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A national, multicentre, web-based point prevalence survey of antimicrobial use and quality indices among hospitalised paediatric patients across South Africa

P.P. Skosana [a,*], N. Schellack [b], B. Godman [a,c,d], A. Kurdi [a,c,e], M. Bennie [c], D. Kruger [a], J.C. Meyer [a]

[a] School of Pharmacy, Sefako Makgatho Health Sciences University, Molotlegi Street, Ga-Rankuwa, Gauteng, South Africa
[b] Department of Pharmacology, Faculty of Health Sciences, University of Pretoria, Pretoria, Gauteng, South Africa
[c] Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK
[d] Centre of Medical and Bio-allied Health Sciences Research, Ajman University, Ajman, United Arab Emirates
[e] Department of Pharmacology, College of Pharmacy, Hawler Medical University, Erbil, Iraq

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ABSTRACT

Objectives: Data on antimicrobial consumption among the paediatric population in public hospitals in South Africa are limited. This needs to be addressed to improve future antimicrobial use and reduce antimicrobial resistance rates. This study aimed to quantify antimicrobial usage and to identify and classify which antimicrobials are used in the paediatric population in public sector hospitals in South Africa according to the World Health Organization (WHO) AWaRe list of antimicrobials.
Methods: A point prevalence survey was conducted among 18 public sector hospitals from nine provinces using a newly developed web-based application. Data were analysed according to the WHO AWaRe list to guide future quality improvement programmes.
Results: A total of 1261 paediatric patient files were reviewed, with 49.7% (627/1261) receiving at least one antimicrobial and with 1013 antimicrobial prescriptions overall. The top five antimicrobials included ampicillin (16.4%), gentamicin (10.0%), amoxicillin/enzyme inhibitor (9.6%), ceftriaxone (7.4%) and amikacin (6.3%). Antimicrobials from the 'Access' classification were the most used (55.9%), with only 3.1% being from the 'Reserve' classification. The most common infectious conditions for which an antimicrobial was prescribed were pneumonia (14.6%; 148/1013) and clinical sepsis (11.0%; 111/1013). Parenteral administration (75.6%; 766/1013) and prolonged surgical prophylaxis (66.7%; 10/15) were common concerns. Only 28.0% (284/1013) of prescribed antimicrobials had cultures requested; of which only 38.7% (110/284) of culture results were available in the files.
Conclusion: Overall, antimicrobial prescribing is common among paediatric patients in South Africa. Interventions should be targeted at improving antimicrobial prescribing, including surgical prophylaxis, and encouraging greater use of oral antibiotics.

1. Introduction

Antimicrobial resistance (AMR) is increasing, especially in low- and middle-income countries (LMICs) where the burden of AMR and infectious diseases is greatest [1]. There are particular concerns in South Africa where there is an increasing incidence of 'superbugs' including carbapenemase-producing Enterobacteriaceae and *Klebsiella pneumoniae* [2]. DeFrancesco et al. also reported high resistance rates to trimethoprim/sulfamethoxazole (54.0%), penicillin (47.1%) and tetracycline (44.8%) among young children in one province of South Africa [3]. However, in their study of paediatric patients hospitalised for *Escherichia coli* bloodstream infections, Malande et al. found that none of the *E. coli* isolates were resistant to carbapenems or colistin [4].

Between birth and 5 years of age, children in LMICs are typically prescribed an appreciable number of antibiotics [5], and exposure to antibiotics among children in many settings including

* Corresponding author. P.P. Skosana. Tel.: + 27 72 923 7269.
E-mail address: phumzile.skosana@smu.ac.za (P.P. Skosana).

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LMICs is high [5–8]. Antimicrobials are also among the most frequently prescribed medicines in hospitals in LMICs [6].

It has been reported that the prevalence of antibiotic use among hospitalised children varies between 33% and 93% across countries [6,8,9]. In addition, the quality of antibiotic use is also of great concern including, for example, a high prevalence of parenteral administration with associated implications including extending the length of hospital stay [1,9]. Ensuring appropriate access to antibiotics while avoiding excess use, especially unnecessary use of broad-spectrum antibiotics, is a major challenge in all settings, but particularly in LMICs [1]. Similar to the adult population, inappropriate and excessive use of antibiotics among hospitalised children has been linked to the emergence of antimicrobial-resistant bacteria that may spread and persist in hospitals and the community [10].

Despite these findings, there are concerns regarding the overall lack of usage data in neonatal and paediatric units, including in South Africa, to guide future practice, although this is changing [7–9]. To address this issue, the World Health Organization (WHO) recommended that all countries develop an antimicrobial consumption surveillance system to monitor antimicrobial utilisation and resistance patterns [11]. Alongside this, there is a critical need for antimicrobial stewardship programmes (ASPs) to identify feasible targets to monitor and modify future antimicrobial prescription patterns in children [1,12,13]. However, in LMICs, ASPs can be challenging as there can be a lack of knowledge about the determinants influencing antibiotic prescribing as well as more limited resources and personnel to undertake ASPs [6,14–16]. Whilst such programmes can be effective in reducing antimicrobial use, the impact on AMR and hospital-acquired infections among children is currently unknown [1,17]. To enhance appropriate prescribing of antibiotics in children, the WHO developed their Model List of Essential Medicines for Children (EMLc), which classifies antibiotics into three groups, namely ‘Access’, ‘Watch’ and ‘Reserve’ (AWaRe) antibiotics [18]. Antibiotics on the Access list are first- or second-line treatments for key infections and should be routinely accessible for appropriate use [19]. Antibiotics on the Watch list are first- or second-choice treatments for specific infections but have a higher potential for resistance development. Antibiotics on the Reserve list should be considered as antibiotics of last resort, to be used under specialist guidance, with specific monitoring and prioritised as key targets for any ASP [18,19].

We are aware of only a limited number of studies undertaken to assess antibiotic utilisation among children in the public sector in South Africa where the majority of patients are treated [20]. The two-tiered health system in South Africa, including both public and private healthcare systems, can be very challenging. Challenges in the public sector, which comprises over 80% of the population, include economic and prescribing difficulties [21–23]. This incorporates shortages of medicines, including antimicrobials, due to procurement, supply and inventory problems despite South Africa being considered a middle-income country [21,22,24]. As a result, necessitating the development of therapeutic interchange polices where pertinent [22]. Problems with procurement and inventory are typically less in the private sector.

In the Global Paediatric Point Prevalence Survey (PPS) [25] as well as a study undertaken by Rogawski et al. [7] from multiple hospitals in different countries, only one hospital from South Africa was included. Other similar studies undertaken in South Africa include a single hospital study by Koopmans et al. in Cape Town [26]. More recently, van der Sandt et al. assessed adherence to guidelines regarding antibiotic use to prevent surgical site infections (SSIs) in children in South Africa as well as adherence to suggestions contained within the South African Standard Treatment Guidelines (STGs) [27]. Some of these studies used retrospective data and some from different data sets. We would like to build on these publications by undertaking a national study among the paediatric population in public hospitals across a range of provinces in South Africa to provide future guidance on potential strategies to improve antibiotic utilisation in children among key stakeholder groups as part of the ongoing National Action Plan to reduce rates of AMR in South Africa [25]. We chose to concentrate on public hospitals in this study since they treat the majority of patients in South Africa, with the cost of care covered by the government under universal healthcare [20,23].

Consequently, in this paper we will describe antimicrobial consumption among paediatric patients in public sector healthcare facilities across South Africa by means of a PPS. The findings will be used to assist the authorities as well as hospital personnel in identifying potential targets and subsequent antimicrobial stewardship activities to improve future antimicrobial prescribing where pertinent.

2. Methods

2.1. Study design

This was a PPS of antimicrobial consumption using data collected from paediatric wards and paediatric intensive care units (ICUs) at 18 purposively selected public sector hospitals in South Africa using a web-based application [28]. This builds on a similar methodology to measure the prevalence of antimicrobial use among the adult population in these public sector hospitals [29].

2.2. Study sites

The 18 purposively selected public sector hospitals included all 9 academic national central and tertiary hospitals in South Africa as well as one district or regional hospital from each of the nine provinces in South Africa [29], conveniently selected considering their proximity to the academic or tertiary hospital used for referral of patients. Table 1 summarises the differences between the types of public sector hospitals in South Africa [29]. Under the universal healthcare system, admission to public hospitals in South Africa is based on patient needs and availability of beds as well as the geographic location rather than any socioeconomic group and their ability to pay [20]. Consequently, we have not included any demographics of parents or guardians in this study.

2.3. Data collection tool and variables recorded

The data collection tool was based on the tools used in the European Centre for Disease Prevention and Control (ECDC) and global PPS studies, and subsequently adapted for sub-Saharan Africa to include potential confounders, including human immunodeficiency virus (HIV), malaria, tuberculosis (TB) and malnutrition [29–31]. The structured paper-based data collection tool was subsequently converted into a web-based application to reduce the time taken for data collection [28].

Data collected included the name and classification of the hospital according to the National Department of Health in South Africa (see Table 1) [29]. Patient-level data recorded included demographic data comprising age, sex, extent of intubation, extent of re-admissions, antimicrobial history and hospitalisation in the last 90 days. The extent of co-morbidities including HIV, TB and malaria was also collected. No attempt was made to split populations into different ethnicities for this study as the primary objective was to gain prevalence data regarding current antimicrobial utilisation across the different public hospital types. In addition, guidelines in South Africa for treating antimicrobial infections do not generally differentiate by ethnicity [27,32–35].

Table 1
Characteristics of the types of public hospitals in South Africa.

- District hospital: bed capacity ranges from 50–600 beds, supporting the primary healthcare sector.
- Regional hospital: bed capacity ranges from 200–800 beds. These hospitals receive outreach patients and support from tertiary hospitals. They must provide health services in at least one of the following specialties: (i) orthopaedic surgery; (ii) psychiatry; (iii) anaesthetics; (iv) diagnostic radiology.
- Tertiary hospital: bed capacity varies. They must provide specialist-level services through regional hospitals as well as provide intensive care services under the supervision of a specialist or specialist intensivist.
- Central hospital: provide tertiary hospital services as well as central referral services, whilst providing national referral services. These hospitals must conduct research and must be attached to a medical school as the main teaching platform. Patients referred to central hospitals are typically from more than one province and they must have a maximum of 1200 beds.
- Specialised hospitals: these hospitals provide specialised health services including psychiatric services, infectious diseases services including tuberculosis services, and rehabilitation services. They have a maximum of 600 beds.

Antimicrobials with the following WHO Anatomical Therapeutic Chemical (ATC) classification system (2019) were included: J01A; J01C; J01D; J01E; J01F; J01G; J01M; J01X; J02A; J04A; J05AB and P01A [36]. Furthermore, the AWaRe classification was used to determine the classes of antimicrobials prescribed as a recent quality indicator especially in children [18,19,25]. As previously mentioned, antibiotics on the Access list are first- or second-line treatments for key infections and should be routinely accessible for appropriate use [19]. Antibiotics on the Watch list are first- or second- choice treatments for specific infections but have a higher potential for antibiotic resistance, and antibiotics on the Reserve list should be considered as such [19,25].

2.4. Patient selection and data collection

For this study, all patients aged <18 years were regarded as paediatrics and were included in the study, similar to the ECDC and global PPS paediatric studies [25,29]. These were further subdivided into the following age categories: neonate (0–28 days); infant (1–11 months); child (1–12 years); and adolescent (13–17 years) [8,37].

For the purpose of calculating the point prevalence of antimicrobial use, the number of patients aged <18 years admitted to any of the paediatric wards and ICUs at 08:00 on the day of data collection were the denominator, whether they were prescribed an antimicrobial or not. The numerator included all patients aged <18 years admitted to any of the paediatric wards and ICUs at 08:00 on the day of data collection who were prescribed antimicrobials. The exclusion criteria included any patient aged ≥18 years as well as those attending accident and emergency departments, admitted for day case surgery or minor procedures, or for chemotherapy in line with other PPS studies [9,29–31].

A detailed national antimicrobial stewardship workshop was conducted coupled with extensive training in order to train pharmacists and academic intern pharmacists who would subsequently assist with data collection using the purposely developed application. This was also similar to other PPS studies [30,31]. Data collection took place during weekdays over a period of 5 months from April–August 2018. Details of the training sessions and the length of time undertaken have been described in our previous publication [29].

2.5. Quality indicators

In addition to assessing antimicrobial utilisation, we also assessed the quality of antimicrobial prescribing using quality indicators based on previous studies [21,30,38]. These included antimicrobial consumption prevalence rates, the mean number of antimicrobials prescribed per patient, and whether the indication for antimicrobial prescribing was recorded. We also reviewed the presence of culture results in the files. We further assessed the duration of antimicrobial prophylaxis to prevent SSIs given current concerns among LMICs, the class of antimicrobial prescribed as well as the extent of intravenous administration [9,30,38]. Surgical prophylaxis is the use of antibiotics before, during or after a surgical procedure to prevent SSI, whereas medical prophylaxis is the prevention of infection in non-surgical situations [30,38]. In addition, the proportion of antimicrobial use from each of the AWaRe categories, calculated as a percentage of the total number of antibiotics, was assessed [18]. We also reviewed whether the antimicrobials used were in line with the STGs [1,30].

2.6. Data management and statistical analysis

The web-based application feeds directly into an MS Excel® database (Microsoft Corp., Redmond, WA, USA), which was subsequently imported into SAS v.9.4 for Windows (SAS Institute Inc., Cary, NC, USA) for analysis. Prior to analysis, the data were cleaned and validated by ensuring that all of the data required were present and that the correct units were used. We also checked for any duplications or errors before analysis in consultation with the statistician. For analysis, the wards in the hospitals were grouped according to the speciality they offer, namely surgical, medical and ICU (paediatric and neonatal).

Antimicrobial prevalence and consumption rates were expressed as percentages (proportional use) and then stratified by ward type, by indication (therapeutic or prophylactic) or according to age category.

Patterns of antibiotic consumption have been described in reference to the 2017 WHO EMLc AWaRe grouping [18]. However, because some of the antibiotics had not yet been classified, we also included an unclassified group.

To assess the relationship between categorical variables, we used the χ^2 test with a *P*-value of <0.05 for statistical significance. For interpretation of practical significance, Cramer's V or phi coefficient ≥0.50 was considered a strong association, 0.30–0.49 a moderate association, 0.10–0.29 a weak association and <0.10 little if any association.

2.7. Ethical considerations

Data collection commenced after receiving ethical approval from the Sefako Makgatho University Research Ethics Committee and permissions from the various study sites. Patient and hospital confidentiality was maintained at all times. Unique study identification numbers were used for hospitals and patients, and no personal identifiers for patients were recorded.

3. Results

3.1. Overview of patient demographics

The 18 included hospitals had 1261 patients reviewed. This comprised eight national central hospitals (54.8%; 691/1261), three provincial tertiary hospitals (14.3%; 180/1261), two regional hospitals (11.7%; 148/1261) and five district hospitals (19.2%; 242/1261).

Table 2
Prevalence of antimicrobial consumption across the different facilities.

Hospital type	No. of patients (children)	No. of patients prescribed an antimicrobial	Prevalence (%) of antimicrobial use	No. of antimicrobial prescriptions	Average no. of antimicrobial prescriptions /per patient (child)
National central	691	323	46.7	540	1.67
District	242	142	58.7	219	1.54
Provincial tertiary	180	95	52.8	140	1.47
Regional	148	67	45.3	114	1.70
Total	1261	627	49.7	1013	

Table 3
Overall antimicrobial consumption by patient demographics.

Demographic	No. (%) of antimicrobial prescriptions
Overall antimicrobials used	1013 (100)
Age	
Neonate (0–28 days)	248 (24.5)
Infant (1–11 months)	266 (26.3)
Child (1–12 years)	410 (40.5)
Adolescent (13–17 years)	89 (8.8)
Sex	
Female	457 (45.1)
Male	555 (54.8)
Transgender	1 (0.1)
Ward type	
Medical	757 (74.7)
ICU	159 (15.7)
Surgical	97 (9.6)

ICU, intensive care unit.

At the time of data analysis, nine of these hospitals were teaching/academic hospitals. Some of the original hospital classifications have changed; however, we kept to the original classifications for accuracy.

The prevalence of antimicrobial consumption was 49.7% (627/1261) among the paediatric patients reviewed, of which more than half were from national central hospitals (51.5%; 323/627) and with the least from regional hospitals (10.7%; 67/627). Overall, 555 antimicrobial prescriptions were received by males (54.8%; 555/1013). Table 2 shows a summary of antimicrobial utilisation across the different facility types, with the highest prevalence of antimicrobial utilisation in the district hospitals (58.7%). Table 2 further shows that the proportion of children receiving antimicrobials differed according to hospital type. However, the number of prescribed antibiotics was highest in the regional hospitals at an average of 1.70 antibiotics per patient.

3.2. Antimicrobial utilisation

A total of 49 different systemic antimicrobials were administered out of a total number of 1013 antimicrobial prescriptions among the 627 children prescribed antimicrobials (Table 2). Medical wards had the highest proportion of prescriptions (757/1013; 74.7%). Of the 1013 antimicrobials prescribed, 847 (83.6%) were given for treatment and the remaining 166 (16.4%) were for prophylaxis.

Table 3 provides further details of the antimicrobials prescribed, including details broken down by age, sex and ward type. The majority of antimicrobial consumption was observed in children aged 1–12 years (40.5%; 410/1013).

Provincial tertiary and district hospitals had the highest percentage of use of antimicrobials from the Access category at 66.4% and 65.3%, respectively. The national central hospitals recorded the highest consumption of antimicrobials from the Watch (32.3%) and Reserve categories (4.4%).

Overall, the top five most prescribed antimicrobials included ampicillin (16.4%; 166/1013 of the total number of antimicrobials prescribed), gentamicin (10.0%; 101/1013), amoxicillin/enzyme inhibitor (9.6%; 97/1013), ceftriaxone (7.4%; 75/1013) and amikacin (6.3%; 64/1013), of which all belong to the Access category except for ceftriaxone, which is in the Watch category. Supplementary Table 1A in the Appendix gives more details about the medicines prescribed. Fig. 1 documents the most commonly prescribed antimicrobials according to their ATC classification per age group.

The most common infectious conditions where antimicrobials were prescribed included pneumonia (14.6%; 148/1013) and clinical sepsis (11.0%; 111/1013). Table 4 shows the breakdown of antimicrobials used for these two conditions according to their AWaRe classification.

3.3. Quality indicators

Most (75.6%; 766/1013) of the antimicrobials were administered intravenously. The majority of antimicrobials prescribed were from the Access and Watch groups (Table 5; Fig. 2), with the highest levels of consumption reported for antimicrobials in the Access group (55.9%; 566/1013). Antimicrobials in the Watch group constituted 27.8% (282/1013) of total use, with limited prescribing of antimicrobials in the Reserve group at 3.1% (31/1013) of total use. However, 13.2% (134/1013) of antimicrobials could not be classified using this terminology (Table 5), with fluconazole and pyrazinamide being the most commonly unclassified antimicrobials.

Most of the patients were receiving antimicrobials for therapeutic treatment (83.6%; 847/1013) and not for prophylaxis (16.4%; 166/1013). Of those receiving antimicrobials for prophylaxis, 91.0% (151/166) of the antimicrobials prescribed were for medical and 9.0% (15/166) were for surgical prophylaxis. In 66.7% (10/15) of cases where paediatric patients were receiving surgical prophylaxis to prevent SSIs, it was for more than one day.

Only 28.0% (284/1013) of prescribed antimicrobials had cultures requested, of which only 38.7% (110/284) of culture results were available in the files, with 51 isolates recorded. The most commonly identified organisms were *Staphylococcus* spp. (18.2%; 20/110;), *Klebsiella* spp. (16.4%; 18/110) and *Acinetobacter* spp. and *Pseudomonas* spp. (each 10.0%; 11/110) (Fig. 3).

4. Discussion

We believe that this study represents one of the first comprehensive, national overviews of paediatric antimicrobial use among public sector hospitals in South Africa. Overall, 49.7% of the admitted patients received at least one antimicrobial, which is higher than the mean rate reported from the worldwide paediatric PPS (36.7%) [9] and by Fink et al. who documented a rate of 24.5% among healthcare facilities in LMICs [5]. This rate is also higher than that seen in similar studies in high-income countries; however, it is significantly lower than other studies in LMICs, including a study conducted in a hospital in South Africa where there was high antimicrobial use (92% of patients) [6,9,26,39,40]. This lower rate of antimicrobial prescribing in South Africa could be due

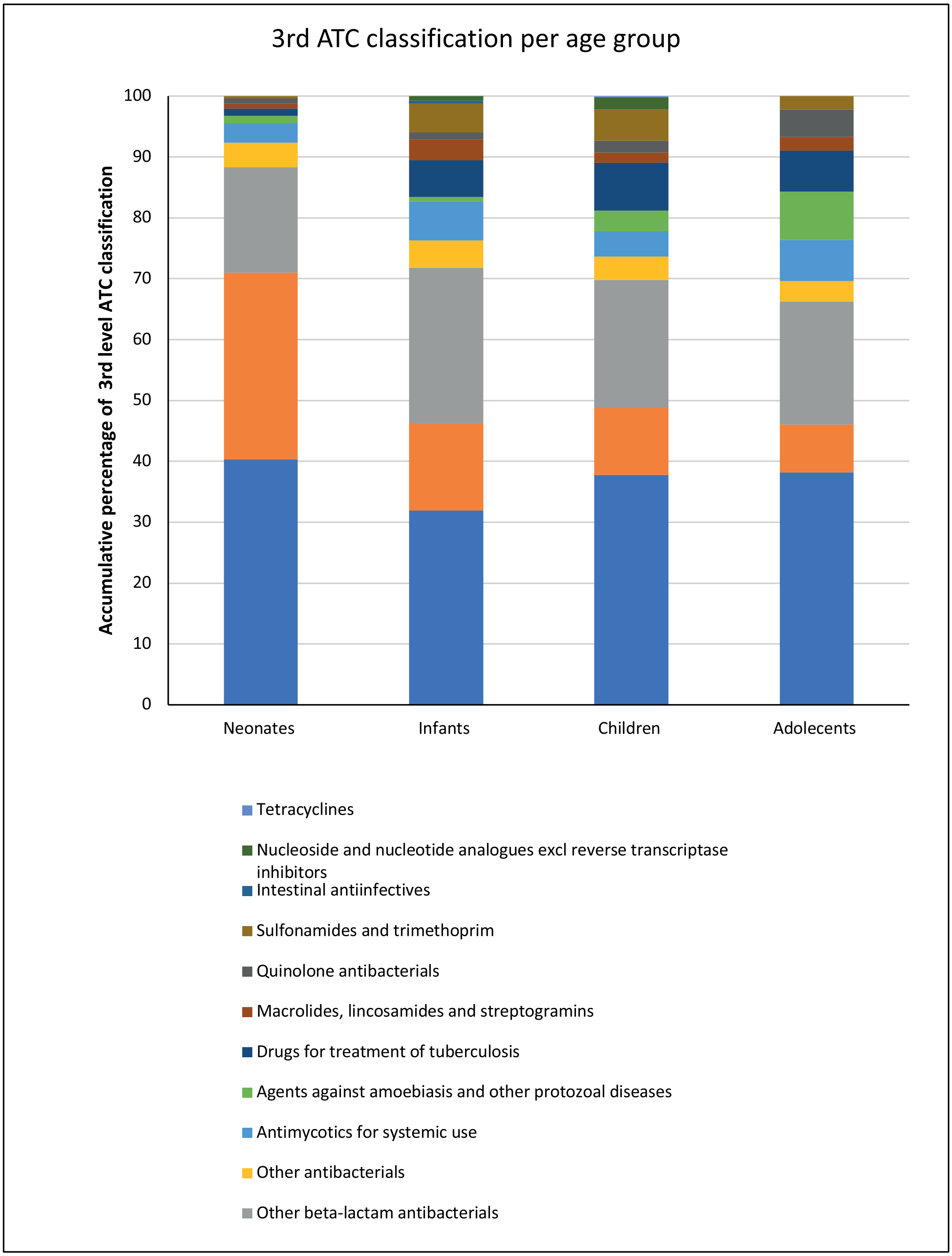

Fig. 1. Classification of antimicrobial use by age group and WHO Anatomical Therapeutic Chemical (ATC) classification.

to the roll out of the ASP across South Africa once the National Strategic Framework was introduced [41] as well as the Expanded Programme on Immunisation (EPI). Pertinent immunisations include the pneumococcal vaccine administered at age 6 weeks, 14 weeks and 9 months as well as the combination hexavalent vaccine, DTaP-IPV-HepB-Hib (diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, heptitis B and Haemophilus influenzae type B) [42,43] given at 6 weeks, 10 weeks, 14 weeks and 18 months, with vaccinations known to prevent an appreciable number of deaths each year [1]. The meningococcal vaccine has been recommended for use and is available in South Africa. Currently, though, only the quadrivalent polysaccharide vaccine (MPSV4) is available in the public sector to those at high risk of contracting meningococcal disease, including well-defined populations during outbreaks [44]. The meningococcal conjugated polysaccharide vaccine (MCV4) is available in the private sector but is subject to full co-payment for those not insured [44]. The influenza vaccine is not part of the standard EPI schedule but it is highly recom-

Table 4
Classification of antimicrobial use for the two most common indications, by AWaRe classification.

Treatment	Pneumonia	N = 148	Clinical sepsis	N = 111
Access	Amikacin; J01GB06	14	Amikacin; J01GB06	6
	Amoxicillin; J01CA04	7	Amoxicillin; J01CA04	1
	Amoxicillin and enzyme inhibitor; J01CR02	8	Amoxicillin and enzyme inhibitor; J01CR02	4
	Ampicillin; J01CA01	47	Ampicillin; J01CA01	21
	Cefazolin; J01DB04	1	Cefazolin; J01DB04	1
	Gentamicin; J01GB03	29	Cloxacillin; J01CF02	3
	Sulfamethoxazole and trimethoprim; J01EE01	3	Doxycycline; J01AA02	1
			Gentamicin; J01GB03	13
			Metronidazole (oral/rectal); P01AB01	1
			Metronidazole (parenteral); J01XD01	1
			Sulfamethoxazole and trimethoprim; J01EE01	2
Total		**109**		**54**
Watch	Azithromycin; J01FA10	5	Cefotaxime; J01DD01	12
	Ceftazidime; J01DD02	1	Ceftriaxone; J01DD04	5
	Ceftizoxime; J01DD07	1	Ertapenem; J01DH03	2
	Ceftriaxone; J01DD04	6	Imipenem and enzyme inhibitor; J01DH51	1
	Ciprofloxacin; J01MA02	2	Meropenem; J01DH02	15
	Ertapenem; J01DH03	1	Piperacillin and enzyme inhibitor; J01CR05	6
	Imipenem and enzyme inhibitor; J01DH51	1	Vancomycin (parenteral); J01XA01	2
	Meropenem; J01DH02	4		
	Piperacillin and enzyme inhibitor; J01CR05	10		
Total		**31**		**43**
Reserve	Colistin (injection/infusion); J01XB01	1	Colistin (injection/infusion); J01XB01	2
	Levofloxacin; J01MA12	1	Ethionamide; J04AD03	1
			Linezolid; J01XX08	3
Total		**2**		**6**
Unclassified	Amphotericin B; J02AA01	2	Amphotericin B; J02AA01	1
	Fluconazole; J02AC01	2	Cefalexin; J01DB01	1
	Isoniazid; J04AC01	1	Fluconazole; J02AC01	4
	Terizidone; J04AK03	1	Tazobactam; J01CG02	1
			Trimethoprim; J01EA01	1
Total		**6**		**8**

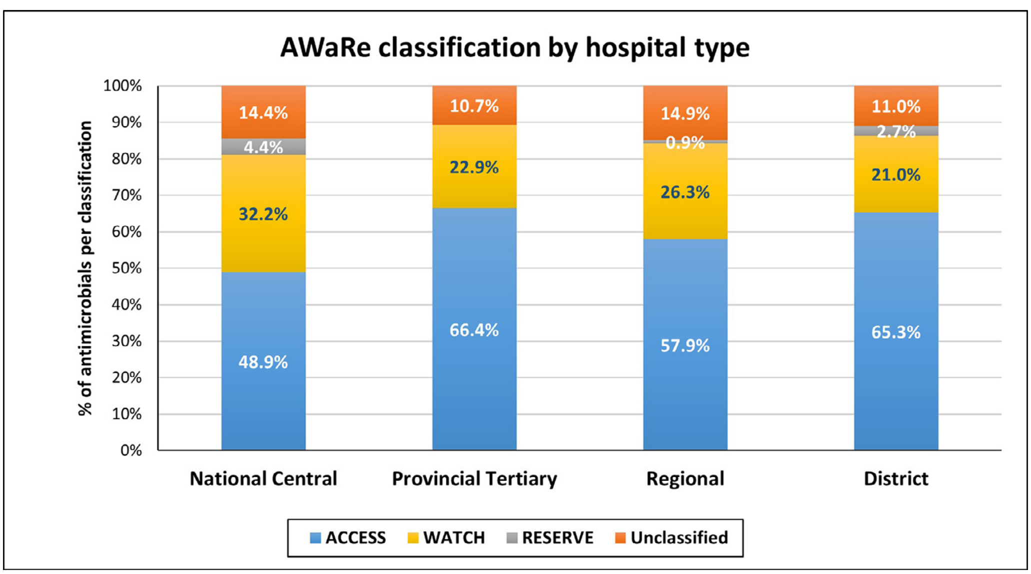

Fig. 2. Percentage of antimicrobial use per hospital type stratified by AWaRe classification.

mended and encouraged from the age of 6 months and above. Due to limited resources, the National Department of Health prioritises certain high-risk groups (children included), making the vaccine available free of charge for them during their annual influenza vaccination campaign [42]. However, there are concerns that the current COVID-19 (coronavirus disease 2019) pandemic has significantly impacted childhood vaccination programmes among African countries, which will appreciably increase morbidity and mortality unless addressed [45,46].

A number of studies have been undertaken regarding the implementation of ASPs in South Africa and their outcomes, potentially resulting in these lower rates [33,47]. However, further research is needed before we can say anything with certainty. The considerable difference in antimicrobial prescribing generally between LMICs and high-income countries, especially among Northern European countries, could be related to multiple factors. These include a higher rate of infectious diseases, limited access to routine diagnostic parameters to help decide the appropriateness and need for antimicrobials following susceptibility testing, limited access to support from specialists such as infectious diseases specialists, and lack of local antibiotic policies and guidelines in LMICs [1,48,49]. However, having guidelines in place does not necessarily

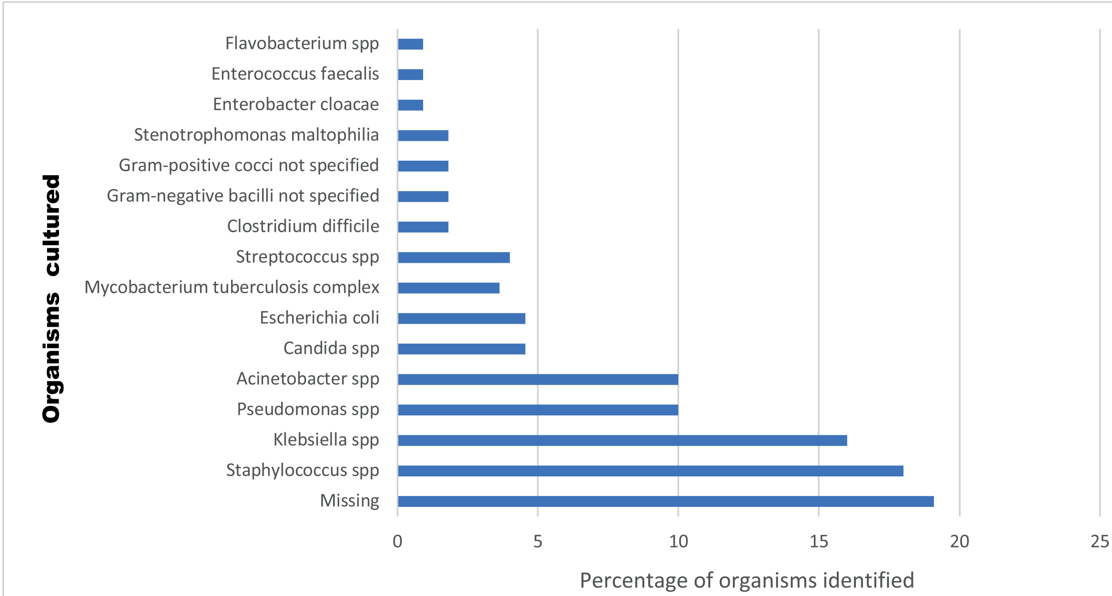

Fig. 3. Organisms identified by culture for paediatric patients.

Table 5
Quality indicators summary.

Indicator	*N* (%)
Route of administration	
Intravenous	766 (75.6)
Oral	236 (23.3)
Intramuscular	11 (1.1)
AWaRe classification [a]	
Access	566 (55.9)
Watch	282 (27.8)
Reserve	31 (3.1)
Unclassified	134 (13.2)
Purpose for use	
Prophylaxis	166 (16.4)
Treatment	847 (83.6)
Item prescribed from SA-EML	
Yes	944 (93.2)
No	69 (6.8)

SA-EDL, South African Essential Medicines List Hospital Level Paediatric Edition 2017.
[a] AWaRe classification based on World Health Organization (WHO) definitions [18].

improve future antibiotic use, with additional programmes including education and follow-up audits typically needed to improve prescribing across sectors and countries [6,34,38,47,50–52].

Similar to other paediatric studies, respiratory tract infections were the most common infection seen among paediatric patients in this study [9,25]. Pneumonia was the most common indication for antimicrobials prescribed (14.6% of prescriptions), similar to other studies conducted in LMICs [53], with ampicillin and gentamicin the two most prescribed antimicrobials (Access category) (Table 4). Clinical sepsis was the second most common indication for antimicrobials (11.0% of prescriptions), again with ampicillin and gentamicin being the two most prescribed antimicrobials (Access category).

We found that the range of antibiotics prescribed is much smaller in neonates than in children, which is also similar to previous studies [9,26]. Our current study also showed high consumption of β-lactam penicillins and aminoglycosides, similar to other studies [8,9]. This may well reflect their recommended use for neonatal sepsis by the WHO [54]. However, we cannot say this with certainty without questioning the prescribers.

Encouragingly, the percentage of antimicrobial use from the Access category was 55.9%, which is better than the findings of Hsia et al. where utilisation of antimicrobials from the Access category was only 33.3% among the hospitals in South Africa taking part in the global PPS [25]. However, this still provides a considerable opportunity for improvement since the majority of antimicrobial use should be from the Access group, with these antimicrobials accounting for 76% of antimicrobials prescribed in the recent global PPS paediatric study [25]. When antibiotics are prescribed, international guidance suggests that narrow-spectrum options, such as amoxicillin or phenoxymethylpenicillin, should be prescribed first [54].

Also encouragingly, <5% of prescribing of antimicrobials across all hospital types was for antimicrobials in the Reserve category, with the majority of prescribing seen among national central hospitals. However, 27.8% of antimicrobials prescribed were from the Watch category (Table 5). These antimicrobials are typically the focus of ASPs since most of these antimicrobials are easily prone to resistance development [19]. Consequently, this can be a focus for future quality improvement programmes with ASPs among the surveyed hospitals in South Africa and wider. The 13.2% of unclassified antimicrobials are also of particular interest for informing future ASPs in South Africa, with further guidance needed on how unclassified antibiotics can be incorporated into the AWaRe classification to facilitate future ASP efforts.

Prophylaxis as an indication for antimicrobial use among paediatric patients in our study was rare (16.4%), which is similar to other studies [26,30]. A concern, however, was that the duration for surgical prophylaxis was greater than the recommended one dose in 66.7% of cases, which is similar to the situation in a number of other LMICs [38,55]. It has been shown that the benefits of antimicrobial prophylaxis are limited to the first 24 hours post-operatively and if continued they can actually lead to adverse effects [38]. The adjusted odds of acute kidney injury increase with each additional day of prophylaxis and the risk of post-operative *Clostridioides difficile* infection demonstrated a similar duration-dependent association [38]. Multiple activities, including educational activities, can help address the situation and improve future antimicrobial prescribing to prevent SSIs across all ages [38].

Of the patients treated with antimicrobials, only 28.0% had at least one microbiology test requested, which is low, similar to other studies in LMICs [53]. We believe this limited use of microbiological laboratories in LMICs may reflect a lack of trust in the value of microbiological results, possibly due to the limited laboratory services, delays in the provision of results, and costs [1,30,38]. We will be following this up in future ASPs since appropriate antimicrobial use will help to reduce AMR. In addition, in hospitals antibiotic prescribing should be governed by appropriate guidelines supported where possible by AMR surveillance. Encouragingly, adherence to the current STGs for paediatric patients was 93.2% in our study, which is similar to the larger PPS in these hospitals (90.2%) and higher than rates seen among children in Zimbabwe and a number of studies in adults [1,6,29]. We will continue to monitor this. In addition, we will seek to introduce quality improvement programmes including reviewing the prescribing of antimicrobials in the Watch category and their use surrounding surgical prophylaxis.

Overall, repeated PPS studies need to be part of paediatric ASPs in order to identify which antimicrobials are being commonly prescribed, their role and AWaRe category, and whether concerns such as susceptibility testing and extended prophylaxis are being addressed. Development of an application with real-time input and analysis allows for timely repeated re-evaluations following any quality improvement initiative [28,29].

We are aware of a number of limitations of this study. These include the fact that only hospital records were analysed for recording of prescriptions and diagnoses, making the findings dependent on the quality of documentation. However, this is similar to other PPS studies. Interpretation of the current data would also have been more useful if this was combined with data on appropriateness, culture-dependent de-escalation and resistance patterns. This again is also similar to other PPS studies. In addition, for the reasons stated, we only concentrated on hospitals in the public sector despite the economic disparities in South Africa. It was also not possible to stratify the ICU results by paediatric or neonatal ICU as both age groups were treated in one ICU at some of the surveyed hospitals. Consequently, we analysed the data just according to ICU status. However, we believe the findings are robust and can be used as a baseline to monitor the long-term impact of future ASP activities and consequently improve future antimicrobial use patterns among paediatric patients in South African hospitals and wider. We are also aware that we only conducted this PPS among 18 hospitals in South Africa. Having said this, we do not believe the findings would have been that different if more public hospitals had been included.

In conclusion, this study shows that there is high prevalence of antimicrobial drug use, especially β-lactam penicillins and aminoglycosides, among paediatric inpatients in public hospitals in South Africa. A number of areas for improvement were identified, which will be the subject of future quality improvement programmes. The developed application makes such re-evaluations easier to undertake and perform, given resource and time constraints within South Africa and may provide guidance for other LMICs.

Data availability

Further details are available from the authors on request.

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Competing interests

None declared.

Ethical approval

Ethical approval for the study was obtained from the Sefako Makgatho University Research and Ethics Committee (SMUREC) [SMUREC/P/36/2018: PG] after review and recommendation by the School of Pharmacy Research Committee. The umbrella study (ENAABLERS) has also been approved by SMUREC [SMUREC/P/233/2017]. The National Department of Health and the provincial departments were consulted for permission to conduct the study in the different public health centres. Permission to conduct the study was sought from the Chief Executive Officers of each of the selected hospitals participating in the study.

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