Conducting surveillance of antimicrobial resistance and residues in the hospital and community environment

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Present focus: Measurement of resistance in clinical settings only

Antibiotics in aquatic environment as vital public health problem undiscovered

Few studies in developing countries reported antibiotics in aquatic environment

Increased use of antibiotics

Insufficient wastewater treatment facilities
Dissemination of antibiotics and antibiotic resistance within agriculture, community, hospital, wastewater treatment, and associated environments.
Scope of Present Presentation ...........

• Community environment
• Hospital environment
• Water and waste water treatment plants
• River and Reservoir Environment

• Not Covered
  • Fish and Aquaculture
  • Poultry
  • Pharmaceutical Plants and related waste
  • Food and related Items
Environmental Surveillance of AMR depends on

- **Time**
  - Short term goals
  - Long term goals

- **Scale**
  - Pan India
  - Few States
  - Few districts

- **Available Resources**
  - Data collection (Primary and Secondary)
  - Analysis cost
  - Result dissemination

- **Feasibility**

- **Organization of Surveillance Activities**
  - Who will do it
  - Part of ongoing initiative
  - Vertical Programme
  - Current capacity
  - Required capacity Building (Laboratory, Analysis etc)
  - Training, ethical issues etc
  - Data Integration and Management
Selection of Antibiotics for residual analysis

• (i) the prescription pattern that area

• (ii) antibiotic residues found in the same setting in previous studies

• (iii) the degree of antibiotic metabolism by the human body

• (iv) environmental stability, and

• (v) the known and suspected environmental impact of an antibiotic
Selection of Antibiotics

Antibiotics for AST Pattern

• Ampicillin, Cefotaxime, Ceftazidime, Cefepime, Imipenem, Meropenem, Ciprofloxacin, Nalidixic Acid, Gentamicin, Amikacin, Nitrofurantoin, Tetracycline, Sulphamethizole, Corimoxazole, colistin

Antibiotics for Residual Testing

• Ciprofloxacin, Enrofloxacin, Erthromycin, Norfloxacin, Ofloxacin, Sulfamethoxozole, Trimethoprim, Metronidazole, Amoxicillin, Ampicillin, Total Residual Antibiotics as beta-lactam
Surveillance of Resistance and Residues in Hospital Environment
Antibiotic residues, metabolites and antibiotic resistance bacteria

Untreated hospital effluent

Antibiotic residues, metabolites and antibiotic resistance bacteria
<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Site 1</th>
<th>Site 2</th>
<th>Site 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ground Water</td>
<td>Municipal Water</td>
<td>At 10:00</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Amikacin</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>--</td>
<td>--</td>
<td>2.2</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

-- = Below Detection Limit
Site 1 = Incoming safe water (received in hospital only once a day)
Site 2 = At the point of exit of inpatient wards of the hospital
Site 3 = 100 metres from the hospital in subsequent drains
Table 1. Concentration of antibiotic released/day/hospital (ng/L).

<table>
<thead>
<tr>
<th></th>
<th>CIP</th>
<th>LEV</th>
<th>OFL</th>
<th>NOR</th>
<th>FQ</th>
<th>MET</th>
<th>SUL</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CS</td>
<td>GS</td>
<td>CS</td>
<td>GS</td>
<td>CS</td>
<td>GS</td>
<td>CS</td>
<td>GS</td>
</tr>
<tr>
<td>Summer</td>
<td>155.5</td>
<td>–</td>
<td>472</td>
<td>35</td>
<td>96</td>
<td>–</td>
<td>–</td>
<td>191</td>
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<tr>
<td>Rains</td>
<td>694</td>
<td>1239</td>
<td>66</td>
<td>88</td>
<td>90</td>
<td>85</td>
<td>40</td>
<td>225</td>
</tr>
<tr>
<td>Winter</td>
<td>245</td>
<td>1836</td>
<td>578</td>
<td>1078</td>
<td>495</td>
<td>475</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>1095</td>
<td>3076</td>
<td>644</td>
<td>1638</td>
<td>620</td>
<td>656</td>
<td>40</td>
<td>225</td>
</tr>
<tr>
<td>Average (Total/3)</td>
<td>365</td>
<td>1025</td>
<td>214</td>
<td>546</td>
<td>206</td>
<td>218</td>
<td>13</td>
<td>75</td>
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</tbody>
</table>

Surveillance of Resistance and Residues in Hospital associated waters

• Starting Point
  • Start with at least 10 Hospital with more than 100 beds
  • Scale up as per resources

• Sampling
  • Four Times in a year (to study seasonality)
  • Hospital waste water
  • Hospital incoming water
  • Continuous or Grab Sampling

  • Hospital Environment (OT, Labour room, surfaces)

• Indicator Bacteria
  • E.coli
  • Klebsiella spp

Analysis
  • CFU
  • Antibiotic Residues
  • AST Patterns, ESBL
  • Antibiotic resistance genes (optional)
  • Inpatient Hospital antibiotic use
Seasonal and Temporal Variation in Release of Antibiotics in Hospital Wastewater: Estimation Using Continuous and Grab Sampling

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Antibiotics and antibiotic-resistant bacteria in waters associated with a hospital in Ujjain, India

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Surveillance of Resistance and Residues in River Environment
Antibiotic resistance and multidrug resistance patterns of *E. coli* isolated from river water samples in different seasons in Kshipra river in India

<table>
<thead>
<tr>
<th>RIVER WATER SAMPLES</th>
<th>Summer n=70*</th>
<th>Rain n=80**</th>
<th>Autumn n=70***</th>
<th>Winter n=83****</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
<td></td>
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<tr>
<td>Ampicillin</td>
<td>12 (17)</td>
<td>27 (33)</td>
<td>32 (45)</td>
<td>33 (39)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>14 (20)</td>
<td>15 (18)</td>
<td>14 (20)</td>
<td>24 (28)</td>
<td>0.4</td>
</tr>
<tr>
<td>Imipenem</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>4 (4)</td>
<td>0.5</td>
</tr>
<tr>
<td>Meropenem</td>
<td>7 (10)</td>
<td>0 (0)</td>
<td>4 (5)</td>
<td>22 (26)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>4 (5)</td>
<td>7 (8)</td>
<td>10 (14)</td>
<td>12 (14)</td>
<td>0.2</td>
</tr>
<tr>
<td>Nalidixic Acid</td>
<td>8 (11)</td>
<td>11 (13)</td>
<td>16 (22)</td>
<td>21 (25)</td>
<td>0.08</td>
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<td>Amikacin</td>
<td>13 (15)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>13 (15)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Sulphamethizole</td>
<td>5 (7)</td>
<td>11 (13)</td>
<td>12 (17)</td>
<td>7 (8)</td>
<td>0.2</td>
</tr>
<tr>
<td>ESBL</td>
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<td>10 (11)</td>
<td>10 (12)</td>
<td>5 (6)</td>
<td>0.4</td>
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<tr>
<td>MDR</td>
<td>2 (2)</td>
<td>15 (17)</td>
<td>19 (24)</td>
<td>20 (23)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Antibiotic resistance and multidrug resistance patterns of *E. coli* isolated from river sediment samples in different seasons in Kshipra river in India

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Rain n= 31*</th>
<th>Autumn n=27**</th>
<th>Winter n=39***</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Ampicillin</td>
<td>9 (29)</td>
<td>9 (33)</td>
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<tr>
<td>Cefotaxime</td>
<td>9 (29)</td>
<td>6 (22)</td>
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</tr>
<tr>
<td>Imipenem</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (5)</td>
<td>0.33</td>
</tr>
<tr>
<td>Meropenem</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>11 (28)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>6 (19)</td>
<td>7 (25)</td>
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<td>11 (40)</td>
<td>11 (28)</td>
<td>0.34</td>
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<tr>
<td>Amikacin</td>
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<td>1 (3)</td>
<td>2 (5)</td>
<td>0.62</td>
</tr>
<tr>
<td>Sulphamethizole</td>
<td>5 (16)</td>
<td>7 (25)</td>
<td>7 (17)</td>
<td>0.65</td>
</tr>
<tr>
<td>Corimoxazole</td>
<td>6 (19)</td>
<td>8 (29)</td>
<td>7 (17)</td>
<td>0.55</td>
</tr>
<tr>
<td>MDR</td>
<td>9 (26)</td>
<td>10 (34)</td>
<td>10 (24)</td>
<td>0.67</td>
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</table>
Antibiotic resistance-coding genes present in the Escherichia coli isolates from river water in different seasons in Kshipra river in India

<table>
<thead>
<tr>
<th>Antibiotic resistance genes</th>
<th>Autumn n(%)</th>
<th>Rain n(%)</th>
<th>Summer n(%)</th>
<th>Winter n(%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTX-M1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9 (50)</td>
<td>10 (31)</td>
<td>8 (23)</td>
<td>8 (19)</td>
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<tr>
<td>CTX-M2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0 (0)</td>
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<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>CTX-M9&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>qnrA.&lt;sup&gt;A&lt;/sup&gt;&lt;sub&gt;b&lt;/sub&gt;</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>qnrA.&lt;sup&gt;B&lt;/sup&gt;&lt;sub&gt;b&lt;/sub&gt;</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>(5)</td>
<td>0 (0)</td>
<td>0.2</td>
</tr>
<tr>
<td>qnrA.&lt;sup&gt;S&lt;/sup&gt;&lt;sub&gt;b&lt;/sub&gt;</td>
<td>2 (8)</td>
<td>6 (23)</td>
<td>2 (10)</td>
<td>7 (16)</td>
<td>0.5</td>
</tr>
<tr>
<td>Sul.1&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3 (13)</td>
<td>4 (12)</td>
<td>2 (5)</td>
<td>4 (12)</td>
<td>0.6</td>
</tr>
<tr>
<td>Sul.2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5 (21)</td>
<td>6 (18)</td>
<td>4 (10)</td>
<td>4 (12)</td>
<td>0.6</td>
</tr>
<tr>
<td>NDM&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
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<tr>
<td>VIM&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>0 (0)</td>
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</table>
Antibiotic resistance-coding genes present in the Escherichia coli isolates from river sediment in different seasons in Kshipra river in India

<table>
<thead>
<tr>
<th>Antibiotic resistance genes</th>
<th>Autumn n(%)</th>
<th>Rain n(%)</th>
<th>Winter n(%)</th>
<th>p-value*</th>
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<tbody>
<tr>
<td>CTX-M1</td>
<td>2 (40)</td>
<td>5 (25)</td>
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<tr>
<td>CTX-M2</td>
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<td>0 (0)</td>
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<tr>
<td>CTX-M9</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>QNR.B</td>
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<td>4 (44)</td>
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<td>2 (33)</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>VIM</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
</tbody>
</table>
Surveillance of Resistance and Residues in River Environment

• Starting Point
  • Major River River System
  • Reservoirs
  • Scale up as per resources

• Sampling
  • Four Times in a year (to study seasonality)
  • Surface water samples
  • Sediment samples
  • During Mass bathing Occasions

• Indicator Bacteria
  • *E.coli*
  • *Klebsiella spp*

Analysis
• CFU
• Basic Water quality and river flow
• Antibiotic Residues
• AST Patterns, ESBL
• Antibiotic resistance genes (optional)
Concept Paper


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5 Department of Microbiology, R.D. Gardi Medical College, Ujjain 456003, India; sharshada1955@yahoo.com
6 R.D. Gardi Medical College, Ujjain 456006, India; uctharc@sancharnet.in
7 India: Initiating for Management of Antibiotic Resistance, Department of Environmental Medicine, R.D. Gardi Medical College, Ujjain 456006, India.
Surveillance of Resistance and Residues in Community
Antibiotic Resistance in Children Stool Samples and its Environment in Rural Ujjain

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>% Resistance (E.Coli)</th>
<th>Human Stool</th>
<th>Animal Stool</th>
<th>Household Drinking Water</th>
<th>Source Drinking Water</th>
<th>Waste Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime</td>
<td></td>
<td>51</td>
<td>14</td>
<td>21</td>
<td>35</td>
<td>30</td>
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<tr>
<td>Cefotaxime</td>
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<td>22</td>
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<td>31</td>
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<td>Ampicillin</td>
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<td>59</td>
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<td>23</td>
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<td>38</td>
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<tr>
<td>Nalidixic Acid</td>
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<tr>
<td>Ciprofloxacin</td>
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<td>15</td>
<td>4</td>
<td>8</td>
<td>9</td>
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<td>Imipenem</td>
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<td>0</td>
<td>3</td>
<td>0</td>
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<td>Meropenem</td>
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<td>4</td>
<td>4</td>
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<td>8</td>
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<td>Sulphamethiazole</td>
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<td>27</td>
<td>17</td>
<td>16</td>
<td>26</td>
<td>27</td>
</tr>
</tbody>
</table>
Surveillance of Resistance and Residues in Community

- **Cohort of Household**
  - Follow-up of all members of cohort
  - Health seeking behavior (common illness)
  - Drug information
- **Sample Collection**
  - Human Stool
  - Drinking Water
  - Source Water
  - Waste Water
  - Animal Stool
One Health
Surveillance of Resistance and Residues in Community

• **Scale**
  • Start with 6 Household Cohorts in selected states
  • Three Urban and Three Rural Cohorts
  • Demographic Surveillance Site (DSS) can be ideal starting points

**Follow up of Cohort (Short Term)**
  • Six Month Initially
  • Sample collection two times

**Follow up of Cohort (Long Term)**
  • Health seeking follow up every three month for one Month duration
  • Sample collection three times in Year

• **Indicator Bacteria**
  *E. coli*

**Analysis**
  • CFU, Basic Water quality parameters, AST
  • Antibiotic Residues and Antibiotic Genes (can be optional)
Protocol: a ‘One health’ two year follow-up, mixed methods study on antibiotic resistance, focusing children under 5 and their environment in rural India

Surveillance of Resistance and Residues in wastewater treatment plants

- **Starting Point**
  - Start with at least 10 wastewater treatment plants
  - Sewage treatment plants
  - Waste water treatment plants (in hospitals)
  - Cooperation from hospital is must
  - Scale up as per resources

- **Sampling**
  - Four Times in a year (to study seasonality)
  - Incoming water waste water
  - Sludge
  - Treated water
  - Continuous or Grab Sampling

- **Indicator Bacteria**
  - *E.coli*
  - *Klebsiella spp*

**Analysis**
- CFU
- Antibiotic Residues
- AST Patterns, ESBL
- Antibiotic resistance genes (optional)
Example of Integrated Surveillance
Setting  Madhya Pradesh

- Urban and Rural Cohort in Ujjain
- Municipal wastewater treatment plants (Ujjain, Bhopal, Indore)
- Hospital wastewater treatment plants  (Ujjain, Bhopal, Indore)
- Hospital waste water  (Ujjain, Bhopal, Indore one hospital each)
Attention are also needed on ............

• Surveillance Biomedical waste management

• Collection and disposal of unused antibiotics in community

• Hospital hygiene and cleanliness surveillance

• Surveillance of antibiotic consumption from Pharmacy (with prescription without prescription)
  • Simulated client study
  • Prescription Audit at Pharmacy
Thanks for attention

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