



# Task Force for AMR : An Initiative of Govt

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# AMR Synonymous with global warming



- The speed with which our antibiotics are rendered ineffective it may not matter that we have antibiotics 5 years from now.
- In such case the fate of advances in medicine like liver, kidney, bone marrow, heart, stem cell Tx. and many more will take a nose dive.
- End result will be a decline in medical wonders
- And lack of faith in medicine of a common man

**We need implementable policies to limit AMR**



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## Characterization of a New Metallo- $\beta$ -Lactamase Gene, *bla*<sub>NDM-1</sub>, and a Novel Erythromycin Esterase Gene Carried on a Unique Genetic Structure in *Klebsiella pneumoniae* Sequence Type 14 from India<sup>∇</sup>

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## Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study



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### Summary

**Background** Gram-negative Enterobacteriaceae with resistance to carbapenem conferred by New Delhi metallo- $\beta$ -lactamase 1 (NDM-1) are potentially a major global health problem. We investigated the prevalence of NDM-1, in multidrug-resistant Enterobacteriaceae in India, Pakistan, and the UK.

**Methods** Enterobacteriaceae isolates were studied from two major centres in India—Chennai (south India), Haryana (north India)—and those referred to the UK's national reference laboratory. Antibiotic susceptibilities were assessed, and the presence of the carbapenem resistance gene *bla*<sub>NDM-1</sub> was established by PCR. Isolates were typed by pulsed-field gel electrophoresis of XbaI-restricted genomic DNA. Plasmids were analysed by S1 nuclease digestion and PCR typing. Case data for UK patients were reviewed for evidence of travel and recent admission to hospitals in India or Pakistan.

**Findings** We identified 44 isolates with NDM-1 in Chennai, 26 in Haryana, 37 in the UK, and 73 in other sites in India and Pakistan. NDM-1 was mostly found among *Escherichia coli* (36) and *Klebsiella pneumoniae* (111), which were highly resistant to all antibiotics except to tigecycline and colistin. *K pneumoniae* isolates from Haryana were clonal but NDM-1 producers from the UK and Chennai were clonally diverse. Most isolates carried the NDM-1 gene on plasmids: those from UK and Chennai were readily transferable whereas those from Haryana were not conjugative. Many of the UK NDM-1 positive patients had travelled to India or Pakistan within the past year, or had links with these countries.

**Interpretation** The potential of NDM-1 to be a worldwide public health problem is great, and co-ordinated international surveillance is needed.

**Funding** European Union, Wellcome Trust, and Wyeth.

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# Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study



Timothy R Walsh, Janis Weeks, David M Livermore, Mark A Toleman

## Summary

**Background** Not all patients infected with NDM-1-positive bacteria have a history of hospital admission in India, and extended-spectrum  $\beta$ -lactamases are known to be circulating in the Indian community. We therefore measured the prevalence of the NDM-1 gene in drinking water and seepage samples in New Delhi.

**Methods** Swabs absorbing about 100  $\mu$ L of seepage water (ie, water pools in streets or rivulets) and 15 mL samples of public tap water were collected from sites within a 12 km radius of central New Delhi, with each site photographed and documented. Samples were transported to the UK and tested for the presence of the NDM-1 gene, *bla*<sub>NDM-1</sub>, by PCR and DNA probing. As a control group, 100  $\mu$ L sewage effluent samples were taken from the Cardiff Wastewater Treatment Works, Tremorfa, Wales. Bacteria from all samples were recovered and examined for *bla*<sub>NDM-1</sub> by PCR and sequencing. We identified NDM-1-positive isolates, undertook susceptibility testing, and, where appropriate, typed the isolates. We undertook Inc typing on *bla*<sub>NDM-1</sub>-positive plasmids. Transconjugants were created to assess plasmid transfer frequency and its relation to temperature.

**Findings** From Sept 26 to Oct 10, 2010, 171 seepage samples and 50 tap water samples from New Delhi and 70 sewage effluent samples from Cardiff Wastewater Treatment Works were collected. We detected *bla*<sub>NDM-1</sub> in two of 50 drinking-water samples and 51 of 171 seepage samples from New Delhi; the gene was not found in any sample from Cardiff. Bacteria with *bla*<sub>NDM-1</sub> were grown from 12 of 171 seepage samples and two of 50 water samples, and included 11 species in which NDM-1 has not previously been reported, including *Shigella boydii* and *Vibrio cholerae*. Carriage by enterobacteria, aeromonads, and *V cholera* was stable, generally transmissible, and associated with resistance patterns typical for NDM-1; carriage by non-fermenters was unstable in many cases and not associated with typical resistance. 20 strains of bacteria were found in the samples, 12 of which carried *bla*<sub>NDM-1</sub> on plasmids, which ranged in size from 140 to 400 kb. Isolates of *Aeromonas caviae* and *V cholerae* carried *bla*<sub>NDM-1</sub> on chromosomes. Conjugative transfer was more common at 30°C than at 25°C or 37°C.

**Interpretation** The presence of NDM-1  $\beta$ -lactamase-producing bacteria in environmental samples in New Delhi has important implications for people living in the city who are reliant on public water and sanitation facilities. International surveillance of resistance, incorporating environmental sampling as well as examination of clinical isolates, needs to be established as a priority.

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# Knowledge is Strength

- We need to know in context of AMR
  1. What to develop &
  2. How to implement
  3. Amount of AMR are we facing
- Once we know what is ailing us we are sure to treat it with all wisdom and strength.
- But imagine in absence of this knowledge what will be the outcome of our precious resource like antibiotic.

**We will be groping in the dark**

# What is the magnitude of problem

- Hospital prevalence of NDM-1

Few case reports

Limited surveillance studies

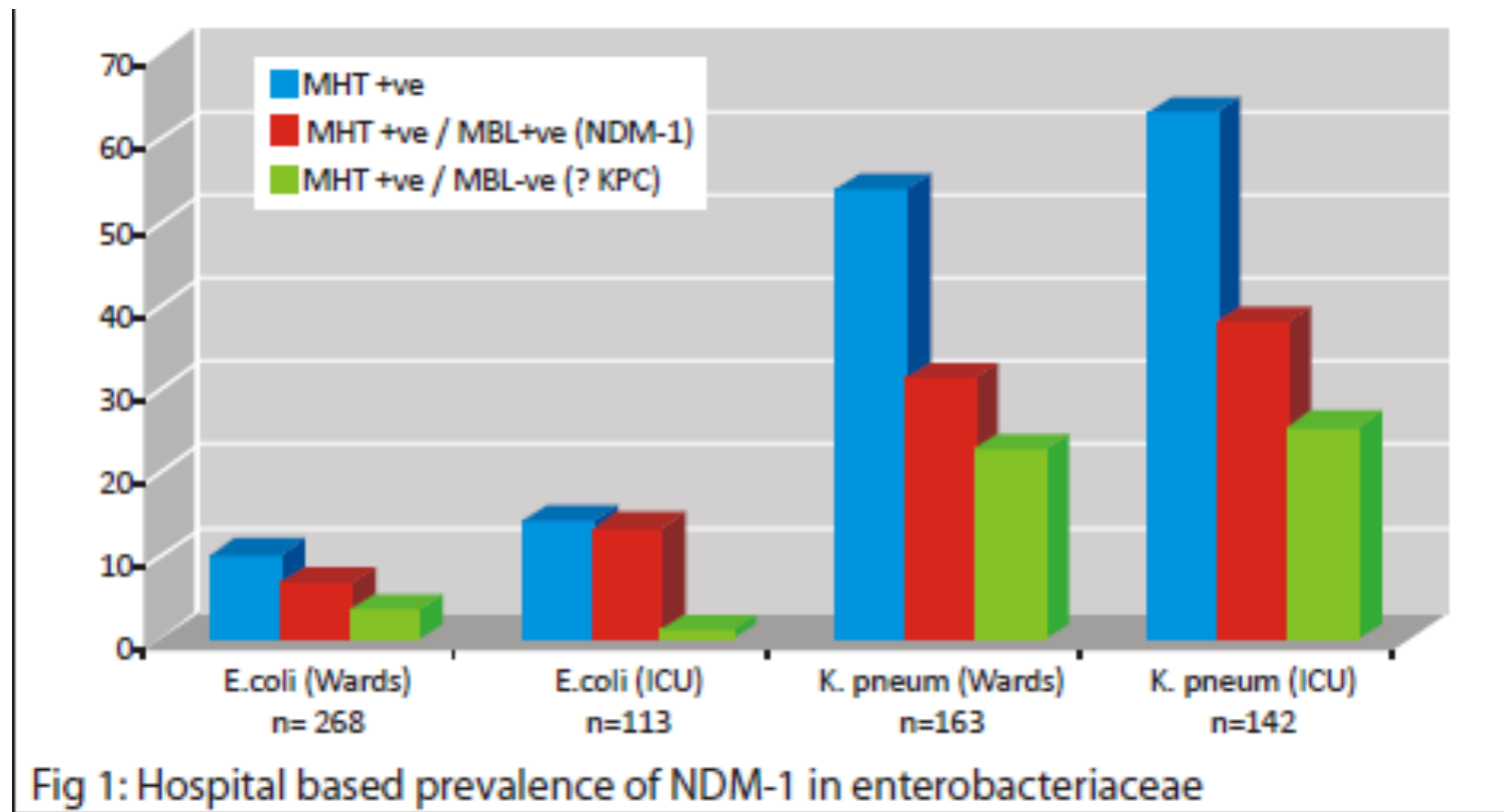
A small study has shown carbapenemase prevalence to be 5.2-7.8%, out of which 86% were NDM-1

- Community prevalence of NDM-1

?

# Prevalence of NDM-1 carbapenemase at SGRH: A pilot study of 5 months

The prevalence of NDM-1 was 6.7% (*E.coli*: wards), 13.3% (*E.coli*: ICU)  
31.3% (*K. pneumoniae*: wards) and 38% (*K. pneumoniae*: ICU)







# Community-Based Surveillance of Antimicrobial Use and Resistance in Resource- Constrained Settings

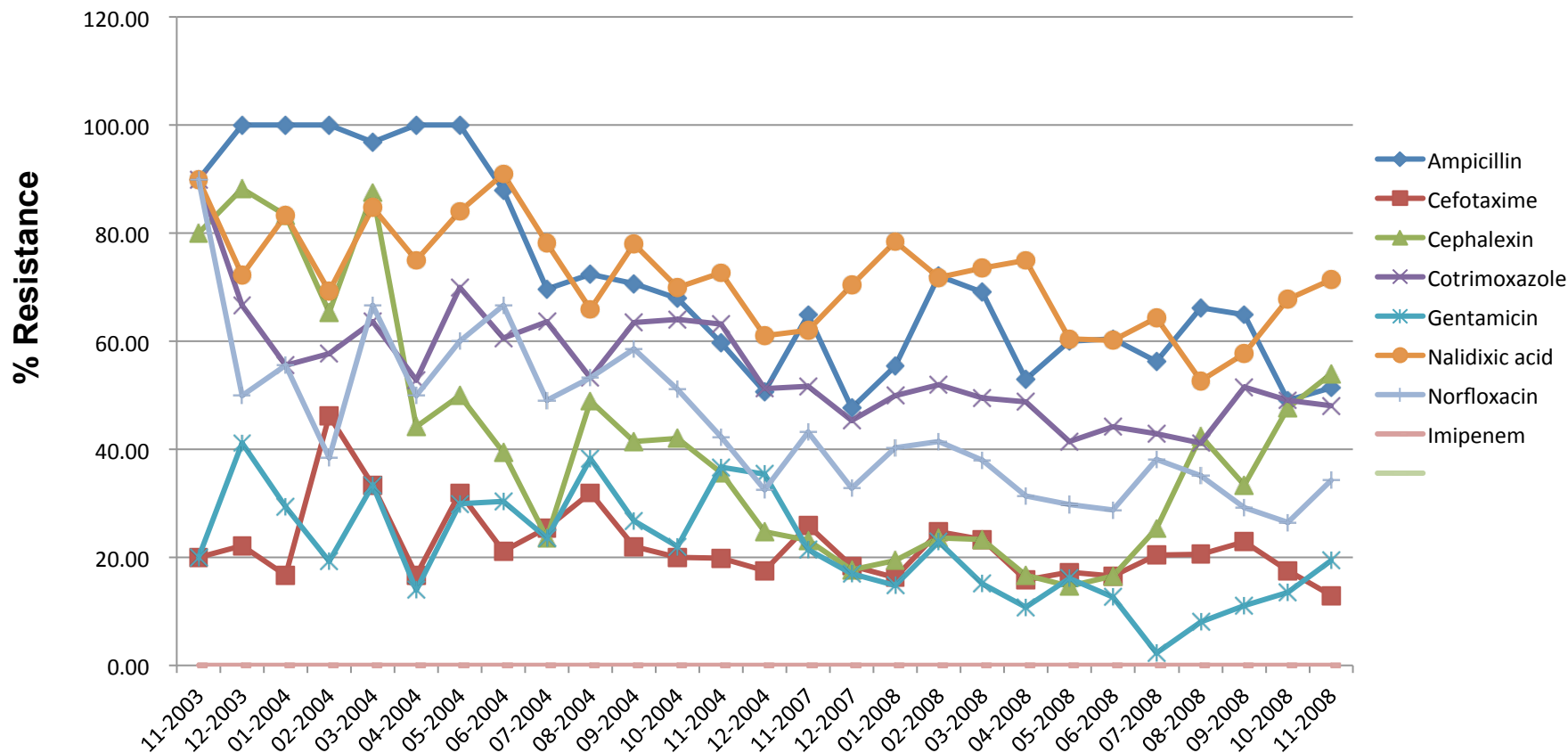
Report on five pilot projects



World Health  
Organization



# CRE in Community E.coli Isolates: Delhi 2003-4, 2007-8





*Journal of*  
**APPLIED THERAPEUTIC RESEARCH**

**Establishing a new methodology for monitoring of  
antimicrobial resistance and use in the  
community in a resource poor setting**

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**In-depth qualitative investigation to  
study antimicrobial use behaviour  
and suggestions for suitable  
interventions**



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## **Antibiotic use in the community: what factors influence primary care physicians to prescribe antibiotics in Delhi, India?**

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# Journal of Clinical Pharmacy and Therapeutics

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ORIGINAL ARTICLE

## Irrational use of antibiotics and role of the pharmacist: an insight from a qualitative study in New Delhi, India

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# To Develop Policies we need to know?

1. How to know what are we faced with in the name of antimicrobial resistance
2. What are the tools that can be used for monitoring AMR with reliable and reproducible results
3. How to interpret this information to formulate and implement policies

**INITIATIVE OF DGHS, MOHEW GOI**



# Task Force

**Assess, Review and Suggest Measures  
On  
Antimicrobial Resistance**



# MoHFW Gol ceased with the problem

- **One or more** central Institutions under Ministry of Health made **coordinating center** at the national level depending on the lab network size
- **Network of Hospital Based AST laboratories**

# FIVE TERMS OF REFERENCE OF THE TASK FORCE COMMITTEE



1. Review the current situation regarding manufacture, use and misuse of antibiotics in the country.
2. Design for creation of a National Surveillance System for antibiotic resistance.
3. Studies documenting prescription patterns and establish a monitoring system for the same.
4. Enforce and enhance regulatory provisions for use of antibiotics in human veterinary and industrial use.
5. Specific intervention measures such as rationale use of antibiotics and antibiotic policies in hospitals which can be implemented, as early as possible



# MEMBERS OF TASK FORCE



- Dr. R. K. Srivastava DGHS-Chairperson
- Prof. Ranjit Roy Chaudhury, Member, Board of Governors, MCI
- Dr. N.K. Ganguly, President, JIPMER, New Delhi.
- Dr. S.K. Bramhachari, Director, CSIR, New Delhi.
- Dr. Surender Singh, Drugs Controller General of India, New Delhi.
- Dr. Randeep Guleria, Prof. of Medicine, AIIMS, New Delhi.
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- Dr. Usha Gupta, Sr. Consultant, Clinical Pharmacology, Fortis Hospital
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- Dr. R.L. Ichhpujani, Director NCDC, Delhi- Member Secretary

[www.nicd.nic.in/ncdc/new-ab\\_policy.pdf.url](http://www.nicd.nic.in/ncdc/new-ab_policy.pdf.url)



# 1. Monitoring Manufacturing ,Use and Misuse of antibiotics

- ‘**Schedule H drug-Warning:** To be sold by retail on the prescription of a Registered Medical Practitioner only’ .
- In order to have separate regulation to check unauthorized sale of antibiotics, a separate schedule as Schedule H1 introduced under the Drugs and Cosmetics Rules to regulate sale of antibiotics exclusively.
  - Corresponding provisions under the Rules could be framed for their implementation. *A system of colour coding of **3<sup>rd</sup> Generation antibiotics and all newer molecules like Carbapenem(Ertapenem, Imipenem, Meropenem), Tigecycline, Daptomycine** may be put in place restricting their access to only tertiary hospitals.*



## 2: Hospital based sentinel National Surveillance System to Monitor antibiotic resistance

- Identification of pathogens/diseases of public health importance
- Creation of network of Antibiotic Susceptibility Testing (AST)
- Standardizing methodology for microbial identification and AST
- The laboratories to perform AST using standardized methods and carbapenem resistance isolates will be stocked and sent to designated central laboratory for further analysis like identification of NDM 1 isolates.
- Strengthen Quality Systems in the network laboratories

[www.nicd.nic.in/ncdc/new-ab\\_policy.pdf](http://www.nicd.nic.in/ncdc/new-ab_policy.pdf)



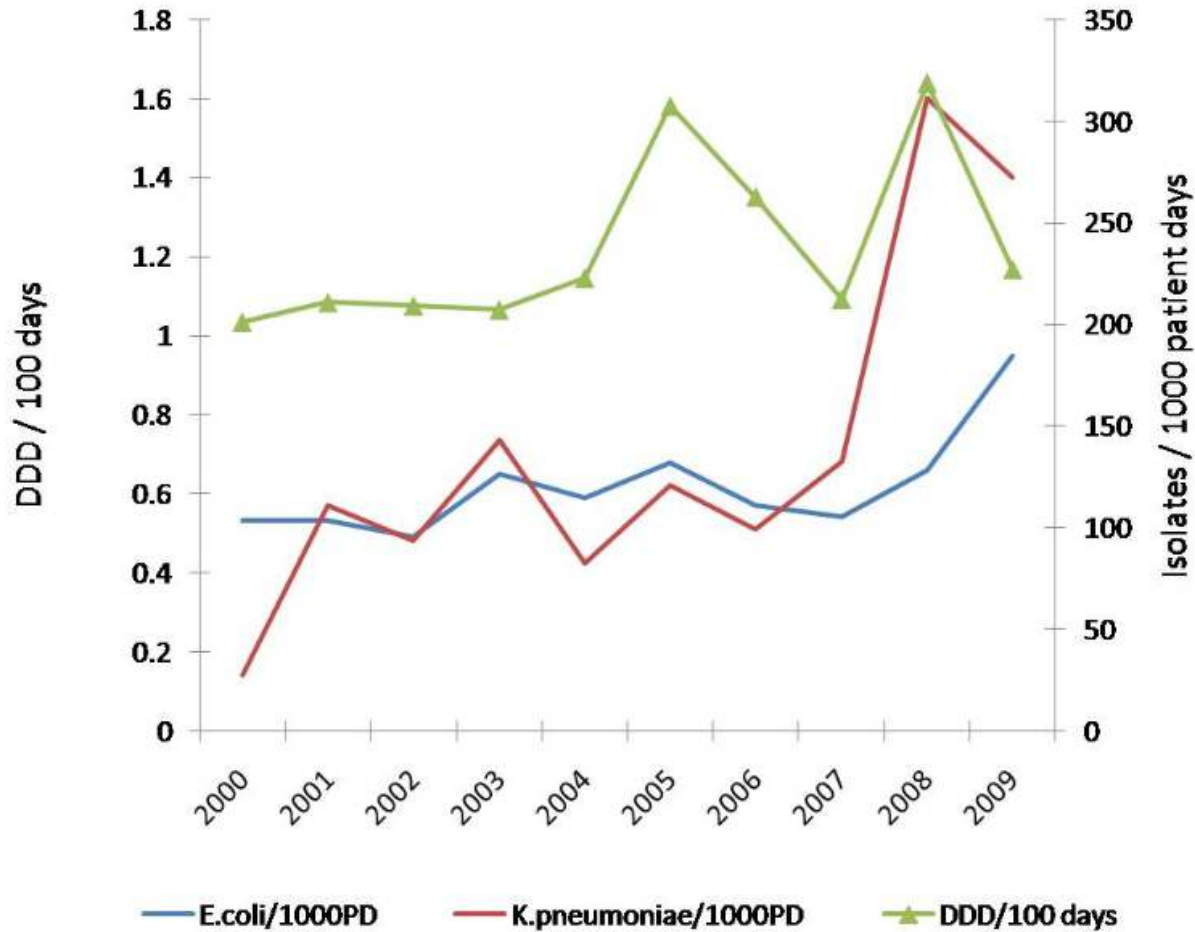


### 3: For Studying the documenting prescription patterns and establishing a monitoring system

- To study the consumption of various antibiotics in tertiary care public hospitals in Delhi under central government and then the rest of the country
- To study the trends in antibiotic use in these hospitals of Delhi
- Data generated will be used for intervention studies for rational use of antibiotics.



### Rising trends of the number of isolates and antibiotic consumption



Ten years trends at SGRH (2000-2009)



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## SHORT REPORT

# Prescription auditing and antimicrobial resistance at a tertiary care hospital in New Delhi, India

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### KEYWORDS

Antibiotic use;  
Antimicrobial  
susceptibility

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**Summary** This paper reports the antibiotic consumption data of Sir Ganga Ram Hospital, New Delhi and bacterial resistance over a seven-year period. Cephalosporins, penicillins and fluoroquinolones were the most widely prescribed antibiotics. A correlation was seen between *Escherichia coli* resistance to third-generation cephalosporins and increased cephalosporin use, as well as resistance to coamoxyclav and its use.

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## Trend analysis of antimicrobial consumption and development of resistance in non-fermenters in a tertiary care hospital in Delhi, India

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**Objectives:** Multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are becoming increasingly important nosocomial pathogens worldwide. To study the evolution of non-fermenters in a tertiary care hospital, we undertook a retrospective 10 year (1999–2008) trend analysis of antimicrobial consumption and resistance in non-fermenters causing bacteraemia.

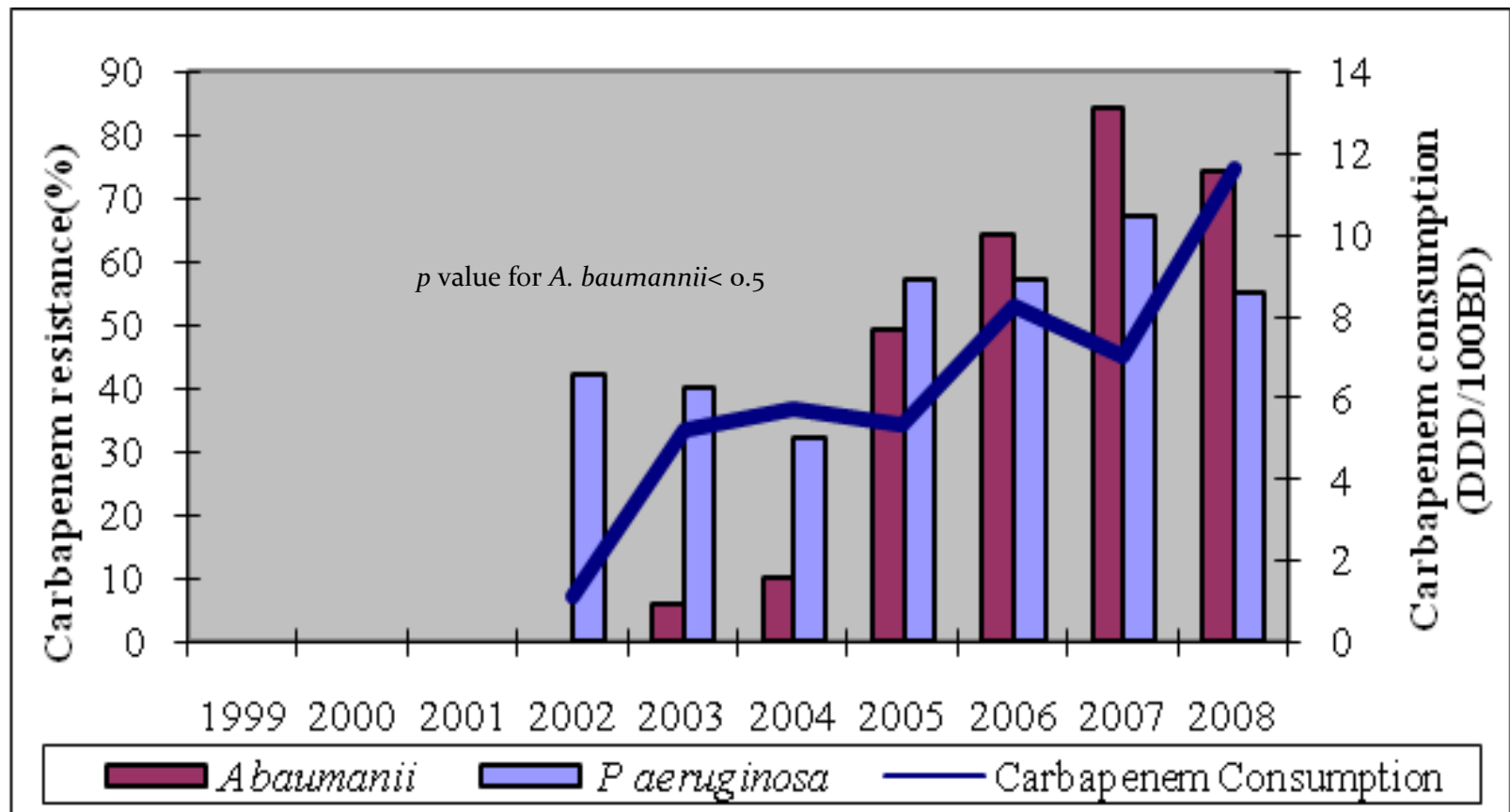
**Methods:** Antibiotic consumption and resistance were analysed by linear regression. The Pearson correlation coefficient was used for assessing correlation between them.

**Results:** A total of 69010 blood cultures were performed, which grew 15465 isolates (22% positivity rate), of which 1525 isolates (771 isolates of *P. aeruginosa* and 754 isolates of *A. baumannii*) were non-fermenters. Overall antibiotic consumption showed an increasing trend, from 158 to 319 defined daily doses (DDDs)/100 bed-days ( $r^2=0.62$ ,  $P=0.007$ ). The largest relative increase in antibiotic consumption was seen for carbapenems ( $r^2=0.68$ ,  $P=0.022$ ), followed by  $\beta$ -lactam/inhibitor combinations ( $r^2=0.45$ ,  $P=0.033$ ), whereas third-generation cephalosporins, fluoroquinolones and aminoglycosides showed no significant changes. A significant increase in resistance in *A. baumannii* to fluoroquinolones ( $r^2=0.63$ ,  $P=0.006$ ), aminoglycosides ( $r^2=0.63$ ,  $P=0.011$ ) and carbapenems ( $r^2=0.82$ ,  $P=0.013$ ) and in *P. aeruginosa* to aminoglycosides ( $r^2=0.59$ ,  $P=0.01$ ) was observed. Carbapenem consumption was associated with the development of resistance in *A. baumannii* ( $r=0.756$ ,  $P=0.049$ ), whereas no such association was observed for other antimicrobials among non-fermenters.

**Conclusions:** Our study highlights the growing problem of high antimicrobial consumption. The increasing prevalence of non-fermenters and the emergence of multidrug-resistant *A. baumannii* are associated with the consumption of carbapenems. The data cannot prove cause and effect.

**Keywords:** *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, carbapenems, DDDs/100 bed-days, bacteraemia

# Association between carbapenem consumption and resistance in *P.aeruginosa* and *A. baumannii* (SGRH)







## 4: For enforcement and enhancement of regulatory provisions for use of antibiotics in human, veterinary and industrial use.

- In India, the antibiotics are used widely in food animals as growth promoters and to prevent and treat infection. Non-therapeutic usage of antibiotics has been especially common in poultry production. However, there is no regulatory provision regarding the use of antibiotics in livestock.
- Establish intersectoral coordination committee with experts from various sectors.
- Develop regulations on usage of antimicrobials in poultry and other animals as well as the requisite labeling requirements in food.



## 5: For rationale use of drugs various strategies in hospitals which can be implemented

- Educational strategy: Training, printing materials, media-based approach
- Managerial strategy: Monitoring & supervision, generic substitution, patient cost sharing (economic incentives) etc
- Regulatory strategy: Enforcement, sanction, drug withdrawal, market control etc
- **Formulation ,implementation & monitoring of the antibiotic policy**
- With quality assured laboratory data in real time develop antibiotic policies that are standard national/local treatment guidelines advocating evidence based immunotherapy or combination therapy. This must include consideration of spectrum of antibiotics, Pharmacokinetics/ Pharmacodynamics, Adverse effects monitoring , Cost and special needs of individual patient groups





## ICU MICROBIOLOGY DATA (Total no. of isolates = 171)

Most Common Pathogens	%	Antibiotics Susceptibility	%
<i>Acinetobacter</i> (n=48)	28%	Colistin / Imipenem (=Amikacin) / Cef/Sul / Piptazo	98%; 9%; 6%; 2%
<i>Klebsiella</i> (n=43)	25%	Imipenem (~Ertapenem) / Amikacin / Piptazo / Cef/Sul	97%; 43%; 33%; 21%
<i>E.coli</i> (n=24)	14%	Imipenem (~Ertapenem) / Amikacin / Piptazo (=Cef/Sul)	100%; 92%; 67%
<i>Pseudomonas</i> (n=20)	12%	Colistin / Pip/Taz / Imipenem / Cef/Sul (=Amikacin)	91%; 62%; 29%; 27%
<i>Staph CNS</i> (n=16)	9%	Vancomycin (~Teicoplanin)	100%

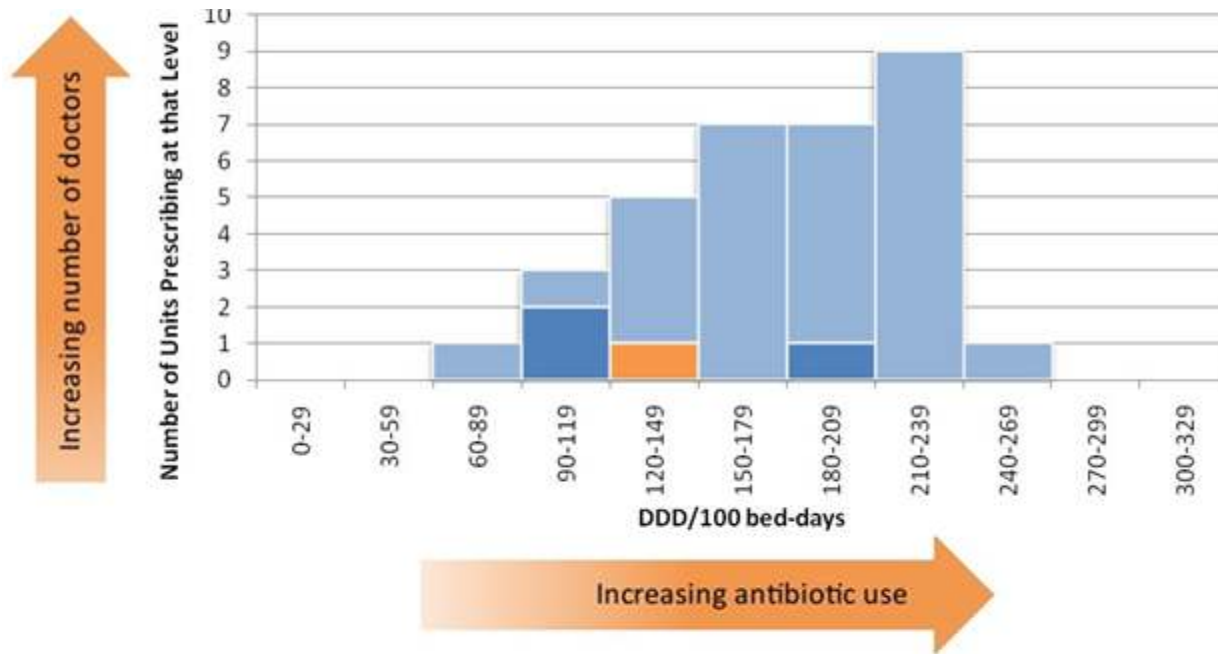
Patient Type 1 (CAI)
No contact with health care system
No prior antibiotic treatment
Patient young with few co-morbid conditions
<b>Send Sample for Culture</b>
<b>PRESUMPTIVE THERAPY</b>
Ampicillin/ Ampicillin-sulbactam/ Amoxi-Clavulanate Ceftriaxone Ciprofloxacin*
<b>After Culture Report</b>
<b>Continue Treatment</b>
S.typhi: Continue the treatment
<b>Stop "De-Escalate "</b>
Continue monotherapy
<b>Consider Escalation</b>
ESBL +ve Enterobacteriaceae including Salmonella: Escalate and treat as patient type 2

Patient Type 2 ( HAI )
Contact with health care system (e.g. recent hospital admission, nursing home, dialysis) without invasive procedure
Recent antibiotic therapy
Patient old with multiple co-morbidities.
<b>Send Sample for Culture</b>
<b>PRESUMPTIVE THERAPY</b>
Ertapenem/Tigecycline** ± Vancomycin/ Teicoplanin
<b>After Culture Report</b>
<b>Continue Treatment</b>
ESBL +ve Klebsiella / E.coli: Continue treatment with monotherapy
<b>Stop "De-Escalate "</b>
Non ESBL Enterobacteriaceae, De-Escalate & Treat it as patients type 1
<b>Consider Escalation</b>
PA/AB: Escalate and treat as Patient Type 3; in case of MRSA add Vancomycin or Teicoplanin

Patient Type 3 (NI)
Long hospitalization and or invasive procedures
Recent & multiple antibiotic therapies
Cystic fibrosis, structural lung disease, advanced AIDS, neutropenia, other severe immunodeficiency.
<b>Send Sample for Culture</b>
<b>PRESUMPTIVE THERAPY</b>
Colistin+Imipenem+Sulbactam ± Vancomycin or teicoplanin
<b>After Culture Report</b>
<b>Continue Treatment</b>
Susceptible PA/AB /MRSA: Continue treatment as monotherapy
<b>Stop "De-Escalate "</b>
ESBL Positive Enterobacteriaceae, De-Escalate and treat as Patients Type 2
<b>Consider Escalation</b>
MDR-PA or AB: Continue 3 Drug Colistin + Imipenem + Sulbactam

\*Avoid Ciprofloxacin since it has potent antipseudomonal activity

# Case Mix Based Antibiotic Consumption Monitoring







*Wisdom is  
the angel  
that lifts us  
to our feet  
when our  
wings have  
troubled  
remembering  
how to fly.*

**Thank You**