Antibiotic Use in Human Health
The India Scenario

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AMR – an alarming situation

Enterobacteriaceae:

*E.coli*: <30% susceptible 3GC & cipro; 85-90% susceptible to carbapenem

*Klebsiella spp*: <35% susceptible to 3GC; < 50% to Pip/Tazo & <55% susceptible to carbapenem

Tigecycline and colistin shows 100% susceptibility

*S Typhi*: A,Ch, SXT is highly susceptible and to avoid cipro

Non-Typhoidal: cipro and ampicillin resistance

*Shigella spp*: quinolones and co trimoxazole resistance is high

Non-fermenters:

*Pseudomonas spp*: ~70 % susceptible to various antibiotics

*Acinetobacter spp*: almost all are <40% susceptible, except colistin
Antibiotic use vs. resistance

Is Antibiotic use is a contributory factor to Antibiotic resistance?

   *Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and metanalysis.* 
   *BMJ.* 2010 May 18; 340: c2096.

   *Outpatient antibiotic use in Europe and association with resistance: a cross-national database study.* 
Antibiotic Use Research in LMIC setting

- Surveillance & challenges
- Measurement issues for antibiotic data & time periods
- Advantages and disadvantages of methods
- Strategic points for collecting data
- Key players in antibiotic use
Examples of Antibiotic Use Monitoring

1. Antibiotic use patterns & surveillance in community

2. Antibiotic practice & misuse in community

3. Patterns of Use in hospital, and measurement of impact of interventions such as Ab guidelines
1. Antibiotic Use Surveillance


- Objective: To determine pattern of antibiotic encounters in health facilities through development of an antibiotic use surveillance system in rural and urban areas of Vellore.

- Design: Surveillance with repeated cross sectional measurement

- Health provider facilities: Hospitals, General Practice (GP) clinics, Pharmacy shops (outlets).

- Two methods:
  1. Individual patient (using % encounters converted to DDD)
  2. Bulk Sales (using DDD)
Patient Method

• Defined daily dose (DDD) calculated for specific antibiotics

• Data collected from each facility included:
  (i) number of encounters with antibiotic - subsequently converted into %
  (ii) type of antibiotics used - subsequently grouped
  (iii) Dose & quantity of antibiotic prescribed or dispensed - for calculation of number of DDDs.

• Ab use expressed as % of encounters with specific Ab
• Converted into DDDs of specific Ab use per 100 patients.
Alternative Method – Bulk Use

• Reviewing sales/purchase records for specific Ab in facilities

• Such records available only in pharmacy shops (outlets) and rural hospitals

• Assessing total amount of specific Ab in records

• Calculating DDDs/100 patients attending specific facility per month.
Main Findings

• In 2 years: 21,600 antibiotic encounters among 52,788 patients

• Overall antibiotic use: 41%

• Patterns of antibiotic use
  
  - Fluoroquinolones and penicillins: widely used
  
  - Cotrimoxazole: rural hospitals use most
  
  - Cephalosporins: urban private hospitals used more

• Antibiotics for respiratory infection symptoms: 41%
Antibiotic Encounters

Antibiotic encounters in all facilities as DDD/100 patients/month

CEP – Cephalosporins, ESP – Extended Spectrum Penicillins, FLQ – Fluoroquinolones, TET – Tetracyclines, SXT – Sulfamethoxazole and trimethoprim

Antibiotic Encounters in health facilities

Antibiotic Encounters as DDD/100 patients
Urban Pharmacy Shops - Phase A

Antibiotic Encounters as DDD/100 patients
Rural Hospitals - Phase A
Antibiotic Bulk Use

Antibiotic sales in facilities measured as DDD/100 patients/month


### Top three antibiotics for patients symptoms

<table>
<thead>
<tr>
<th>Symptom group</th>
<th>Patient encounters (n=10800)</th>
<th>Most common antibiotic</th>
<th>Antibiotic encounters (%)</th>
<th>Second most common antibiotic</th>
<th>Antibiotic encounters (%)</th>
<th>Third most common antibiotic</th>
<th>Antibiotic encounters (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchial</td>
<td>292</td>
<td>AMX</td>
<td>97 (33)</td>
<td>SXT</td>
<td>63 (22)</td>
<td>DOX</td>
<td>40 (14)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>435</td>
<td>PEN</td>
<td>404 (93)</td>
<td>AMP</td>
<td>7 (2)</td>
<td>SXT</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Dental</td>
<td>353</td>
<td>AMX</td>
<td>150 (42)</td>
<td>TET</td>
<td>42 (12)</td>
<td>DOX</td>
<td>35 (10)</td>
</tr>
<tr>
<td>Ear and Eye</td>
<td>243</td>
<td>AMX</td>
<td>52 (21)</td>
<td>SXT</td>
<td>38 (16)</td>
<td>CIP</td>
<td>32 (13)</td>
</tr>
<tr>
<td>Fever</td>
<td>2292</td>
<td>CIP</td>
<td>737 (32)</td>
<td>AMX</td>
<td>364 (16)</td>
<td>SXT</td>
<td>184 (8)</td>
</tr>
<tr>
<td>Fever and Cough</td>
<td>332</td>
<td>AMX</td>
<td>96 (29)</td>
<td>CIP</td>
<td>70 (21)</td>
<td>SXT</td>
<td>35 (11)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>705</td>
<td>NOR</td>
<td>300 (43)</td>
<td>SXT</td>
<td>143 (20)</td>
<td>CIP</td>
<td>93 (13)</td>
</tr>
<tr>
<td>Gynaecological</td>
<td>185</td>
<td>DOX</td>
<td>114 (62)</td>
<td>CIP</td>
<td>15 (8)</td>
<td>SXT</td>
<td>15 (8)</td>
</tr>
<tr>
<td>Lower Respiratory</td>
<td>1241</td>
<td>AMX</td>
<td>424 (34)</td>
<td>OFX</td>
<td>114 (9)</td>
<td>CIP</td>
<td>93 (7)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>187</td>
<td>CIP</td>
<td>43 (23)</td>
<td>OFX</td>
<td>36 (19)</td>
<td>AMX</td>
<td>28 (15)</td>
</tr>
<tr>
<td>Surgery related</td>
<td>340</td>
<td>CTX</td>
<td>85 (25)</td>
<td>SXT</td>
<td>73 (21)</td>
<td>CIP</td>
<td>53 (16)</td>
</tr>
<tr>
<td>Skin Soft tissue</td>
<td>568</td>
<td>AMX</td>
<td>80 (14)</td>
<td>CIP</td>
<td>76 (13)</td>
<td>SXT</td>
<td>62 (11)</td>
</tr>
<tr>
<td>Urinary</td>
<td>516</td>
<td>NOR</td>
<td>195 (38)</td>
<td>CIP</td>
<td>73 (14)</td>
<td>DOX</td>
<td>58 (11)</td>
</tr>
<tr>
<td>Upper Respiratory</td>
<td>2132</td>
<td>AMX</td>
<td>652 (31)</td>
<td>SXT</td>
<td>161 (8)</td>
<td>RXM</td>
<td>158 (7)</td>
</tr>
<tr>
<td>Wound</td>
<td>979</td>
<td>LEX</td>
<td>176 (18)</td>
<td>AMX</td>
<td>134 (14)</td>
<td>AMP</td>
<td>126 (13)</td>
</tr>
</tbody>
</table>


Challenges in surveillance

• Permission from facilities.

• Difficult to compare with studies using fixed populations or inhabitants as denominator.

• Many facilities did not have or would not reveal sales records or not organized in a systematic manner.

• Huge data set.

• Intensive effort for data entry, verification, cleaning and analytical issues eg., combination drugs, number of brands

• Multidisciplinary team approach needed for surveillance.

• Funding and leadership support needed for sustainability
2. Antibiotic Practice & Misuse


■ Objectives:
1. To determine proportion of patients prescribed antibiotics having URI /fever/ diarrhoea
2. To describe antibiotic pattern and related factors

■ Design: Cross sectional survey with cluster sampling

■ Setting:
Govt. facilities: Hospitals (Urban) & PHCs (Rural)
Private facilities: Hospitals, Private Clinics (Urban & Rural)
Method - % prescriptions

- Government rural stratum - 20 PHCs randomly selected.
- Government urban stratum - 2 district & 4 taluk hospitals.
- Private rural stratum – 20 GP clinics
- Private urban stratum - 20 GP clinics & hospitals
- 100 prescriptions from govt urban hospitals, 30 prescriptions from all other facilities
# Antibiotic use by strata

<table>
<thead>
<tr>
<th></th>
<th>Overall  (N = 4058)</th>
<th>Rural  (N = 1548)</th>
<th>Urban  (N = 2510)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>3041 (74.9 %)</td>
<td>1199 (77.5 %)</td>
<td>1842 (73.4 %)</td>
</tr>
<tr>
<td></td>
<td>Gov't  (N = 2517)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>3041 (74.9 %)</td>
<td>1959 (77.8 %)</td>
<td>1082 (70.2 %)</td>
</tr>
<tr>
<td></td>
<td>Private  (N = 1541)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Top 10 antibiotics in gov’t & private facilities

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>GOVT (N= 2178)</th>
<th>PVT (N=1236)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>1109</td>
<td>50.9</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>391</td>
<td>18.0</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>56</td>
<td>2.6</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>161</td>
<td>7.4</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>73</td>
<td>3.4</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>119</td>
<td>5.5</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>3</td>
<td>0.2</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>158</td>
<td>7.3</td>
</tr>
<tr>
<td>Cefalexin</td>
<td>8</td>
<td>0.5</td>
</tr>
</tbody>
</table>
## Top 10 antibiotics in Rural & Urban facilities

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>RURAL (N=1336)</th>
<th>URBAN (N=2078)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>665</td>
<td>49.8</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>179</td>
<td>13.4</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>67</td>
<td>13.5</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>106</td>
<td>7.9</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>64</td>
<td>4.8</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>66</td>
<td>4.9</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>7</td>
<td>0.5</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>92</td>
<td>6.9</td>
</tr>
<tr>
<td>Cefalexin</td>
<td>2</td>
<td>0.1</td>
</tr>
</tbody>
</table>
Objective: To assess consumption of antibiotics over ten years & evaluate role of policy guidelines in containing antibiotic use

Method
- Pharmacy computer system: antibiotic dispensation data
- Number of DDDs calculated monthly for individual antibiotic
- Divide by patients occupying beds per month - bed days
- To assess impact of guidelines: Interrupted time series (ITS)
- Monthly data points before & after policy implementation
- Segmented Regression Analysis
Findings - Patterns of Use

Calendar plot showing patterns of use for tetracyclines

Impact of Policy Guidelines

Overall antibiotic use with segments demarcated by vertical lines.

1 – Before guidelines booklet dissemination
2 – Stakeholder involved guideline booklet dissemination
3 – No active guideline booklet dissemination
4 – Revised guideline booklet dissemination
5 – Revised guideline booklet dissemination & intranet access

Patterns and Trends of Use

Calendar plot showing patterns & trends of use for other Beta-Lactams

Needs for Surveillance

1. Models of monitoring/surveillance in different contexts
2. Prioritizing key microbes & antibiotics for monitoring
3. Training for health professionals, academics & field staff in surveillance methods
4. Specific software for uniformity, validity & evidence base
5. Sustainability planning for continuance of surveillance
Surveillance in LMIC

– a challenge,

but the need is paramount

Thank You