Antibiotic Resistance in India

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Disclaimer/Disclosures

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- No other Conflicts of Interest
Percentage of third generation cephalosporin resistant Escherichia coli, by country (2011–2014)
Percentage of carbapenem-resistant Klebsiella pneumoniae, by country (2011–2014)
Why India has high antibiotic resistance prevalence?
Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data

Thomas P Van Boeckel, Sumanth Gandra, Ashvin Ashok, Quentin Caudron, Bryan T Grenfell, Simon A Levin, Ramanan Laxminarayan

Summary

Background Antibiotic drug consumption is a major driver of antibiotic resistance. Variations in antibiotic resistance across countries are attributable, in part, to different volumes and patterns for antibiotic consumption. We aimed to assess variations in consumption to assist monitoring of the rise of resistance and development of rational-use policies and to provide a baseline for future assessment.

In 2010- India is the largest consumer of antibiotics, followed by China and the United States
Percentage change in antibiotic consumption per capita 2000–2010

Antibiotic consumption: 2014

Trends in antibiotic consumption in India: 2000-2010

Source: Laxminarayan R et al. PLOS Medicine, 2016.
Trends in antibiotic consumption in India

Source: IMS Health
Peak month of antibiotic consumption

Fixed Dose Combination (FDC) Antibiotics - India

- 118 (at least) FDC antibiotics are available in India
  - Cefixime + Azithromycin
  - Cefixime + Linezolid
  - Azithromycin + Levofloxacin
  - Cefixime + Levofloxacin

In India, faropenem has been approved for respiratory, urinary tract, skin and soft-tissue, and gynecological infections.
Attitude and Behavioral Aspects

• Reasons for prescribing antibiotics:

  **Private Sector**
  – Patient Pressure
  – Fear of losing patients
  – Lack of follow up
  – For profit

  **Public Sector**
  – Huge workload
  – Lack of diagnostic facilities
  – Pressure to use short-dated medicines

Kotwani A et al. IJMR in press
Global Antimicrobial Consumption in Food Animals

Some Hot spots:
Southeast coast China
South coast of India, Mumbai, Delhi

Van Boeckel et al PNAS- 2015
Countries with Highest Antimicrobial consumption in Food Animals

2010

Van Boeckel et al. PNAS. 2015.
Countries with Highest Antimicrobial consumption in Food Animals

Van Boeckel et al PNAS. 2015.
### Colistin sulphate for growth promotion in Food Animals- India

<table>
<thead>
<tr>
<th>Company</th>
<th>Brand Name</th>
<th>Antibiotic present</th>
<th>Information on label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venky’s</td>
<td>Bamylate</td>
<td>Bacitracin</td>
<td>For increased weight gain and improved feed efficiency</td>
</tr>
<tr>
<td></td>
<td>Tylomix</td>
<td>Tylosin</td>
<td>A growth promoter. In broilers it provides uniformity in growth</td>
</tr>
<tr>
<td></td>
<td>V-FUR 200</td>
<td>Furazolidone</td>
<td>V-Fur 200 is an ideal growth promoter for adult birds</td>
</tr>
<tr>
<td>Biomir Venture LLP</td>
<td>LINCO-MIR</td>
<td>Lincomycin</td>
<td>Helps to increase the growth, body weight with Colistin sulphate economical FCR in broilers</td>
</tr>
<tr>
<td></td>
<td>CO-MIR</td>
<td>Doxycycline</td>
<td>Helps to increase growth and body weight in broiler</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colistin sulphate</td>
<td>Improves feed consumption efficiency. Act as best performance booster</td>
</tr>
<tr>
<td></td>
<td>CON - MIR</td>
<td>Lincomycin Neomycin</td>
<td>Helps to increase the growth, body weight with economical FCR in broilers</td>
</tr>
<tr>
<td>Vetline India</td>
<td>Furavet</td>
<td>Furazolidone</td>
<td>An essential growth promoter. Ensures better growth, weight gain and feed conversion</td>
</tr>
<tr>
<td></td>
<td>Progrovet</td>
<td>Doxycycline</td>
<td>Better feed conversion hence increased weight gain in broilers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colistin sulphate</td>
<td></td>
</tr>
<tr>
<td>Ayugen Pharma Pvt. Ltd.</td>
<td>Lincomax</td>
<td>Lincomycin Metranidazole Colistin sulphate</td>
<td>Improves weight gain and F.C.R in broilers Helps in improving growth and performance</td>
</tr>
</tbody>
</table>

Source: Center for Science and Environment
Effluent Pollution From Antibiotics Manufacturing Units

• China supplies up to 90 percent active pharmaceutical ingredients (API) for antibiotics

• APIs mostly exported to India, processed and sold on to markets around the world
Effluent Pollution From Antibiotics Manufacturing Units

• ‘Good Manufacturing Practices’ (GMP), do not include environmental safeguards

• Unfortunately, environmental regulation are currently left up to national regulators
Ciprofloxacin concentration in Effluent from drug manufacturers, Hyderabad, India- 2006

- Up to 31,000 µg/L

- “Discharge load of 45 kg per day = amount consumed in Sweden (population nine million) over 5-days”
Corresponding microbiological analyses revealed carbapenemase-producing Enterobacteriaceae (carrying mainly *bla*OXA-48, *bla*NDM, and *bla*KPC) in more than 95% of the samples.

Lubbert C et al. *Infection*, April 2017
Conditions suitable for rapid spread of resistance genes in India
Risk of Extended Spectrum Beta-lactamase (ESBL) Enterobacteriaceae colonization for a traveler

- South Asia: 55%
- Asia (except South Asia): 39%

Hassing RJ et al. Eurosurveillance 2015
Kuenzli E et al. BMC ID 2014
Most Common Organisms Isolated from Early Onset Neonatal Sepsis Cases in India

Delhi Neonatal Infection Study- Lancet GH, October 2016
Perfect conditions for emergence of Superbugs

HUMAN SECTOR

- Human medicine
  - Therapeutic use

- Hospital
  - Community

- Antibiotics (Urine and faeces)
- Resistant bacteria

ANIMAL SECTOR

- Animal husbandry
  - Therapeutic and preventive use or growth promotion

- Plant production
  - Aquaculture

- Food

- Antibiotics (Urine and faeces)
- Resistant bacteria (Direct spread or run-off)

BREEDING GROUND

- Lakes, rivers and soils

PHARMA SECTOR

- Pharmaceutical industry
  - Accidental and intentional release of antibiotics from production plants

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI
Initiatives by Indian Government

- **National Policy for Containment of AMR-2011** (Ministry of Health & Family Welfare)

- **AMR Surveillance Network** establishment by ICMR and NCDC in 2011

- **Schedule H1** in March 2014- Selected group of antibiotics cannot be sold without prescription
Initiatives by Indian Government

• “Medicines with Red Line”: Public awareness campaign in February 2016

• Banned 63 antibiotic FDCs in March 2016, but......
Initiatives by Indian Government


1. Improve awareness and understanding of AMR through effective communication, education and training
2. Strengthen knowledge and evidence through surveillance
3. Reduce the incidence of infection through effective infection prevention and control
4. Optimize the use of antimicrobial agents in health, animals and food
5. Promote investments for AMR activities, research and innovations
6. Strengthen India’s leadership on AMR
India-UK Bilateral Agreement on AMR

• UK–India AMR Research Programme agreement- November 2016

• RCUK and Dept. of Biotechnology, India will oversee AMR research

• Call for Scoping report on “Mapping AMR Research in India” June 2017

• CDDEP selected to do the Scoping report which will be submitted by August 31st, 2017.
AMR Research Landscape in India

• Task 1- A concise overview of AMR situation in India
  – Literature search in “Pubmed”, “Google Scholar” and web search for grey literature for last five years
  – Include AMR situation in humans, agriculture, environment
  – Factors driving AMR
  – Policy initiatives

• Task 2- Mapping current AMR research
  – From Literature search in Task1, current AMR research will be collated in all areas (humans, agriculture, environment)
  – Identify major manufacturers of antibiotics (CDSCO, OPPI, FICCI) and their research programs into antimicrobial compounds

• Task 3- Information on AMR relevant data sources
  – From Literature search from Task1 AMR data sources will be identified
Thank you

ResistanceMap

ResistanceMap is an interactive collection of charts and maps that summarize national and subnational data on antimicrobial use and resistance worldwide.

Antibiotic Resistance
Choose a pathogen and compare resistance to different antibiotics across countries. World map, in-country trends over time, and charts to compare between countries.

Antibiotic Use
Compare use rates between countries and over time. World map, charts, and breakdowns by antibiotic class.

Explore by Country
Focus on a single country and explore maps and charts on either antibiotic use or antibiotic resistance. Sub-national data is available for the United States.

http://resistancemap.cddep.org/