southeast Asia and Middle East. Table-10 below shows export of fish and fish products over a period of five years from 2007 to 2011. [20]

Major export items of fish products are raw shrimp block

**Table-10: Export of Fish and Fish Products in years from 2007 to 2011**

| SL | Year | Fish Production (Metric Ton) | | Other Fish Production (Metric Ton) | | Total |
|---|---|---|---|---|---|---|
| | | Quantity (MT) | Value (Crore Taka) | Quantity (MT) | Value (Crore Taka) | Value (Crore Taka) |
| 1. | 2010 -2011 | 54891 | 3568.2 | 41578 | 1035.63 | 4603.83 |
| 2. | 2009-2010 | 51599 | 2885.21 | 26044 | 523.31 | 3408.52 |
| 3. | 2008-2009 | 50368 | 27 44.12 | 22520 | 499.29 | 3243.41 |
| 4. | 2007 -2008 | 49907 | 2863.92 | 25992 | 532.36 | 3396.28 |
| 5. | 2006-2007 | 53361 | 2992.33 | 20343 | 360.56 | 3352.89 |

frozen; IQF shrimp and white fish; PUD and P&D shrimp block frozen; consumer pack of raw frozen shrimp; chilled & frozen Hilsa; dry, salted and dehydrated fish; live fish; Eel fish & Crab and a little quantity of value added fish and shrimp products. Production of Crab through fattening in 2010 was 7,756 metric tons of which 634.7 metric tons was exported by earning Tk. 375.88 Crore. DoF has three inspection and quality control stations located at Khulna, Chittagong and Dhaka equipped and facilitated with testing laboratories. DoF is entrusted with the responsibility to ensure the quality of the products as competent authority. [20]

**5.6.9 Fisheries Legislations, Acts, Rules and Ordinances:** For fisheries resource conservation, management and maintenance of quality of the fish, and fish products, the following major acts, rules and ordinances have been enforced (Table-11). [20]

**Table-11: Types of Acts, Rules and Ordinances related to Fish and Fish Products**

| SL | Year | Types of Acts, Rules and Ordinances |
|---|---|---|
| 1. | 1939 | Tank Improvement Act 1939 |
| 2. | 1950 | Fish Protection & Conservation Act 1950 (amended in 1995) |
| 3. | 1983 | The fish & fish Products (Inspection & Quality Control) Ordinance 1983 |
| 4. | 1983 | The Marine Fisheries Ordinance 1983 |
| 5. | 1983 | The Marine Fisheries Rules 1983 |
| 6. | 1985 | The protection and Conservation of Fish Rules 1985 (amended in 2008) |
| 7. | 1992 | Shrimp Culture Avikor Act 1992 |
| 8. | 1993 | Shrimp Culture Avikor Rules 1993 |
| 9. | 1997 | The fish & fish Products (Inspection & Quality Control) Rule 1997(amended in 2008) |
| 10. | 1998 | National Fisheries Policy Bangladesh 1998 |
| 11. | 2010 | Fish Feed and Animal Feed Act 2010 |
| 12. | 2010 | Fisheries Hatchery Act 2010 |
| 13. | 2011 | Fish Feed Regulation 2011 |
| 14. | 2011 | Fish Hatchery Regulation 2011 |
| 15. | 2012 | Pond Development Act 2012 |
| 16. | 2013 | National Shrimp Policy 2013 |
| 17. | 2014 | National Shrimp Policy 2014 |
| 18. | 2015 | Code of Conduct Shrimp 2015 |

**5.6.10 Fish Production and Resource Conservation Campaign:** Campaign for boosting fish production and resource conservation, the country observes fish week "Campaign for Boosting Fish Production and Resources Conservation" usually in between July and September every year. Raising awareness of the people through the country for the conservation and management of fisheries resources is also an objective of this campaign. It is a national program and is inaugurated by the Prime Minister of the Government of the People's Republic of Bangladesh. Table-12 (page 115) shows the fisheries resources information in Bangladesh in 2010 to 2011. [20]

**5.6.11 Common Fish Diseases:** Aquaculture has been expanding throughout Bangladesh for the last three decades to meet the protein demand of the fast growing population of the country. Due to scarcity of land, farmers tend to maximize the speed of growth and total fish production. With the growing demand for finfish and shellfish, there has been a shift from traditional to semi-intensive and intensive aquaculture system, so that they can get greater yield.

A wide variety of parasites and pathogens can and do infect fish. Most disease agents are naturally present in low numbers and normally do not cause problems. The natural defence mechanisms of fish (i.e. undamaged skin, mucus covering the skin, and various components of the immune system) keep disease agents in check. However, when fish already crowded in culture operations are further stressed (e.g., by low dissolved oxygen, nutritionally inadequate feeds, excessive handling) their natural disease defence systems

**Table-12: Fisheries Resources Information in Bangladesh (2010-2011)**

| SL | Fisheries Resources Information in Bangladesh | | FY 2010 -2011 |
|---|---|---|---|
| 1. | Sources wise Water Areas for Fish Production | | Areas in Hector |
| | A. | Closed Water Body (Culture & Capture based) | 653,289 |
| | | a. Pond & Ditches | 371,309 |
| | | b. Oxbow lake | 5,488 |
| | | c. Shrimp Farm | 276,492 |
| | B. | Open Water Body (Capture based) | 3,847,234 |
| | | a. River & Estuaries (without Sundarban) | 853,863 |
| | | b. Beel | 114,161 |
| | | c. Kaptai Lake | 68,800 |
| | | d. Flood Plain | 2,810,410 |
| | C. | Marine Fisheries ( Sq. Nautical Miles) | 68,520 |
| | | a. Territorial Water | 2,680 |
| | | b. Exclusive Economic Zone | 41,040 |
| | | c. Continental Shelf | 24,800 |
| | D. | Length of the Coast line (km) | 710 |
| 2. | | Fish Production in Metric Tons | 3,061,687 |
| | | a. Open Water (Inland Capture) | 1,054,585 |
| | | b. Closed Water (Inland Culture) | 1,460,769 |
| | | c. Marine Fisheries | 546,333 |
| 3. | A. | Export of Fish & Fish Products | |
| | | a. Quantity (in Metric Tons) | 96,469 |
| | | b. Value (BDT in Crore) | 4,604 |
| | | c. Contribution to export earnings (%) | 2.73 |
| | B. | Number of Fish Processing Plants (n) | 162 |
| | C. | Number of EU approved Plants (n) | 74 |
| 4. | A. | Contribution in GDP (%) | 4.43 |
| 5. | A. | Fish Intake/Demand | |
| | | a. Per Capita Annual Fish Intake (kg) : | 18.94 |
| | | b. Annual Total Fish Needed (Million Metric Tons) | 2.04 |
| | | c. Contribution in Animal Protein Supply (%) | 60 |
| 6. | A. | Fish Hatchery/Nursery | |
| | | a. Number Fish hatchery (Public – 76 and Private 845) | 921 |
| | | b. Number of Fish Nursery (Public – 76 Private 845) | 921 |
| | | c. Fingerling Production (in million) | 8.2 |

may be weakened and the ability of the fish to protect themselves against infectious diseases may be reduced.

Disease induced catastrophic mortalities are frequently the result of, and response to, a stressful experience. The common causes of fish diseases are as follows:

(I) Bacterial disease (caused by Aeromonas and *Pseudomonas* bacteria), finrot (caused by *Aeromonas*, *Pseudomonas* or *Flexibacter* bacteria), Cotton-wool disease (caused by Flexibacter); vibriosis is one of the most prevalent fish diseases (caused by Vibrio anguillarum) which is of major importance to salmonid fish culture industry and is also known as Red pest of eels;

(ii) Fungal disease called Saprolegniasis (caused by Saprolegnia and *Achlya*);

(iii) Parasite diseases such as *Cryptocaryoniasis, Trichodiniasis, Lernaeosis, Glugea* disease and Sanguinicolosis; and

(iv) Other fish disease are fish with ulcer, fish with cloudy eye, dropsy, fish with white spot, swim bladder disorder and Lymphocystis *(iridovirus)*.

**5.6.12 Fish Disease Burden in Bangladesh:** It was found in a study conducted at Chittagong, Bangladesh in 2016 among the fish farmers (n=196) that 24% of the fish disease occured immediately after stocking, 21% disease occurred during rainy season and 19% disease occurred in winter season. Mortality, abnormal swimming and feeding behavior, unusual appearance, some localized lesions and reduced growth are the main clue to recognize and diagnose the fish disease. The most frequently observed diseases were epizootic ulcerative syndromes (18.7%) followed by tail and fin rot (13.2%), red spot (11.5%), gill rot (9.4%), parasitic disease (9.0%), broken prawn antennae (7.2%), and other environmental and nutritional diseases. [35]

Under the program of investigation and identification of emerging fish diseases and development of their control strategies, Bangladesh Fisheries Research Institute (BFRI) in

their annual report (2012-2013 and 2014-2015) documented a total of 85 bacterial strains from 120 samples of infected shing fish *(Heteropneustes fossilis)*. The isolation frequencies of these 85 strains upon anatomical parts of infected shing were: infected skin and fin 32.9%, gill 14.1%, liver 11.8% and kidney 38.8%. On the other hand, bacteria of Streptococcus sp. were isolated from diseased tilapia fish *(Oreochromis nilotica)* that isolated bacteria showed grams positive coccus. Isolates Streptococcus sp1 and Streptococcus sp2 were showed γ-haemolysis but Streptococcus sp3 was showed α-haemolysis in blood agar.[36]

Bangladesh Fisheries Research Institute (BFRI) investigated shrimp/prawn diseases and their control strategies in South-Western region of Bangladesh. The investigation included 24 randomly selected water bodies (Gher in local language) to identify immerging diseases of shrimp in context to aqua ecology and pathogens. Most of the water bodies (70%) found to be in trouble due to poor pond preparation, inadequate feeding and lower water depth. [36]

Due to lower water depth and sudden rainfall, 80% of the water bodies having shrimp *(Penaeus monodon)* attacked by white spot syndrome virus (WSSV) in March to May. However, the water depth tend to rises from late May towards June and onward, stocked golda shrimp *(M. rosenbergii)* were badly infected by the complex form of infection by different group of bacteria. The initial treatment, therefore, replied with reducing the mortality to 5% and successful moulting of over 37% of larvae to PL. PCR test for the presence of MrNV was also performed but found negative.[36]

**5.6.13 Use of Chemotherapeutics in Fish/Shrimp:** It is evident that disease can cause huge fish/shrimp mortality, the largest single reason of economic loss in aquaculture systems. In order to control fish diseases, farmers are tempted to apply a wide range of chemotherapeutics with the advocacy of pharmaceutical/pesticide companies, drug sellers, GO/NGO personnel, reputed farmers and even neighbors. BFRI identified at least 55 chemotherapeutics, disinfectants, water treatment compounds, biological products, probiotics, vitamins & minerals, feed additives, antibiotics and hormones.[38]

These chemicals and drugs are being used in aquaculture systems indiscriminately without proper understanding /diagnosis of the disease/problem. Unfortunately, most of the persons advocating in favor of using drugs in aquaculture are neither qualified enough nor having any legal basis to prescribe any drugs.

**Table-13: Different antibiotics were used against various fish diseases**

| Antibiotics Use (Fish and Shrimp) | Purpose of use in Diseases/ Bacterial infection | Dosage Ranges (suggested by different companies/traders) |
|---|---|---|
| Chlorsteclin | Tail and gill rot, dropsy, EUS | 4-10 mg/kg feed |
| Oxy-tetracycline | Tail and gill rot, dropsy, EUS,Gram positive and Gram negative Bacteria, EUS, Edwardsiellosis, Columnaris | 2 6mg/kg feed |
| Azithromycin | Columnaris, Edwardsielbsis, Motile Aeromonas septecemia, Vibriosis, Mycobacteriosis, EUS, | 1-2g / kg feed |
| Erythromycin | Applied against infection for brood stock maintenance, preventing infectious diseases | 20 ppm |
| Nitro furans (Prefuran) | Aeromonas, Vibrio sps ,usage for treating larvae and post larvae in shrimp | 1 ppm in shrimp hatcheries for treating larvae and post larvae treatment/ 2-4 ppm for brood stock maintenance |
| Furazoliodine | Broodstock maintenance, treating larvae and post larvae in shrimp | 3-5 ppm Vibriosis, |
| Amoxicillin | Columnaris, Edwardsiellosis, Mycobacteriosis | 3-7mg/kg feed |
| Chloramphenicol | After eye ablation infection, Shrimp hatcheries and Brood stock maintenance | 10 ppm |
| Sulphadiazine & Trimethoprim | Effective against wide range of Bacteria | mixed with feed: 50g/kg body weight, 5-7 days |
| Chlortetracycline | Aeromonas, Vibrio sps, Gram positive and Gram negative Bacteria | 3-7 mg/kg feed |

Antibiotics with different trade names were seen in the market as well as used by the fish farmers. Thus, the farmers fetch considerable pressure from the commercial companies to use a variety of products in their farms. Several products have been sold without any explanation of their action.

### Antibiotic Sensitivity Test

Haque et al. (2012) reported that A. *hydrophilla* is 100% resistant to streptomycin and ampicillin. About 86% of Aeromonas isolates showed resistance to ampicillin and 25% to streptomycin. [39] Ahammed et al. (2016) reported that the isolated *Aeromonas hydrophilla* were tested against ten commercially available antibiotics and the results of their sensitivity are presented in here. Most of the bacterial samples were sensitive against ciprofloxacin (92%), and levofloxacin (84%), ntermediate against gentamicin (40%) and resistant against Novobiocin (84%), ampicillin (100%) and penicillin (92%). [38]

Similar study was carried out by Monir et al. (2016) using five bacterial strains isolated were tested against 10 antibiotics where all of the isolates were found to be sensitive to Ciprofloxacin, Levofloxacin, Azithromycin and Gentamicin but most of the remaining isolates were found resistant or less sensitive to Tetracycline, Chlortetracycline and Oxytetracycline. Ciprofloxacin and Levofloxacin were highly effective whereas Ampicillin and Penicillin were found fully resistant. Since Tetracycline, Chlortetracycline and Oxytetracycline are being used in fish culture system indiscriminately resulting in transfer of resistant genes to the isolated bacterial strains. [37]

**Table-14: Antibiogram profile of isolated *Aeromonas hydrophilla***

| Antibiotics | No (%) | | |
|---|---|---|---|
| | Sensitive | Intermediate | Resistant |
| Ciprofloxacin (5µg) | 23 (92) | 2 (8) | 0 (0) |
| Levofloxacin (5µg) | 21 (84) | 4 (16) | 0 (0) |
| Gentamicin (10µg) | 15 (60) | 10 (40) | 0 (0) |
| Azithromycin (15µg) | 12 (48) | 8 (32) | 3 (12) |
| Tetracycline (30µg) | 4 (16) | 12 (48) | 9 (36) |
| Oxytetracycline (10µg) | 1 (4) | 10 (40) | 14 (56) |
| Chlortetracycline (25µg) | 3 (12) | 13 (52) | 9 (36) |
| Novobiocin (5µg) | 0 | 4 (16) | 21 (84) |
| Ampicillin (10µg) | 0 | 0 | 25 (100) |
| Penicillir | 0 | 2 (8) | 23 (92) |

**Table-15. Antibiotics sensitivity test on isolated bacteria from infected Shing *(H. fossilis)***

| Antibiotics | *Aeromonas hydrophilla* | *Aeromonas salmonicida* | *Aeromonas sobria* | *Pseudomonas anguiseptica* | *Vibrio anguillarum* |
|---|---|---|---|---|---|
| Ciprofloxacin (5µg) | +++ | +++ | +++ | +++ | ++ |
| Levofloxacin (5µg) | +++ | +++ | +++ | +++ | ++ |
| Gentamicin (10µg) | ++ | ++ | ++ | +++ | ++ |
| Azithromycin (15µ g) | ++ | ++ | ++ | ++ | + |
| Tetracycline (30µg) | + | + | + | + | + |
| Oxytetracycline 10µg) | - | + | + | + | + |
| Chlortetracycline (25µg) | - | - | + | + | + |
| Novobiocin (5 µg) | - | - | - | - | +++ |
| Ampicillin (10µg) | - | - | - | - | - |
| Penicillin (10µg) | - | - | - | - | - |

- No inhibition, + inhibitory zone between 5-12mm, ++ inhibitory zone between 13-20mm, +++ inhibitory zone between 21-30mm above. (Monir et al. 2016)

## 5.7 USE OF ANTIMICROBIALS IN AGRICULTURE SECTOR

The risk of antimicrobial resistance in agriculture appears to be high particularly in countries where legislation, regulatory surveillance and monitoring systems on the use of antimicrobials, and the prevention and control of antimicrobial resistance are weak and/or inadequate. This is where government should play a key role in supporting the national drug regulatory authority, drug manufacturers/producers, retail and whole sale traders, international agencies and other stakeholders to move towards the responsible use of antimicrobials in agriculture, thus helping to reduce antimicrobial resistance in agricultural systems and across the agriculture sector.

It is important that these life-saving drugs remain available and appropriately accessible to agriculture. Estimates of the total annual global consumption of antimicrobials in agriculture vary considerably. This is due to poor surveillance and data collection in many countries. For example, only 42 countries in the world have systems to collect data on the use of antimicrobials in livestock. Estimated global antimicrobial consumption in the livestock sector in 2010 was 63,151 metric tons. But the quantity of antimicrobials used for crop production is calculated to be relatively low in comparison to that used in livestock production, with estimates ranging from 0.2 to 0.4 percent of total agricultural consumption.

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