POLICY BRIEF

A point prevalence survey of paediatric antimicrobial use and healthcare-associated infections in three academic hospitals in South Africa

Prakash Jeena1,2, Terusha Chetty3,4, Ashendri Pillay1, Moherndran Archary5, David P Moore6,7, Jeané Cloete5,8, Maria Karsas5, Tarylee Reddy9,10, Yusentha Balakrishna9, Firdose Nakwa5, Ruth Lancaster11, Ameena Goga3,12

1 Department of Paediatrics and Child Health, University of KwaZulu-Natal, Durban, South Africa
2 Department of Paediatrics and Child Health, Inkosi Albert Luthuli Central Hospital, Durban
3 HIV and Other Infectious Diseases Research Unit, South African Medical Research Council, South Africa
4 Department of Public Health Medicine, University of KwaZulu-Natal, Durban, South Africa
5 Department of Paediatrics and Child Health, Chris Hani Baragwanath Academic Hospital, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
6 South African Medical Research Council Vaccine and Infectious Diseases Analytics (VIDA) Research Unit, University of the Witwatersrand, Johannesburg, South Africa
7 Department of Paediatrics and Child Health, Steve Biko Academic Hospital, University of Pretoria, Pretoria, South Africa
8 Maternal and Infant Health Care Strategies Research Unit Centre, University of Pretoria, Pretoria, South Africa
9 Biostatistics Research Unit, South African Medical Research Council, Durban, South Africa
10 School of Mathematics, Statistics and Computer Science, University of KwaZulu-Natal, Durban, South Africa
11 Affordable Medicines Directorate, National Department of Health, South Africa
12 Department of Paediatrics and Child Health, University of Pretoria, Pretoria, South Africa
Background
In South Africa, a high HIV and tuberculosis (TB) prevalent low-middle income country (LMIC) with a significant COVID-19 burden, antimicrobial usage for paediatric community-acquired infections (CAI) and healthcare-associated infections (HAI) are largely unknown.

This study aimed to provide antibiotic and antifungal point prevalence estimates for the treatment of CAI and HAI, or for prophylaxis, in the setting of academic hospitals in South Africa.

Aim
To evaluate antimicrobial usage for the treatment of neonatal and paediatric CAI and HAI, or prophylaxis, among hospitalised children at three academic hospitals in South Africa.

Study design
This cross-sectional study included all newborns and children (0-15 years) admitted to three hospitals in KwaZulu-Natal and Gauteng provinces, South Africa. We used the World Health Organization (WHO) methodology for conducting antimicrobial point prevalence surveys in hospitalised children.

Study sites
Inkosi Albert Luthuli Central Hospital, Steve Biko Academic Hospital and Chris Hani Baragwanath Academic Hospital.

Participants
All children (newborn and children up to 15 years of age) in the wards at 08h00 on each Wednesday during the study period were eligible. Study duration varied by site, as recruitment ended once approximately 400 children were enrolled at each site.

Inclusion criteria:
• All children hospitalised at the respective neonatal and paediatric wards (including neonatal and paediatric intensive care units (ICUs)) at 08h00 on each day of the survey; and
• All hospitalised children with an antimicrobial prescription.

Exclusion criteria:
• Children previously recruited into the study during the same admission;
• Children undergoing treatment and discharged on the same day;
• Children presenting to outpatient departments or awaiting transportation; and
• Children receiving outpatient parenteral antibiotic therapy, or hospitalised children receiving only topical or ophthalmologic antibiotics.

Data collection: Anonymised data were collected from 22 September 2021 to 05 January 2022.

Data Analysis
Descriptive statistical methods were used to assess frequency distributions and cross-tabulations. Overall antimicrobial prescribing prevalence, and prescribing prevalence stratified by ward and site were calculated. For the purposes of reporting, antimicrobials analysed included antibiotics, antituberculosis agents, and antifungals. Key indicators included: (i) the antimicrobial prescription prevalence rate; (ii) the indication for an antimicrobial prescription (CAI, HAI, or prophylaxis); (iii) the antimicrobial spectrum prescribed (antibacterial, antituberculosis, antifungal) and the proportional contribution to overall antimicrobial usage; (iv) the WHO AWaRe classification of prescribed antibiotics. Multivariable logistic regression analyses were conducted to test associations with HAI.

DESCRIPTION OF THE STUDY POPULATION
• At least one antimicrobial was prescribed for 1191 (22.9% (95 confidence interval (CI) 15.5-32.5%)) of the 5200 children that were hospitalised in the surveyed wards during the study period.
• Of the hospitalised children on antimicrobials (n=1191):
  • children under one year of age comprised 66.7% of the study population on antibiotics and antifungals
  • children aged 1-5 years and >5-15 years comprised 27.2% and 19.5% of the study population, respectively
  • 54 (4.5%) had COVID-19
  • 33 (2.8%) were living with HIV

ANTIMICROBIAL USE IN THREE ACADEMIC HOSPITALS
• Overall, 1,946 antimicrobials were prescribed to 1,191 children.
• The commonest prescribed antibiotics in children less than 1 year of age were beta-lactamase sensitive penicillins, aminoglycosides and carbapenems. Older children (1-15 years) were frequently prescribed combination penicillins and carbapenems, respectively (Figure 1).
• Antimicrobials were selected appropriately at the three academic hospitals in line with the AWaRe classification (Figure 2).
• The primary reason for which antimicrobials were prescribed were HAI, clinical sepsis, surgical prophylaxis (SP), medical prophylaxis (MP) and lower respiratory tract infections (Figure 3). HAI more commonly occurred in children with an underlying diagnosis of congenital anomalies.
Special Situations

COVID-19: High rates of antibiotic use (48.2%) in SARS-CoV-2 infected participants was due to high rates of co-infection in these children. However, given the small sample size (n=54), more data are needed to understand the appropriateness of antibiotic use in these children.

HIV infection: Few HIV-infected children were enrolled on this study (n=33), and almost all (84.8%) were on antiretroviral therapy, reflective of a well-functioning PMTCT programme. HIV infection was not a risk factor for HAI or the excessive use of antimicrobials.

Accumulative percentage of drug classification

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Drug Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate (0 - 28 days)</td>
<td>100.0%</td>
</tr>
<tr>
<td>Infant (29 - 364 days)</td>
<td>90.0%</td>
</tr>
<tr>
<td>Child (1 - 12 years)</td>
<td>80.0%</td>
</tr>
<tr>
<td>Adolescent (13 - 15 years)</td>
<td>70.0%</td>
</tr>
</tbody>
</table>

Primary reason for antimicrobial use

<table>
<thead>
<tr>
<th>Reason</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAI: Healthcare-associated infections</td>
<td>24.1%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>32.1%</td>
</tr>
<tr>
<td>SP: Surgical prophylaxis</td>
<td>10.3%</td>
</tr>
<tr>
<td>LRTI: Lower respiratory tract infections</td>
<td>7.7%</td>
</tr>
<tr>
<td>MP: Medical prophylaxis</td>
<td>5.0%</td>
</tr>
<tr>
<td>Gastroenteritis or colitis of infections origin</td>
<td>3.3%</td>
</tr>
<tr>
<td>Upper respiratory tract infections</td>
<td>2.1%</td>
</tr>
<tr>
<td>Bone and soft tissue infections</td>
<td>1.8%</td>
</tr>
<tr>
<td>Infections of the genitourinary tract</td>
<td>1.3%</td>
</tr>
<tr>
<td>Central nervous system infection</td>
<td>0.3%</td>
</tr>
<tr>
<td>Other</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Percentage prescriptions according to AWaRe classification

<table>
<thead>
<tr>
<th>Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reserve</td>
<td>31.8%</td>
</tr>
<tr>
<td>Watch</td>
<td>36.9%</td>
</tr>
<tr>
<td>Access</td>
<td>31.3%</td>
</tr>
</tbody>
</table>

Figure 1. Classification of antimicrobial use by age group and WHO Anatomical Therapeutic Chemical (ATC) classification at three academic hospitals in South Africa, 22 September 2021 – 05 January 2022 – Most prescribed

Figure 2. Classification of antimicrobial use by indications and AWaRe classification

*CAI = Community acquired infections; HAI = Healthcare-associated Infections; MP = Medical prophylaxis; SP = Surgical prophylaxis; O = Other

Figure 3. Primary reason for antimicrobial use in 1191 children at three academic hospitals in South Africa, 22 September 2021 – 05 January 2022
The study had 4 main findings, for which we make the following recommendations

**Finding 1**
There was variation in overall antimicrobial prescribing prevalence between sites (29.1% at Hospital A, 40.8% at Hospital B and 14.1% at Hospital C). The site with the lowest antimicrobial prescriptions had a policy of routinely stopping all empiric antimicrobial use at 72 hours.

**Recommendation 1**
Health care facilities need policies to routinely de-escalate or stop all empiric antimicrobials at 72 hours, with justification required for recontinuation of antimicrobial therapy. The use of electronic technology to link microbiological results to antimicrobial prescribing should be explored, especially where there is a shortage of medical personnel. This could help reduce AMR.

**Finding 2**
Most children were distributed across paediatric medical (24.6%), surgical (20.3%), and high-risk wards (20.2%).

**Recommendation 2**
Antimicrobial stewardship programs should target wards/units/sub-specialties with high antimicrobial point prevalence.

**Finding 3**
The prevalence of antimicrobial prescribing to treat HAI was extremely high (45.6%). This was attributed to the study sites serving as referral facilities for children with complicated illnesses whose prolonged hospitalisation placed them at risk for developing HAI.

**Recommendation 3**
Health care personnel should optimise infection prevention and control (IPC) practices, in general, and especially for children with prolonged hospitalisation or using invasive or advanced monitoring or fluid delivery systems. While there was an appropriate selection of antimicrobials according to the AWARe classification, the duration, dose, and relationship to microbiological isolates need to be considered.

**Finding 4**
Neonates and infants had a ~1.6-fold and adolescents had ~2.1-fold greater risk of an antimicrobial prescription for HAI compared to children 6-12 years of age. Being preterm and underweight was also associated with having an antimicrobial prescription for HAI.

**Recommendation 4**
A special focus on antimicrobial policies in younger children, preterm and underweight is warranted. Antimicrobial policies should also focus on adolescents with oncological conditions.

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