Scoping Report on Antimicrobial Resistance in India - Key findings

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UK-India tackling AMR in the environment from antimicrobial manufacturing waste - Partnership workshop
AMR scoping report

Identified AMR research gaps in India
METHODOLOGY

- PubMed and Google Scholar databases were used.
- Following search terms: “antimicrobial OR antibiotic AND resistance AND India” were used.
- The search was limited to the last five years (July 1, 2012, to June 30, 2017).
METHODOLOGY

- Each article was assigned to one of the following eight categories:
  - Humans
  - Animals
  - Environment
  - Novel agents
  - Diagnostics
  - One health
  - Reviews/editorials
  - Miscellaneous
Antibacterial Resistance Situation in Humans, Animals and Environment in India
Carbapenem resistance among various bacteria in Humans

- E. coli: 11.5% (Gandra S et al. 2016), 16.2% (ICMR 2015)
- K. pneumoniae: 56.6% (Gandra S et al. 2016), 56.6% (ICMR 2015)
- P. aeruginosa: 46.8% (Gandra S et al. 2016), 41.8% (ICMR 2015)
- A. baumannii: 70.9% (Gandra S et al. 2016), 67.3% (ICMR 2015)
Carbapenem resistance genes among bacteria isolated from Humans

• NDM-1 has been the predominant gene encoding for carbapenem resistance in Enterobacteriaceae

• Recent studies indicate increasing occurrence of OXA-48

• More worrisome is increasing co-expression of both NDM-1 and OXA-48
Antibacterial Resistance Situation in Humans—Colistin resistance

• Colistin resistance among gram-negative bacteria has emerged in India

• Bloodstream infections due to colistin-resistant *K. pneumoniae* are associated with 69.3% mortality among Indian patients

• Plasmid-mediated colistin resistance genes *mcr-1* and *mcr-2* were not detected frequently
Antibacterial Resistance Situation in Food animals

- NDM-1 and vancomycin-resistant *Staphylococcus aureus* (VRSA) strains in milk samples obtained from cows with mastitis have been reported.

- NDM-1 strains **have not been** reported from poultry and fish.

- *mcr-1/mcr-2* gene-producing bacteria conferring resistance to colistin **have not been** reported in food animals.
Antibacterial Resistance Situation in Environment

• NDM-1 and OXA-48 genes have been detected in major rivers like Ganga, Yamuna and Cauvery

• *mcr-1* gene conferring resistance to colistin was detected in Mutha river, Pune
Factors Driving Antibiotic Resistance in India
Human Antibiotic consumption: 2014

High consumption of broad-spectrum antibiotics in humans

- Trends in antibiotic consumption 2000-2015
Lack of availability of narrow-spectrum agents

Number of formulation companies manufacturing various antibiotics for human use
Fixed Dose Combination (FDC) Antibiotics

• 118 (at least) FDC antibiotics are available in India
  – Cefixime + Azithromycin
  – Cefixime + Linezolid
  – Azithromycin + Levofloxacin
  – Cefixime + Levofloxacin ........
Social Factors

Among general public
- self-medication
- access to antibiotics without prescription
- use of pharmacies and informal healthcare providers as sources of healthcare
- lack of knowledge about when to use antibiotics

Healthcare providers in private sector
- perceived patient demand
- fear of losing patients if asked for diagnostic investigations
- diagnostic uncertainty
- economic incentives from pharmaceutical companies
- lack of continuing medical education

Healthcare providers in public sector
- heavy patient load
- pressure to use short-dated medicines
- lack of diagnostic facilities
- lack of continuing medical education
Cultural Activities

NDM-1 levels are **20 times greater** in the Ganga river at the time of pilgrimage season when compared to non-pilgrimage season.
Antibiotic consumption in animals

- It is estimated that India was the fifth-largest consumer of antibiotics in food animals (poultry, cattle and pigs) in 2010.

- Antibiotic use is projected to grow by 312%, making India the fourth-largest consumer of antibiotics in food animals by 2030.
Antibiotic consumption in animals

• Use of antibiotics as growth promoters in food animals and poultry is a common practice; however, the true extent of this practice is unknown

• Concerning issue is the use of colistin for growth promotion, prophylaxis, and therapeutic purposes in poultry
Pharmaceutical industry pollution

• It is estimated that 80% of the antibiotics sold by multinational pharmaceutical companies on the global market are manufactured in India and China.

• Effluents coming from manufacturing units contain antibiotic residues.

• Regulation of environmental discharges from the manufacturing units is left to the local governments.

• Current pollution standards do not include antibiotic residues, and thus they are not monitored in the pharmaceutical industry effluent.
Antibiotic API manufacturer hotspots

There are at least 40 antibiotic API manufacturers in India
Effluent Pollution From Antibiotics Manufacturing Units

• ‘Good Manufacturing Practices’ (GMP), do not include environmental safeguards
Antibiotic Formulation companies hotspots

At least 250 antibiotic formulation companies in India

Cities/towns with 5 or more drug (antimicrobials and/or others) manufacturing units

Cities/towns with 4 or fewer drug (antimicrobials and/or others) manufacturing units
Poor Environmental Sanitation

Population without access to improved sanitation facilities, 2015
Inability to remove antibiotic resistant bacteria and genes in Sewage treatment Plants (STPs)

*E. coli* resistance to third-generation cephalosporins among STPs

- **STP receiving domestic waste**: 25%
- **STP receiving domestic and hospital waste**: 70%
- **STP receiving hospital waste**: 95%
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

- **Acinetobacter spp**: 27.1%
- **CONS**: 16.6%
- **Klebsiella spp**: 15.7%
- **E.coli**: 14%
- **S. aureus**: 10.5%
- **Enterococcus spp**: 6%
- **Pseudomonas spp**: 5.9%
- **Enterobacter spp**: 4.3%

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

HUMAN SECTOR

ANIMAL SECTOR

PHARMA SECTOR

BREEDING GROUND
AMR policy update in India

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

- **AMR Surveillance Network** establishment by ICMR and NCDC in 2013

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

- Publication of National Treatment Guidelines for Antimicrobial Use in Infectious Diseases by NCDC and ICMR- 2016

- National address by Prime Minister on the issue of antibiotic resistance in his *Man Ki Baat* (a radio program hosted by the honorable prime minister of India) in August- 2016
AMR policy update in India

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

• National Action Plan on AMR 2017-2021: April 2017

• The Food Safety and Standards (Contaminants, Toxins and Residues) Regulations in food animals- June 2017
AMR Research Landscape in India
AMR publications in eight categories (n=2152)

- Humans: 48%
- Novel agents: 18%
- Miscellaneous: 12%
- Review/Editorial: 13%
- One Health: 1%
- Environment: 4%
- Diagnostics: 1%
- Animals: 3%
- Miscellaneous: 12%
Top 10 institutions with AMR publications

CMC Vellore  AIIMS Delhi  Manipal University  Aligarh Muslim University  Banaras Hindu University  Panjab University  NICED Kolkata  PGIMER Chandigarh  Assam University  VIT University

Animals  Environment  Humans  Novel agents  Miscellaneous  Diagnostics  One health
AMR research in India

• AMR research studies in India were of limited scope in all areas, including humans, animals and environment

• Most of them are surveillance based studies

• Novel agent studies were limited to in vitro experiments

• Limited number of studies on novel diagnostics and there were no “one health” studies

• Studies examining the impact of various policies were also lacking
Recommendations for future studies

• Burden of antibiotic resistance in various groups (neonates, children, young adults, the elderly)

• Interdisciplinary studies (one health approach) to understand the relative contribution of different reservoirs (humans, animals, environment) to the burden of AMR problem

• Studies on waste management to reduce the contamination of rivers during religious mass gatherings

• Developing novel technologies to remove antibiotic-resistant bacteria and genes from sewage treatment plants
Recommendations for future studies

• Conducting large-scale studies on antibiotic use for various purposes (growth promotion, prophylaxis, treatment) among food animals, especially in poultry

• Developing standards and detection tools for antibiotic residues in pharmaceutical industrial effluents

• Focusing on supply systems and market dynamics of antibiotic production for animal use
Thank you

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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/
Percentage of third generation cephalosporin resistant *Escherichia coli*, by country (2011–2014)

State of the World’s Antibiotics Report, CDDEP 2015
Percentage of carbapenem-resistant *Klebsiella pneumoniae*, by country (2011–2014)

State of the World’s Antibiotics Report, CDDEP 2015