Global antibiotic use rises, fueled by economic growth

cidrap.umn.edu/news-perspective/2018/03/global-antibiotic-use-rises-fueled-economic-growth

Chris Dall | News Reporter | CIDRAP News | Mar 26, 2018

Editor's note: *This story was updated late on Mar 26 with comments from Debbie Goff, PharmD.*

A large new study of antibiotic use in humans shows an alarming rise in consumption around the world, driven predominantly by rising living standards in low- and middle-income countries (LMICs).

The study, published today in the *Proceedings of the National Academy of Sciences,* found that overall global antibiotic use rose by 65% from 2000 through 2015, while the antibiotic consumption rate increased by 39%. Over that period, antibiotic consumption in LMICs more than doubled, with some LMICs having consumption rates that surpassed those of high-income countries (HICs). The increase was correlated with growth in per capita gross domestic product (GDP).

The rise in consumption comes despite an increasing international focus on the threat of antibiotic resistance, which is driven by antibiotic use. Even though antibiotic consumption levels in many LMICs remain far below those of wealthier nations, the concern is that the pattern will continue as living standards rise around the globe and more people have access to antibiotics. And that could have a profound impact on public health.

"If things continue at the same rate they're going, without any sort of deviation, things are just going to get worse," study co-author Eili Klein, PhD, a professor in the department of emergency medicine at Johns Hopkins University and fellow at the Center for Disease Dynamics, Economics & Policy (CDDEP), told CIDRAP News.

Growth is driven by poorer nations

To come up with the global consumption estimates, researchers from CDDEP, Princeton University, the Institute of Integrative Biology in Zurich, and the University of Antwerp used pharmaceutical sales data from 76 countries, broken down between the retail and hospital sectors. Because there is no global body collecting antibiotic consumption data, Klein said, these are the best data currently available.

The investigators also looked for associations between consumption and economic and health indicators, including per capita GDP, measles vaccination coverage, and physician density per 1,000 inhabitants.

Overall, the researchers found that antibiotic consumption in the 76 countries increased from 21.1 billion to 34.8 billion defined daily doses (DDDs)—the standard measure of drug consumption—over the 16-year study period, while the antibiotic consumption rate rose from 11.3 to 15.7 DDDs per 1,000 inhabitants per day. Based on these data, total global consumption of antibiotics in 2015 was estimated to be 42.3 billion DDDs.

In LMICs, the total antibiotic consumption grew by 115%, climbing from 11.4 to 24.5 billion DDDs, and the consumption rate increased 78%, from 7.6 to 13.5 DDD per 1,000 inhabitants per day. Although the total amount of antibiotics consumed in HICs rose from 9.7 to 10.3 billion DDDs (6%), the consumption rate dropped by 4%, from 26.8 to 25.7 DDDs per 1,000 inhabitants per day.

A finding that underscores the rising use of antibiotics in lower-income countries was the fact that in 2015, the two countries with the highest consumption rate were LMICs—Turkey and Tunisia. Algeria and Romania were in fifth and sixth place, respectively. In 2000, the highest consumption rates were found in France, New Zealand, Spain, Hong Kong, and the United States. But the rate of consumption in most LMICs remains far below those in wealthier nations.

The largest increases in overall antibiotic consumption were also seen in LMICs—India (103%), China (79%), and Pakistan (65%). The total amount of antibiotics consumed in LMICs in 2015 was nearly 2.5 times that in wealthier nations.

The data also showed that the consumption of broad-spectrum penicillins increased by 36% from 2000 to 2015, with the greatest increase in LMICs (56%). LMICs also saw increases in consumption of cephalosporins (399%), quinolones (125%), and macrolides (119%), while consumption of these drugs dropped in HICs. Consumption of newer and last-resort antibiotics like carbapenems and polymixins increased across all countries, though consumption rates in LMICs remain much lower than in HICs.

Rising GDP tied to rising consumption

When Klein and his colleagues looked at factors affecting consumption, they found a positive association between per capita GDP growth and increasing antibiotic consumption in LMICs, but no such association in wealthier nations. No other indicators had a statistical impact. What this suggests, Klein explained, is that the antibiotic use is rising in these countries because more people can afford to buy them.

"In most lower-income countries, clearly the physician is not the primary barrier," Klein said. "The primary barrier to access is mostly related to the cost of the antibiotic. Economic growth allows increased access to antibiotics, which is most likely driving a significant proportion of the increase that we see."

While more people having access to antibiotics is beneficial, the question is whether the drugs are being used for the right reasons. Although this study could not determine whether any of the antibiotic consumption was inappropriate, Klein said that a certain amount of unnecessary use is likely, given that inappropriate outpatient antibiotic use in the United States and other developed nations is between 30% and 40%, and many low-income countries don't have stringent controls on use of the drugs.

"You have to assume that a huge proportion, or at least some of it, is due to inappropriate prescribing," he said.

The fact that antibiotic use in wealthy nations was not associated with GDP growth indicates that differences in consumption rates in these countries, some of which are significant, have less to do with access and more to do with attitudes toward antibiotic use and prescribing.

"What that sort of suggests is that once you hit a point of saturation, where access is no longer the barrier, it then becomes something much more related to norms," Klein said. Differing norms around antibiotic use might explain, for example, why antibiotic consumption rates in southern European countries like Greece are much higher than those in northern European countries such as the Netherlands.

Based on the data, Klein and his colleagues estimated that if no policies are implemented and all countries' antibiotic consumption increases at the current growth rate, total global antibiotic consumption will grow 202% by 2030.

"If there was ever a paper written that described why antibiotic stewardship must be implemented in every hospital, clinic, and outpatient setting in every country, this paper is it," said Debbie Goff, PharmD, an infectious disease and antibiotic resistance specialist at The Ohio State University Medical Center.

Strategies for reducing antibiotic use

Klein said that going forward the challenge will be to determine what strategies have proved effective in driving consumption rates down in a country like Singapore—which saw a drop of roughly 10 DDDs per 1,000 inhabitants per day over the study period—and importing those strategies into LMICs and wealthier nations where consumption remains high. But Goff, who was not involved in the study, said that won't be an easy process.

"Many LMICs, such as Algeria, are still struggling to figure out how to implement antibiotic stewardship," she said.

And Klein and his co-authors note that reducing consumption in poorer nations, which bear a higher burden of infectious disease, has to be achieved without limiting access to critically needed drugs.

An alternative, they suggest, is to focus on reducing the burden of disease in these countries by improving sanitation and water quality and increasing access to vaccines. Since antibiotics are often used as a surrogate for infection control in LMICs, this strategy could play a significant role in curbing rising consumption.

"When you look at the history of the 20th century, one of the big things that drove down the mortality rate in current high-income countries was improvements in infrastructure and sanitation…which dramatically reduced diarrheal diseases," said Klein. "So, in many of these low-and middle-income countries where antibiotic use is ramping up, investments in infrastructure and vaccines, both of which can reduce preventable diseases, would probably have a big effect in driving down antibiotic use as well."

Klein also suggested that antibiotic consumption targets could be an option as well. But this will require greater investments in surveillance to get more accurate assessments of antibiotic use. "These are good estimates, and the broadest and most up-to-date, but there's still no real harmonized, global consumption data," he said.

While Goff agrees that better surveillance is needed, she argues that, ultimately, healthcare providers in both poor and wealthy nations need to be better stewards of a dwindling resource. "All the surveillance in the world will not make a dent in antibiotic use if healthcare providers continue their current antibiotic prescribing behaviors," she said.

See also:

Mar 26 *Proc Natl Acad Sci USA* study