Antimicrobial consumption among hospitalized neonates and children in Punjab Province, Pakistan

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Abstract

Background: Periodic surveillance of antibiotic consumption in the form of point prevalence studies is a quick and robust methodology to evaluate prescribing trends in hospitals. The current study was undertaken to document antibiotic consumption among neonates and children from hospitals in Pakistan. **Methods:** This large multicenter study using the World Health Organization standardized methodology and AWaRe (Access, Watch, and Reserve) classification examined antibiotic consumption for suspected bacterial infection among neonates and children admitted hospitals in Punjab, Pakistan. **Results:** A total of 708 beds of children wards of the 16 health facilities were examined. Almost all (97%) hospitalized children were prescribed antibiotics on the day of the assessment with 2.6 antibiotics per patient. The three most common indications were respiratory tract infections (31.58%), sepsis (26.52%), and prophylaxis for medical problems (10.30%). The three most frequently prescribed antibiotics were ceftriaxone (24.2%), amikacin

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(23.2%), and ampicillin (16.7%). Almost half of the antimicrobials were prescribed from the "Access" (49.5%) and "Watch" (45.5%) categories under the AWaRe classification. However, no antimicrobial was prescribed from the "Reserved" category. **Conclusion:** Our findings indicate that empirical antimicrobials use among hospitalized children is highly prevalent in Pakistan. The utilization of "Watch" category of antimicrobials is frequent, stressing immediate action.

Keywords: Antimicrobials, antibiotics, children, empirical use, Pakistan, point prevalence survey, prescribing, surveillance

1. Introduction

Infectious diseases are the leading cause of morbidity and mortality among children [1]. Globally, more than five million children die every year principally from preventable causes, including diarrhea, malaria, and pneumonia, with South Asia and Sub-Saharan African countries contributing more than 80% of this burden [2]. Pakistan is ranked third in countries with the highest child mortality rate, followed by Nigeria and India [1]. Naz and colleagues reported that 20-30% of child deaths in Pakistan are related to respiratory tract infections [3]. We are aware that hospitalized children are usually given multiple antibiotics to treat their illnesses in lower- and middle-income countries (LMICs) [4-8]. Moreover, they are frequently prescribed with broad-spectrum antibiotics in conditions where narrow-spectrum antibiotics can provide beneficial effects. This increases the risk of multidrug-resistance (MDR) and extensively drug-resistance (XDR) bacterial infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), *Salmonella typhi*, *Carbapenems-resistant Pseudomonas aeruginosa*, *Enterobacteriaceae, Streptococcus pneumonia*, *Mycobacterium tuberculosis*, and *Vancomycin-resistant* enterococci (VRE) in hospitals [9-11].

Antimicrobial resistance (AMR) is one of the top ten biggest threats concerning global health, requiring rigorous measures to reduce associated morbidity, mortality, and costs [12-15]. Overall, AMR is associated with worse patient outcomes, including treatment failure, prolonged hospital stays, adverse drug reactions, and deleterious effects on gut microbiota and immune system, increasing health care costs and mortality [16, 17]. Hospitals, particularly in LMICs, are associated with the inappropriate use of antibiotics, including prolonged use to prevent surgical site infections (SSIs) and healthcare-associated infections generally (HAIs) [18-21]. Inappropriate antibiotics prescribing patterns, the transmission of resistant bacterial infections among patients and from health care providers to patients, lack of diagnostic facilities and standard treatment guidelines are significant factors in AMR development [21-23]. Overall, approximately 20-50% of antibiotic consumption among the hospitalized population is reported to be inappropriate [21]

A global action plan was put forward to combat the ongoing crisis of AMR in the World Health Assembly in 2015 [24]. It aimed to improve awareness and understanding of AMR, strengthen knowledge through surveillance and research, reduce the incidence of infections, and optimize the use of antibiotic agents [25]. A key area was the development of national action plans (NAPs) to combat AMR, with Pakistan no exception [26, 27], although there are ongoing concerns with the rate of implementation of the NAP in Pakistan [28]. Surveillance of antibiotic consumption could reduce the irrational use of antibiotics under the umbrella of antimicrobial stewardship programs (ASPs), including prescribing for children [29-34]. Higher-income countries have implemented ASPs. The data regarding ASPs and their impact from LMICs is limited due to a lack of sources; however, this is changing [7, 30, 35-42].

The World Health Organization (WHO) has developed a standardized methodology to acquire baseline information regarding antibiotic use among hospitalized patients from their medical records in a specific time, which is named point prevalence surveys (PPS) [43]. In 2019, the WHO AWaRe Classification on antibiotics was developed to guide different antibiotics to prescribe [44, 45]. This classification has been proven as an excellent tool of AMS at the local, national, and international levels as a first step to enhance appropriate antibiotic use and subsequently curb growing AMR rates [46-48]. In Pakistan, few PPS studies have been conducted to examine antibiotic consumption among hospitalized individuals. The majority of these studies were from metropolitan areas estimating the antibiotic consumption in the adult population [35, 36]. To the best of our knowledge, no study examing antibiotic consumption among neonates and children throughout Pakistan. Consequently, we sought to address this by conducting a large, multicenter study among hospitalized children in Pakistan.

2. Methodology

2.1 Ethical approval

The Human Research Ethics Committee, Department of Pharmacy Practice, The University of Lahore (REC/DPP/FOP/34) provided the ethical approval for this study. Permission to conduct this study was obtained from the administration of participating hospitals before conducting this study. Participants' data were coded and stored in a password-protected file accessible only to the researchers. No personal data are disclosed and reported as de-identified data.

2.2 Inclusion and exclusion criteria

All the hospitalized patients stayed overnight and remained in the wards at 8:00 AM on the study day and prescribed any antibiotic for a bacterial infection, administered via the parenteral, oral, rectal, or inhalational route. Moreover, the neonates before the said time were also included in the current study. The excluded patients from this study were patients who stayed for short outpatient appointments and patients attending long-term care departments, including dialysis and accident and emergency wards.

2.3 Sample frame

This large multicenter study was conducted using the WHO standardized methodology [43]. The WHO PPS methodology builds on the Global PPS and ECDC [30, 49]. More than 180 antibiotics were subsequently classified as Access, Watch, or Reserve in the WHO essential medicine list [44, 45]. Since continuous surveillance may be laborious, expensive, and time-consuming, a one day study is a prompt way to assess the pattern of antibiotics prescribing and consumption within hospitals before the use of web-based applications become more widespread [38, 41, 50].

The data extracted from medical records were used to evaluate the prescribing pattern of antibiotics for suspected bacterial infections at the hospital, pediatric ward, and patient level. The study settings of the current study were District Headquarter (DHQ) and Tehsil Headquarter (THQ) hospitals from the Punjab province of Pakistan. The Government healthcare departments are bifurcated into two divisions; (1) Specialized Healthcare and Medical Education Department (SHCME) and (2) Primary and Secondary Health Department (P&SHD). SHCME deals with the tertiary/teaching public sector hospitals throughout Punjab. At the same time, the P&SHD is the controlling authority of district headquarter (DHQ) hospitals, tehsil headquarter (THQ) hospitals, rural health centers (RHCs), and basic unit heads (BHUs) in all the districts of the province. Only DHQ and THQ level hospitals were approached to participate in this study as these are the principal hospitals dealing with neonates and child care in the province. Each hospital within these categories had functional children’s wards. The majority of these hospitals had a neonatal medical ward, neonatal intensive care unit (ICU), and a children's general ward. All the hospitalized patients are provided care free of charge, i.e., no co-payments, including essential and other medicines from the Government of Punjab. All these hospitals had the necessary number of treating physicians, pharmacists, nursing, and other supporting staff to provide maximum patient care. We chose Punjab for this initial study of children as Punjab is the most populous Province in Pakistan [35]. We also purposely did not include private hospitals as we believe this may have distorted the findings. We are aware that there can be differences in prescribing between public and private hospitals driven by expectation and other factors [51].

Participating pharmacists and pharmacy technicians currently working in DHQ and THQ hospitals were contacted and briefed about the design and purpose of the study. All those willing to participate were provided with complete training by the principal investigators regarding data collection procedures. Sixteen hospitals were subsequently included in this study from different geographical locations throughout the Punjab Province.

2.3 Sampling procedure

The target population was sampled from the neonatal medical ward, neonatal intensive care unit (ICU), and a children's general ward of DHQ and THQ level hospitals. Data on antibiotics consumption were collected via a data collection form. Data collection was completed in two months (October-November 2020). On the day of study, investigators visited the children's ward at 8:00 AM and searched the medical records of these children thoroughly to gather the required information. In case of any confusion or ambiguity, treated physicians or nursing staff were approached for clarification.

2.4 Data collection tool

A data collection form was designed to collect the necessary data at the three different levels; hospital, children's ward, and individual patient’s level, based on the WHO PPS methodology (WHO 2018). The data collection form had the following three sections. **Section-I** was designated to collect detailed descriptions of the health facility, including the hospital's name, administrative control, the total number of beds in the hospital, the various operations in the hospitals, and the availability of essential antibiotics in the concerned hospital. **Section-II** was used to record details of the children's ward, including the functional status of its sub-departments and the total number of beds in the ward. **Section-III** captured the information about the age, gender, any surgical procedure, and diagnosis or reason for hospitalization. The rationale behind the choice of antibiotic was collected from the patients’ notes. Details of prescribed antibiotics, including name, preferably the generic name (INN – International Non-proprietary Name) and ATC code [52], route of administration, dose, dosing frequency, duration, and stop date/time, were also collected if recorded. The frequency of antibiotics prescribed referred to the number prescribed. This could be from the same ATC class or a different class. We were aware that ATC coding might be complex, especially for some fixed-dose combinations (FDCs) in Pakistan. However, this is the international standard.

Moreover, detailed information about the indication, type of indication, including treatment or prophylaxis, were recorded. Furthermore, if prophylaxis, then whether this was medical or surgical prophylaxis. For surgical prophylaxis, the duration of prescribed antibiotics was also noted due to ongoing concerns regarding the extent of extended prophylaxis among LMICs [19]. Antibiotics prescribed for the infection were subsequently differentiated into the community or hospital-acquired infections. Community-acquired infections (CAIs) would include infections if symptoms appeared >48 hours from hospital admission. Hospital-acquired infections (HAIs) were recorded if symptoms were showing after 48 hours from hospital [30]. The status of targeted or empiric therapy and culture facilities was also documented.

2.5 WHO AWaRe Classification

The Access group of antibiotics consists of antibiotics that should be routinely available and prescribed against commonly encountered susceptible pathogens while manifesting lower resistance. The Watch category includes high-priority antibiotics with greater resistance potential among pathogens; consequently, should be carefully managed. The Reserve group contains antibiotics class that should only be prescribed against multi-drug resistance infections to reduce their resistance potential [38, 44, 45, 53]. Certain antibiotics combinations are also classified as not recommended due to a lack of evidence-based effectiveness at a fixed dose.

2.6 Statistical analysis

All statistical analyses were performed using Microsoft Excel and Statistical Package for the Social Sciences (SPSS) version 24, with 0.05% as a significance level. Descriptive statistics were used to present frequency, and percentage.

3. Results

3.1 Characteristics of the sample

Of 122 tehsil and district health district facilities approached, 16 agreed and participated in this study. On the study day, 607 beds were occupied, with bed occupancy of 85.7% (607/708 beds).

The majority of the study population were male (53.8%). The study population, divided into four groups according to their age groups, included neonates (33.1%), infants (21.1%), young child (19.9%) and child (25.8%) as shown in **Table 1**. 97.5% (592/607) of the children were prescribed antibiotics, and the total number of antibiotics prescribed among the children was 1,224.

Table 1: Demographics of the study participants and hospitals related information

Variables	**Total N (%)**
Total number of beds in the hospitals	2550
Total number of beds in the childrens' ward	708
Total patients in children ward at 8:00 AM	607 (85.73)
Total number of children prescribed an antibiotic	592 (97.52)
Age	
Neonates (0-28 days)	196 (33.10)
Infants (29 days-1year)	125 (21.11)
Young child (>1-5 years)	118 (19.93)
Child (>5-12 years)	153 (25.84)
Gender	
Male	319 (53.88)
Female	273 (46.11)
Route of administration	
Oral	51 (4.16)
Parenteral	1173 (95.83)
Sub specialty	
Medical	973 (79.49)
Surgical	19 (1.55)
ICU	232 (18.95)

The frequency of patients having one, two, and ≥ three prescribed antibiotics were 8.3%, 58.83%, and 32.8%, respectively, with an average of 2.06 antibiotics per patient (**Table 2**). Furthermore, more than 95% (1173) of antibiotics were prescribed for parenteral administration, with only 4.1% of antibiotics prescribed for oral administration. Other anti-infective agents such as antivirals, antifungals, or antiprotozoals were infrequently prescribed in this study population.

Table 2: Information related to antimicrobials prescribed and types of infection

Variables	**Total n (%)**
No. of antibiotics prescribed	1,224
No. of Antibiotic(s) per patient	
One antibiotic	102 (8.33)
Two antibiotics	720 (58.82)
≥ Three antibiotics	402 (32.84)
Other anti-infective agents	
Antiviral	6 (0.4)
Antifungal	16 (1.28)
Antiprotozoal	4 (0.32)
Indications	
Therapeutic use	1,127 (92.07)
Prophylaxis use	92 (7.51)
Unknown	5 (0.40)
Indications for prophylaxis	
Medical	61 (10.30)
Surgical	31 (5.23)
Surgical prophylaxis	
Single dose	2 (6.45)
One day	11 (35.48)
More one day	18 (58.06)
Type of infection	
Community-acquired	1,044 (85.29)
Hospital-acquired	88 (7.1)
Reasons on notes	
No	1,070 (87.41)
Yes	154 (12.58)
Empirical therapy	1,224
Targeted therapy	-

The majority (79.4%) of the antibiotics were prescribed in the medical subspecialty of the children's wards, followed by the intensive care units (18.9%) and surgical wards (1.5%). As far as the therapeutic and prophylaxis use of antibiotics is concerned, 1127 (92.0%) antibiotics were prescribed for therapeutic use. Only 92 (7.5%) antibiotics were prescribed for prophylaxis. This included 61 antibiotics for medical prophylaxis and 29 antibiotics for surgical prophylaxis. Medical prophylaxis indications mainly included cystic fibrosis, non-vaccinated or immunocompromised children and certain non-incision procedures. Among the surgical prophylaxis patients, 18 antibiotics were prescribed for more than a single day, while only 11 antibiotics were prescribed for a single day. The majority (85.2%) of the antibiotics were prescribed for CAIs, with 7.1% prescribed for HAIs. We found that majority of the antibiotics (87.4%) were prescribed without mentioning any reason or indication for their use on the medical records. All antibiotics were prescribed empirical without any culture or sensitivity testing. In addition, start and stop date information was typically not recorded. However, only 4 of the 16 hospitals taking part had facilities to undertake culture and sensitivity testing within their hospital.

3.2 Frequent indications and antibiotic consumption

3.2.1 *Neonates*

Our study revealed that respiratory tract infections (RTIs) were the leading cause of antibiotic consumption among neonates (**Table 3**). 41.3% of neonates presented with such infections, followed by sepsis (32.1%) and febrile neutropenia (12.2%). The top three antibiotics prescribed among neonates were amikacin (26.4%), ampicillin (21.2%), and cefotaxime (18.6%), as shown in table 4. Other antibiotics prescribed in this age group were ceftazidime (13.9%) and ceftriaxone (7.8%), respectively.

Table 3: Indications for antibiotics for suspected bacterial infections according to age groups

Type of Infection for which an antibiotic was prescribed	Neonates n (%)	Infants n (%)	Young children n (%)	Older children n (%)	Total n (%)
Respiratory tract infections	81 (41.32)	51 (40.80)	31 (26.27)	24 (15.68)	187 (31.58)
Sepsis	63 (32.14)	32 (25.60)	30 (25.42)	32 (20.91)	157 (26.52)
Prophylaxis for medical problems	21 (10.71)	10 (8.00)	10 (8.47)	20 (13.07)	61 (10.30)
Febrile neutropenia or fever	24 (12.24)	16 (12.80)	06 (5.08)	11 (7.18)	57 (9.62)
Gastrointestinal infections	7 (3.57)	06 (4.80)	13 (11.01)	29 (18.95)	55 (9.29)
Skin and soft tissue infections	-	03 (2.40)	14 (11.86)	20 (13.07)	37 (6.25)
Prophylaxis for surgical diseases	-	7 (5.6)	09 (7.62)	13 (8.49)	29 (4.89)
Other infections	-	-	5 (4.23)	4 (2.61)	9 (1.51)

3.2.2 *Infants*

Similar to neonates, RTIs were the major indication (40.8%) for antibiotics utilization among infants in our survey (Table 3). The three most frequently used antibiotics in this age group were amikacin (28.5%), ceftriaxone (21%), and ampicillin (14.2%).

3.2.3 *Young children*

As shown in Table 3, the predominant reasons for antibiotics use in young children (> 1-5 years of age) were again RTIs (26.2%) followed by sepsis (25.4%) and skin and soft tissue infections (11.8%). The three most commonly prescribed antibiotics in this age group were ceftriaxone (38.4%), amikacin (18.2%), and ampicillin (17.5%).

3.2.4 *Older Children*

The most commonly reported indications for antibiotics among children 5-12 years were sepsis (20.91%) followed by gastrointestinal infections (18.95%) and RTIs (15.68%). Skin and soft tissue Infections and prophylactic use for medical problems were the indications in 13.07% children. The most frequently prescribed antibiotics in this age group was ceftriaxone (32.4%), followed by amikacin (19.8%) and ampicillin (13.1%) (**Table 4**).

Table 4: Prescribed antibioticsfor suspected bacterial infections according to age group

Antibiotics (ATC Code)	**ATC class**	**Neonates n (%)**	**Infants n (%)**	**Young child n (%)**	**Child n (%)**	**Total population n (%)**
Ceftriaxone (J01DD04)	Third-generation cephalosporin	27 (7.84)	56 (21.05)	116 (38.41)	98 (32.41)	297 (24.26)
Amikacin (D06AX12)	Aminoglycoside	91 (26.45)	76 (28.57)	55 (18.21)	62 (19.87)	284 (23.20)
Ampicillin (J01CA01)	Aminopenicillins	73 (21.22)	38 (14.28)	53 (17.54)	41 (13.14)	205 (16.74)
Cefotaxime (J01DD01)	Third-generation cephalosporins	64 (18.60)	22 (8.27)	11 (3.64)	-	97 (7.92)
Ceftazidime (J01DD02)	Third-generation cephalosporins	48 (13.95)	16 (6.01)	9 (2.98)	2 (0.64)	75 (6.12)
Ciprofloxacin (J01MA02)	Fluoroquinolones	3 (0.87)	9 (3.38)	13 (4.30)	36 (11.53)	61 (4.98)
Cefepime (J01DE01)	Fourth-generation cephalosporins	10 (2.90)	06 (2.25)	07 (2.31)	11 (3.52)	34 (2.77)

Metronidazole (J01XD01)	Imidazole derivatives	2 (0.58)	6 (2.25)	13 (4.30)	10 (3.20)	31 (2.53)
Azithromycin (J01FA10)	Macrolides	9 (2.61)	9 (3.38)	4 (1.32)	7 (2.24)	29 (2.36)
Meropenem (J01DH02)	Carbapenems	6 (1.74)	7 (2.63)	4 (1.32)	4 (1.28)	21 (1.71)
Piperacillin+ enzyme inhibitor (J01CR05)	piperacillin and enzyme inhibitor	3 (0.87)	5 (1.87)	-	9 (2.88)	17 (1.38)
Cefixime (J01DD08)	Third-generation cephalosporins	-	-	5 (1.65)	11 (3.52)	16 (1.30)
Others		8 (2.32)	16 (6.01)	12 (3.97)	21 (6.73)	57 (4.65)
Total antibiotics		344 (28.10)	266 (21.73)	302 (24.67)	312 (25.49)	1224

3.2.5 Antibiotics utilization according to AWaRe classification

Our survey revealed that nearly half (49.5%) of the children were prescribed antibiotics from the “Access” category of antibiotics, with antibiotics from the “Watch” category prescribed among 45.5% of cases (**Figure 1**). No antibiotic from the “Reserved” was prescribed in the sample population. Furthermore, 61 (4.98%) antibiotics were prescribed from the ‘not recommended’ group of antibiotics.

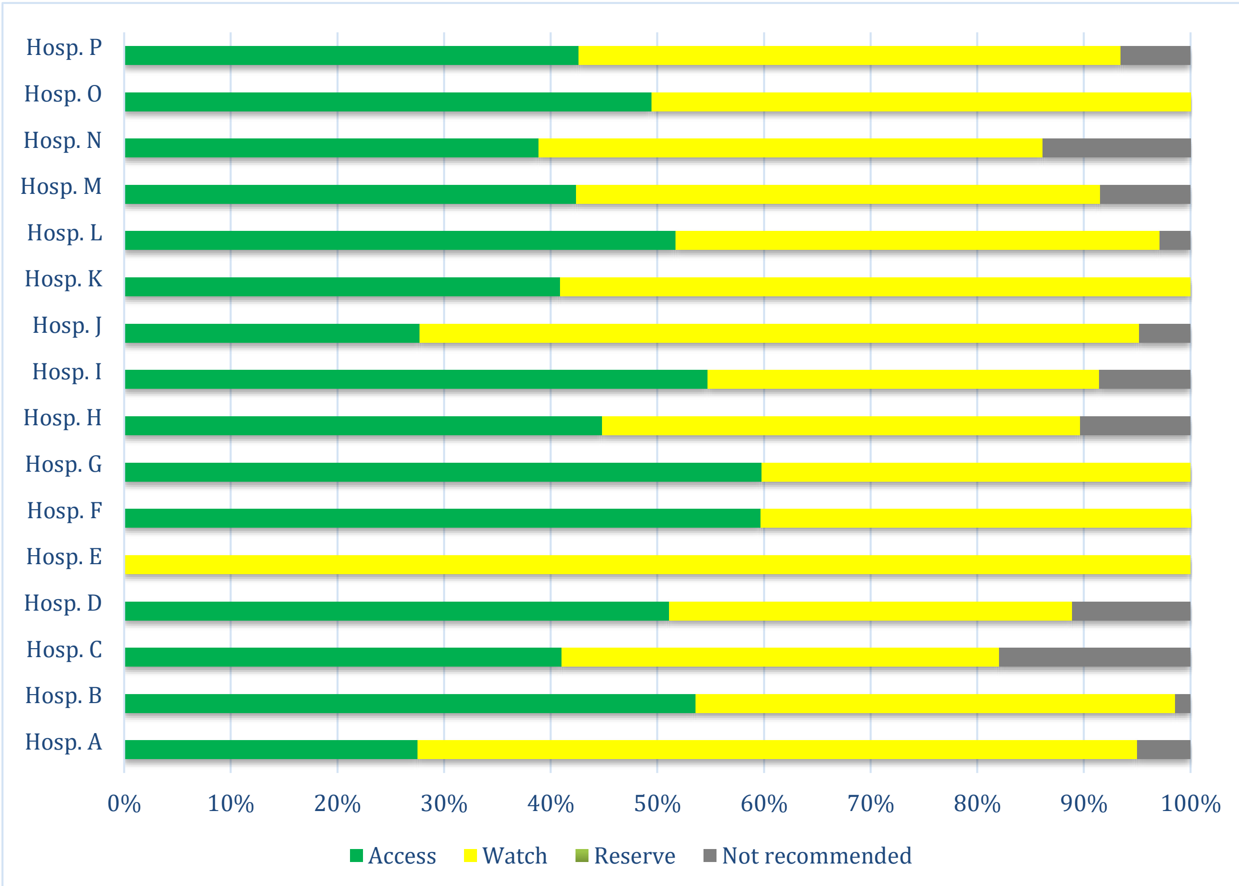

Figure 1: Antibiotic consumption among children and neonates in all the hospitals according to the WHO AWaRe classification.

4. Discussion

To the best of our knowledge, this is the first study among pediatric patients in Pakistan, building on studies conducted among adults in Pakistan [35, 36]. We found that nearly all hospitalized children received at least one antibiotic, which was comparable to the results of a previous study conducted in South Africa [54]. However, appreciably higher than studies from Switzerland, the Global PPS study in children and Turkey where only 36%, 36.7%, and 54.6% of pediatric patients respectively received antibiotics during their hospital stay [55-57]. In addition, appreciably higher than a rate of 24.5% seen in other LMICs treating children [58]. The average number of antibiotics prescribed per patient in our survey was almost double the findings of Zhang et al. in China [59]. Our findings that parenteral administration was the most frequently employed route to treat hospitalized children is similar to Zhang et al. [59]. However, we were aware of a study conducted in Norway where only 73% of the pediatric population were prescribed antibiotics via the parenteral route [60]. The high rate of intravenous (IV) administration is a concern as (IV) administration can be associated with harmful effects, including phlebitis, extravascular injury, and local or systemic infections, including bacteremia. While IV routes of administration can be preferred to achieve rapid action in severe infections, oral routes of administration should be adopted where possible to conserve costs and hasten early discharge [61-64]. We believe the high use of IV antibiotics in our study may be related to fears of infection while patients are in hospital, with the IV route seen as more effective by both patients and physicians [61, 64, 65]. However, further research is needed before we can say anything with certainty. This is being planned as part of follow-up activities.

Antibiotics were prescribed more often in the medical wards of the participating hospitals than in either intensive care units or surgical wards in our study. A previous study from India also reported similar antibiotic prescribing trends [7]. Contrary to our results, De et al. reported that one-third of the pediatric population were prescribed antibiotics prophylactically [66]. This may reflect a higher proportion of patients undergoing surgery in this study. RTIs were the principal reason for antibiotics in our study, followed by sepsis, medical prophylaxis, and fever. Similar trends were reported in the earlier multinational study [46]. RTIs as pneumonia were also the principal reason for antibiotic prescribing among pediatric patients in other hospitals in in Pakistan as well as in LMICs [67,68].

In the present survey, amikacin was the most frequently prescribed antibiotic in neonates and infants, as one-fourth population of said age groups were prescribed with amikacin. These findings are consistent with an earlier study conducted in India where 17.3% of the total pediatric population were prescribed amikacin [7]. Ceftriaxone was one of the most prescribed antibiotics in children aged > 1-12 years, followed by amikacin and ampicillin. These findings were also consistent with the results of a previous study from Saudi Arabia, where ceftriaxone was prescribed to 11.7% of the hospital population [69]. However, unlike other studies, beta-lactam penicillins and aminoglycosides were the most prescribed antibiotics in children and neonates [7, 57]. The high use of broad-spectrum antibiotics such as ceftriaxone in our study may reflect a general trend of not performing sensitivity testing, which may have been exacerbated by only four of the sixteen facilities having facilities on site for culture and sensitivity testing. We are aware that culture testing is pivotal for diagnosing and appropriate selection of antibiotics to combat infections.

Disappointingly, we found that not a single sample was sent to the laboratory for such testing in our study. This contrasts with a recent study from the USA where most neonates were prescribed antibiotics after the confirmation from culture testing [70]. The lack of requests for culture and sensitivity testing could be due to poor knowledge of how to request such tests especially with lack of testing onsite for many of the hospitals taking part coupled with the belief of more rapid resolution of infections with IV administration resulting in high IV use from the outset with broad-spectrum antibiotics. This is a concern as such practices can promote the overuse of broad-spectrum antibiotics. As a result, the rationale behind the current culture of a lack of testing among the hospitals in our study will be evaluated further including ways to increase testing facilities within hospitals, along with high IV use, with similar concerns in other LMICs [71]. The findings will subsequently be the subject of future quality improvement programs in these and other hospitals in Pakistan, given the considerable potential for inappropriate antibiotic prescribing without routine testing. There were also concerns with the extent of surgical prophylaxis beyond the operation in our study's small number of such patients. This is a concern across LMICs, including pediatric patients, and again will be the subject of future quality improvement programs building on the success of such programs in other LMICs [19, 48, 51].

Finally, AWaRe is now recognized as a useful tool to identify and reduce inappropriate prescribing of antibiotics and subsequent AMR. Our survey showed that half of the surveyed children were prescribed ‘Access’ category antibiotics, while the others included ‘Watch’ category antibiotics. This is a concern since, as mentioned, antibiotics classified as ‘Watch’ include those having broad-spectrum activity with the potential for higher resistance rates. These antibiotics were prescribed to nearly 46% of the surveyed population, which may well be due to a lack of culture and sensitivity testing. This will also be the subject of future quality improvement programs among hospitals in our study and wider in Pakistan as part of planned ASPs. While encouragingly, no antibiotics were prescribed from the reserve group; 5% of total antibiotics were prescribed from the ‘not recommended’ class, which needs to be investigated further. Encouragingly, these findings were in contrast to a multinational survey (56 countries) concerning the AWaRe classification of antibiotics among children, which showed that nearly one-third of antibiotics in Pakistan were from the unclassified antibiotics category [46].

We are aware that there were several limitations to our study. Firstly, the study data was only gathered from 16 public sector hospitals (DHQ and THQ hospitals) of the Punjab Province and not from other Provinces in Pakistan. In addition, no private hospitals and no teaching/tertiary hospitals were involved for the reasons stated. Consequently, the findings may not be generalizable to the entire hospitalized children population of the country. We are also aware that we did not collect any data on the culture and sensitivity testing as these were typically not requested with all antibiotics prescribed as empirical therapy. Finally, we want to remind readers of the fundamental limitation inherent in the study's cross-sectional design, which is the inability to establish underlying relationships and causation. However, despite having several limitations, we believe our findings are robust, providing direction for the future especially key targets for any ASPs.

5. Conclusion

Our findings indicate that antibiotics use among hospitalized children is highly prevalent in Pakistan. The majority of hospitalized children were prescribed antibiotic therapy empirically and mainly via the parenteral route of administration. Both need be addressed on a priority basis to reduce over use of broad-spectrum antibiotics along with reducing costs. Promoting the use of culture and sensitivity testing would enhance future rational antibiotic prescribing among children in Pakistan, which can be facilitated by increasing such facilities within hospitals in Pakistan. Furthermore, an appreciable number of antibiotics prescribed were from the "Watch" category. This again stresses the need for active ASPs to be instigated within public hospitals in Pakistan to enhance the rational prescribing of antibiotics. Targeted ASP activities should also include reducing the extent of IV administration and extended prophylaxis as well as the extent of testing coupled with instigating routine start and stop dates. We will be following this up in future research projects.

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Declaration of interests

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in

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Author contribution statement

ZUM and MS made substantial contributions to the study design, data collection, data analysis, interpretation of the results, and manuscript drafting. MY, HAM, MK, MI, MBR, were involved in data collection and interpretation. BG, KH and SSH revised the manuscript for important intellectual content including English language. All authors have read and approved the final version of the manuscript.

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Declaration Statements for Original Research Articles

The current study was conducted after the approval number from the ethics committee of The Department of Pharmacy Practice, Faculty of Pharmacy, The University of Lahore REC/DPP/FOP/34. As we only searched, the medical records of the patients that were discharged from the hospital, therefore, the ethic committee allowed us to use this patient's medical record after their approval.

Data availability

The datasets used during the current study are available from the corresponding author on reasonable request.

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