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Prescription Errors in Pediatric In-patients with Infectious Diseases at Mbagathi District Hospital

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ABSTRACT

Background: Medicines are the most common health-care intervention, and the errors they cause are a preventable iatrogenic problem. Prescription errors are a type of medication errors in the choice of administration of drugs Literature suggests that children experience prescription errors three times more than adults. This study sought out to find the occurrence of prescription errors in one of the major public district hospitals in Nairobi County.
Methods: The study entailed prospective review of patient files of pediatric in-patients on antimicrobials aged 0-12 years at Mbagathi District Hospital pediatric ward between April and June 2019. Patient data was collected and reviewed for prescription errors**.**
Results: 206 participants (median age 9months) recruited. Common diagnoses included pneumonia (36.5%), acute diarrheal disease (21.5%), meningitis (10.3%), neonatal sepsis (7.3%), and malaria (4.7%). 502 antimicrobials were prescribed. Antibacterials were most prescribed (87%). Most patients were on two antimicrobials (40.3%). Prescribing errors were 1298. Each prescription had at least one prescribing error. These were incomplete prescriptions (53.2%), dosing errors (25.3%), indication errors (10.9%) and documentation errors (10.6%). Weight was a significant dosing error predictor that children receiving artesunate were 30.5 times more likely to be under-dosed (cOR=30.5: 95% CI: 9.3, 99.7, p=<0.001) and 28.7 times more likely to be overdosed (cOR 28.7: 95% CI: 1.95, 422.7, p=<0.001). Benzyl penicillin and ceftriaxone had most dosing errors.
Conclusion: The prevalence of prescribing errors was high. Interventions are in place to promote safe prescribing for pediatric patients.

Keywords: Antimicrobial, Dosing errors, Medication errors, Patient safety, Pediatric, Prescription errors

1.0 INTRODUCTION

In health care systems, a safe environment is of high priority. Safety culture has been defined as *"the product of individual and group values, attitudes, perceptions and patterns of behaviour that determine a group or organization's commitment to safety management in general or particularly in certain processes"*. [1] Safe use of medicines is the most important determinant of the overall patient safety in healthcare facilities. Medicines are important for curing communicable diseases, preventing chronic disease problems and relieving pain with the aim of improving the quality of life. However, these very useful drugs may lead to unwarranted harm if not correctly used or if incorrectly prescribed.

Medication errors are a major global concern and might have critical clinical consequences in patients. These errors constitute 2 to 14% of in-patients in the United States, with 1 to 2 per cent of them being harmed or occur in 6 out of 10 adult health center admissions and 5 out of one

hundred medicinal drug orders. Majority of the errors are due to poor prescribing. A systematic review by way of Miller and colleagues showed that, the most recurrent types of medicine errors in pediatric sufferers were administration (72-75%), documentation (17-21%), dispensing (5-58%) and prescribing errors (3-37%). [2]

These errors cause a wide range of complications in patients, starting from mild pain to significant morbidity, which may motive prolonged hospitalization or death. Drug errors kill an estimate of about 7,000 patients per year and account for almost 1 in 20 admissions in the USA. [6] The Institute of medicine (IOM) file for 1999 implicates medication mistakes, partly, as a direct cause of approximately 98,000 deaths yearly. Medication errors related to disease and death increases facility healthcare prices by up to $4700 per admitted patient, or $2.8 million for a 700-capacity hospital. Furthermore, time spent by the healthcare group to minimize mistakes, may affect on the available time for direct patient care. The Physician Insurers Association of the USA noted that, medicinal mistakes are the 5th most common misadventure for pediatricians in a survey of medical legal responsibility fits filed from January 1985 thru December 2000. Over 30% of these cases resulted in a quest for payment of $14.7 million in total compensation. The general monetary burden of healthcare from drug mistakes inside the USA alone exceeds $100 billion annually. [3]

Prescription errors make up for a large proportion of medication errors. These errors also result in a large number of unfavorable drug events in patients. Prescription errors are a significant public health burden contributing to 18.7–56 % of all drug events among hospitalized patients. [4] About one third of adverse drug events (ADEs) are related to medicinal drug errors, which are preventable. [5]

Children represent a big percent of the population, and are particularly prone to ailments and suffer the harmful effects of medication due to the differences in pharmacodynamics and pharmacokinetics. [6] This places them at greater danger than adults of experiencing medicine errors because they have an immature physiology and developmental obstacles, which affect their capability to talk and self-administer drugs. Besides, majority of drugs are formulated in adult dose concentrations and pediatric warning signs and pediatric dosage instructions are regularly not included in a drug product. [7] Therefore, drug doses are usually tailored to the needs of pediatric patients. They are individually calculated on age, weight and condition basis of the patient.

In this regard, there are extended possibilities of prescription mistakes in pediatric patients. The 1995–1999 study conducted by the US Pharmacopeia (USP), Medication Errors Reporting Program confirmed a remarkably higher medication error rate leading to either harm or death in young patient populations (31%), compared to the adult one (13%). Adverse Drug Events (ADEs) in pediatric (5.7%) and adult patients (5.3%) occurred at the same rate in a more recent study. However, potential ADEs (errors that do not cause harm) occurred three times more in pediatric patients than in adults. [8]

In this study, prescription errors in pediatrics were classified into four major subgroups: First type, indication errors (contraindicated drug, incorrect drug use and therapeutic duplication); dosing errors (overdose, under-dose and wrong frequency); incomplete prescriptions (which may lack information about unit dose, formulation, number of doses per day, the hour of administration, or any other particular instructions for use in hospitalized patients) and wrong documentation errors (use of brand names, dangerous abbreviations, illegibility and trailing zeros).

Consequently, pediatric patients are a specific populace who need special care. [9] For this reason, this study was conducted to evaluate the prevalence of various types of prescribing errors in hospitalized children on antimicrobial agents in Mbagathi District

Hospital. This hospital is the second largest public health facility in the capital city of Kenya and is a specialist facility for infectious diseases. Given that dosing errors are the most serious type of prescribing error, risk factors for dosing errors were identified.

2.0 METHODS

2.1 Study design and site

This was a hospital-based cross sectional study which entailed the prospective review of treatment sheets and patient files of pediatric inpatients admitted with an infectious disease at the General Pediatric Ward at Mbagathi District Hospital (MDH). The hospital is located in Langata District of Nairobi County, Kenya. It is a 38 bed pediatric ward that has a monthly average admission of approximately 340 children aged less than 12 years. This ward was divided into 5 smaller ward rooms. The hospital serves mostly the urban poor of Nairobi.

2.2 Study Population and Eligibility criteria

The study population included children aged 0-12 years admitted at the Mbagathi District Hospital general pediatric ward with infectious disease during the study period April 2019 to June 2019. The child had to be on at least one antimicrobial. The caregiver had to give an informed consent for the child to participate in the study. Patients whose treatment sheets were missing from their files were excluded.

2.3 Sample size, Sampling methods and participant recruitment

The Cochran formula [10] was applied to determine the sample size. The level of significance was set at 0.05 and precision was 0.05. In the study on the incidence and determinants of medication errors among pediatric in-patients aged 0-5 years at Kisii Level 5 Hospital, 75.8% of the prescriptions contained errors. [4] Working on the assumption of 75% as the prevalence of medication related problems among these patients, the calculated sample size (n) was a minimum of 203 patients after adjusting for a finite population. This figure was adjusted upwards by 10% to cater for any loss to follow-up or incomplete information, a minimum of 224 treatment sheets and files was sampled at the end of the study.

Consecutive sampling was employed, whereby every patient meeting the inclusion criteria was included in the study as they were admitted until the target (pediatric) sample size was achieved. Treatment sheets and patient files were picked from the nursing station and reviewed if they met the eligibility criteria for recruitment with the aid of the Eligibility Screening Form.

2.4 Data collection

A pre-designed data collection tools was adapted from the Institute for Safe Medication Practices (ISMP) [11] were used to collect data on patient demographics, diagnosis and medication prescribed. Data collection was done within 48 hours of admission so as to capture any prescribing errors that could have occurred. To avoid interrupting the normal activities of the wards, the treatment sheets were abstracted after the ward rounds were complete.

For each participant data on medications, formulation, dosage, frequency, and duration of use, were noted exactly as it was recorded on the prescription/treatment sheet. Attendant information on drug treatment, including monitoring of high-risk medications was recorded. The cadre of the prescribers was also noted. The treatment sheets were review every two days after admission for a minimum of four days or until discharge if this happened sooner. Each patient's prescription/treatment sheets were evaluated for prescribing errors. The types of prescribing errors included indication errors (contraindications and incorrect drug), documentation errors (use of brand names, illegibility or use of abbreviations and completeness of prescriptions).

The correctness and adequacy of the prescribed dosage for each prescribed drug

was also assessed. To determine under-doses and overdoses, the Pedi-Stat Application from QxMD Medical Software Inc (https://qxmd.com/pedi-stat) was used to check the correctness of the prescribed dose. Pedi-Stat is a decision supporting tool used to guide dose selection for pediatric patients. This utility could be used to calculate weight-based and age-specific medication doses for pediatric patients. [6]

If a prescription error was encountered, the health practitioner (medical officer or nurse) on duty was immediately alerted so that prescription could be reviewed and corrective action taken. Furthermore, a follow-up on the affected patient was done within 24 hours to confirm that appropriate measures were taken to mitigate the prescription error of concern.

2.5 Variables and Data analysis

The outcome variables were the various kinds of prescribing errors. For the purpose of regression analysis, we focused on dosing errors which included over and under dosing. Descriptive data analysis was conducted and all continuous variables were expressed as either the mean and standard error, or median and inter-quartile range. Categorical variables were then presented as proportions and percentages. Inferential analysis was done using the Chi square, Mann-Whitney and student T-tests.

The risk factors for medication errors were determined using multivariable logistic regression. Variable selection was done using a forward stepwise model building approach. The covariates used for regression analysis included patient socio-demographic characteristics, medication history, diagnoses and co-morbidities. STATA version 13.0 software was used for data analysis. The level of significance was set at 0.05.

2.6 Ethical considerations

Approval to carry out this study was sought from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UoN-ERC) (Reference number: KNH-ERC/A/89, Appendix A). To implement the study, permission was also sought from the relevant hospital management authorities at Mbagathi District Hospital.

Informed consent for participation was sought from the patients' parents or guardians. In addition, assent was obtained for participants with some degree of capacity to understand the research and make decisions, but did not have the legal authority to provide informed consent. This was done for children over the age of 7 years.

3.0 RESULTS

3.1 Participants recruited and reasons for exclusion

Figure 1 summarizes the number of number of participants who were recruited into the study. Between April and June 2019, three hundred and eleven (311) children were admitted at Mbagathi District Hospital. Two hundred and ninety two (292) caregivers (93.9%) expressed interest in participating. Seventy five (75) children were excluded for not meeting the eligibility criteria and a further eleven (11) were excluded because caregivers did not give consent. Two hundred and six (206) treatment sheets and files from the General Pediatric Ward (GPW) at Mbagathi District Hospital (MDH) met the inclusion criteria and these records were evaluated for prescription errors.

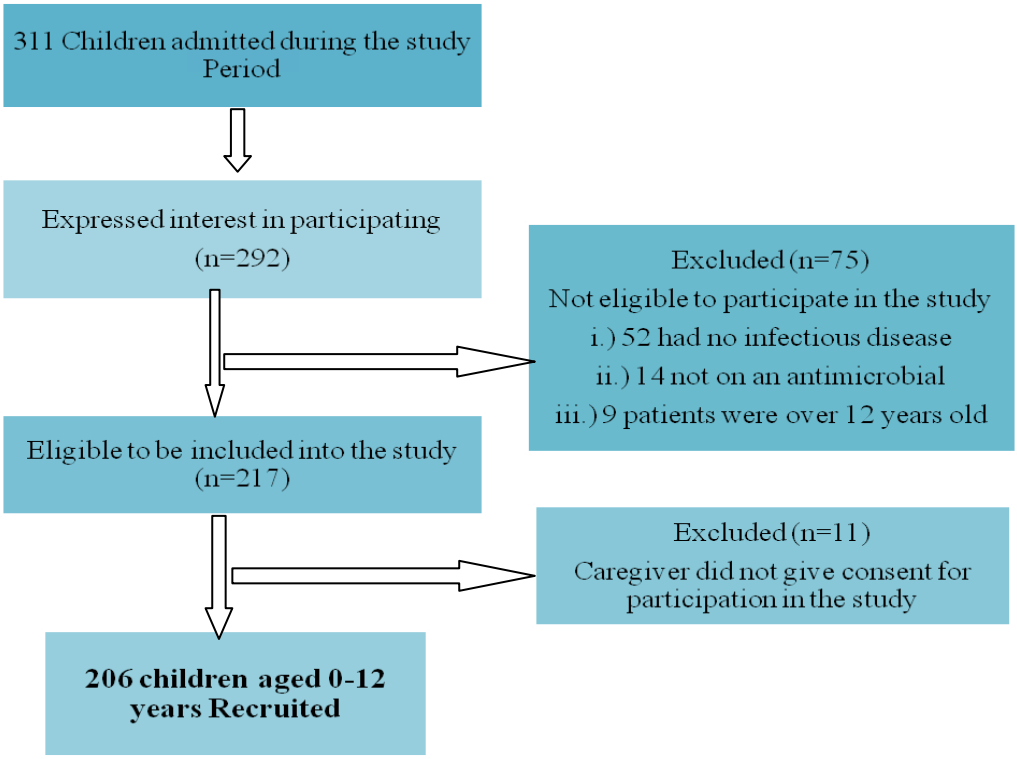

Figure 1: Consort diagram for recruitment of children hospitalized at Mbagathi Hospital

3.2 Baseline Characteristics of Study Participants

The socio-demographic traits of the participants are summarized in Table 1. Among the 206 pediatric patients recruited into the study, 57.3% were admitted in the acute room ward. The acute room is equipped with emergency equipment and supplies, and is reserved for critically ill patients. These patients are admitted here before being moved to the other ward rooms for recuperation when the patient is more stable. Room 1 is reserved for children who are stable but less than one year old and housed 19.9% of the participants. The rest of the rooms (2, 3 and 4) were for stable older children. Thirty two patients (15.5%) were admitted in room 2; 1 (0.4%) was admitted in room 3 and 14 (6.8%) were admitted in room 4.

Slightly more than half (108, 52.4%) of the patients were male while the rest 98 (47.6%) were female. The median age at admission was 9 months and ranged from 1 day to 144 months. The median weight was 6.6 kg, the lowest was 3.8 kg and highest was 10 kg. The median height was 62.3 cm and ranged from 48.1 to 75 cm. The median basal surface area was 0.4 [range 0.2, 0.5].

Table 1: Socio-demographic characteristics of study participants

	Frequency (%) Or Median [Range]	**Ward**	**n (%)**
Gender n (%)		Acute room (ward 1)	118 (57.3)
Male	108 (52.4)	Room 1	41 (19.9)
Female	98 (47.6)	Room 2	32 (15.5)
Baseline characteristics		Room 3	1 (0.4)
Median (range)		Room 4 (ward 5)	14 (6.8)
Age (months)	9 [1, 144]	**Total**	**206**
Weight (kg)	6.64 [3.8, 10]		
Height (cm)	62.25 [48.1, 75.0]		
Basal surface area	0.35 [0.2, 0.49]		

3.3 Clinical presentation, diagnoses and co-morbidities of children on antimicrobials admitted at Mbagathi District Hospital

Most of the children who were admitted with an infection (138, 67%) presented with a high fever as well. Only 26, (12.6%) of patients had elevated white blood cell (WBC) counts. Collectively, over two thirds (69.9%) were admitted with one or two diagnoses. Few patients had in excess of three diagnoses. For instance, only four patients had six diagnoses and ten had five diagnoses.

There were 233 infections in total noted amongst 197 of the children who were included in the study. Nine children (4.4%) did not have an infection but were on antimicrobials. The primary diagnoses were defined as infections that were the main reason for admission. The highest proportion of patients was admitted due to pneumonia (85, 36.5%). Acute diarrheal disease was a major reason for admission (50, 21.5%), then meningitis (24, 10.3%), neonatal sepsis (17, 7.3%), and malaria (11, 4.7%). About 10% of the patients had two or three infections. There was a higher incidence of patients who had malaria with meningitis than those who had malaria with pneumonia and malaria with pneumonia. Only two patients were admitted with malaria, meningitis and pneumonia. Most patients did not have a second infection.

About 50% of the participants had co-morbidities in addition to the primary infection. The most prevalent co-morbidity was severe acute malnutrition followed by dehydration and neonatal jaundice. A significant number of patients (40, 38.1%) had two or more co-morbidities. This information is represented in Table 2.

Table 2: Clinical presentation, diagnoses and co-morbidities of children on antimicrobials admitted at Mbagathi District Hospital

	n (%)	**Infection**	**Number of infection cases (%)**	**Patient co-morbidity**	**n (%)**
Fever status		Pneumonia	85 (36.5)	Multiple co-morbidities	40 (38.1)
Febrile	138 (67)	Acute diarrheal disease	50 (21.5)	Severe acute malnutrition	14 (13.2)
Not febrile	68 (33)	Meningitis	24 (10.3)	Dehydration	13 (12.4)
Level of white blood cells		Neonatal sepsis	17 (7.3)	Neonatal jaundice	13 (12.4)
Elevated WBCs	26 (12.6)	Febrile convulsions	12 (5.2)	Asthma	5 (4.8)
No elevated WBCs	180 (87.4)	Malaria+Meningitis	11 (4.7)	Anemia	5 (4.8)
Number of diagnoses per child		Malaria	11 (4.7)	Sickle cell anemia	4 (3.7)
1	75 (36.4)	Meningitis+Pneumonia	6 (2.6)	Congenital heart defect	2 (1.9)
2	69 (33.5)	Malaria+Pneumonia	4 (1.7)	Cerebral palsy	2 (1.9)
3	32 (15.5)	Bronchiolitis	3 (1.3)	Failure to thrive	2 (1.9)
4	16 (7.8)	HIV	2 (0.9)	Rickets	2 (1.9)
5	10 (4.9)	Malaria+Meningitis+Pneumonia	2 (0.9)	Adenoid hypertrophy	1 (1)
6	4 (1.9)	Cellulitis	1 (0.4)	Nephrotic syndrome	1 (1)
Total	**206 (100)**	Oral candidiasis	1 (0.4)	Sturge Weber Syndrome	1 (1)
		Sepsis	1 (0.4)		
		Septic cord	1 (0.4)		
		Rheumatic fever	1 (0.4)		
		Abscess	1 (0.4)		
		Total	**233 (100)**		

3.4 Types of medications prescribed for in-patient children at Mbagathi Hospital

The medication information is represented in Table 3. All the 206 participants were on one or more antimicrobials. The median of the number of drugs that was prescribed per patient was 2. A substantial number of patients were on five or more drugs (65, 31.6%) followed by those on three drugs (57, 27.7%) then those on four drugs (46, 22.3%).

The antimicrobials prescribed were grouped into different classes: antibiotic, antifungal, antiparasitic or antiviral. Five hundred and two (502) antimicrobials were prescribed in total to the 206 patients.

Antibacterials were most prescribed antimicrobials with 437 (87%) out of the 502 instances. Antiparasitics were 43 (8.6%) were, and the least prescribed antimicrobials were antifungals and antivirals at 3.6% and 0.8% respectively. Majority of the patients were on two antimicrobials 83 (40.3%) followed by those on three antimicrobials 59 (28.7%). Those on one and four or more antimicrobials had 32 (15.5%) number of patients each.

The most prescribed antimicrobial was benzyl penicillin (133, 26.5%), then gentamicin (111, 22.1%) and then ceftriaxone (92, 18.3%). The most prevalent frequency of administration was once daily (166, 33.1%) followed by four times daily dosing (139, 27.7%) then twice daily dosing (135, 26.9%). The most used route for antimicrobial administration was the intravenous route (278, 55.4%). Slightly over a third of the patients had no route of administration indicated.

Table 3: Types of medications prescribed for in-patient children at Mbagathi Hospital

Number of drugs per patient	n (%)	Number of antimicrobials per patient	n (%)
1	4 (1.9)	1	32 (15.5)
2	34 (16.5)	2	83 (40.3)
3	57 (27.7)	3	59 (28.7)
4	46 (22.3)	>4	32 (15.5)
≥ 5	65 (31.6)	**Total**	**206 (100)**
Type of antimicrobial			
Antibacterial	437 (87)		
Antiparasitic	43 (8.6)		
Antifungal	18 (3.6)		
Antiviral	4 (0.8)		
Total	**502**		

3.5 Prescribing errors identified in treatment sheets of children admitted at Mbagathi Hospital

The prescribing errors detected were 1298 in total. Of these, majority were incomplete prescriptions/missing information errors 691 (53.2%), followed by dosing errors (328, 25.3%), indication errors (142, 10.9%) and then documentation errors (137, 10.6%).

Excluding incomplete prescriptions/missing information errors, there were 607 (46.8%) other types of prescribing errors realized. Majority of the errors were dosing errors (328, 54%) followed by indication errors (142, 23.4%) and then documentation errors (137, 22.6%).

All the 206 (100%) patients' prescriptions had missing information. Therefore, the overall prevalence of prescription errors in this study was 100%. The most prevalent missing information per prescription was drug formulation 203 (98.5%). The least common type of missing information was name of the patient and name of the drug.

The inappropriate abbreviations included '*xpen'* instead of benzyl penicillin, '*genta'* instead of gentamicin, '*ABZ'* for albendazole and '*AL'* instead of artemether-lumefantrine. The brand names used included, Coartem™, for artemether-lumefantrine Flagyl™ instead of metronidazole, Septrin™ for cotrimoxazole and Candid B™ instead of clotrimazole-betamethasone.

The most common indication error that was observed in this study was incorrect drug. An example was prescribing gentamicin for acute diarrheal disease and malnutrition. Dosing errors which included under-doses and overdoses were attributed to use of estimated doses according to guidelines instead of actually individualizing the doses based on weight. Wrong frequencies of administration were also very common; more-so for antibacterial drugs where pediatric age and weight was a determining factor of the dosing frequency. The prescribing errors are summarized in Table 4.

Table 4: Errors in prescriptions for pediatric in-patients at Mbagathi District Hospital

Prescription errors	n (%)	Prescription errors	n (%)
Dosing errors		**Missing information**	
Under-dose	126 (9.7)	Drug formulation	203 (15.6)
Overdose	129 (9.9)	Prescriber's name/signature	175 (13.5)
Wrong frequency	73 (5.7)	Date of the prescription	136 (10.5)
	328 (25.3)	Route of administration	92 (7.1)
Indication errors		Duration of drug intake	25 (1.9)
Contraindicated error	4 (0.3)	Strength of the drug	19 (1.5)
Incorrect drug	60 (4.6)	Frequency of the drug	14 (1.1)
Unnecessary drug	78 (6.0)	Gender	11 (0.8)
	142 (10.9)	Amount of drug dispensed	5 (0.4)
Documentation errors		Age	4 (0.3)
Use of brand names	9 (0.7)	Amount of drug prescribed	3 (0.2)
Dangerous abbreviation	121 (9.3)	Name of the patient	1 (0.1)
Illegibility	4 (0.3)	Name of the drug	1 (0.1)
Trailing zero	3 (0.2)		**691 (53.2)**
	137 (10.6)		

3.6 Risk Factors for Dosing Errors

Multivariable logistic regression analysis was undertaken to identify the risk factors associated with under- and over dosing errors. Separate analysis was done for each type of error.

3.6.1 Risk Factors for Under-dosing of antimicrobials

On comparison of the distribution of variables across those who experienced under-dosing errors and those who did not, there was a statistically significant difference for the weight, height, body surface area, creatinine levels, age, ward admitted in, frequency of dosing, diagnosis and the antimicrobial class. There were no statistical significant associations for the variables gender, elevated white blood cells and fever status. Gentamicin (p=0.005), body surface area (p=0.048) and the room the patient was admitted (p=0.005) were statistically significant risk factors for under-dosing as well as presented in Table 5. The associations between the various types of predictors with under-dosing are presented separately.

Table 5: Risk factors for under-dosing errors

Variable	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Sepsis	6.600 (2.625, 16.590)	**<0.001**	4.463 (1.638, 12.160)	**0.003**
Malaria	0.921 (0.314, 2.700)	0.88	-	
Meningitis	0.082 (0.052, 2.488)	0.853	-	
Pneumonia	2.152 (1.304, 3.552)	**0.003**	-	
Diarrhea	1.828 (0.927, 3.604)	0.081	-	
BSA^2	1.787 (1.076, 2.968)	**0.025**	1.744 (1.006, 3.022)	**0.048**
Ward5	1.952 (1.032, 3.692)	**0.04**	2.867 (1.379, 5.920)	**0.005**
Age (months)	0.681 (0463, 1.004)	**0.052**	-	
Height	1.724 (1.048, 2.839)	**0.032**	-	
Weight (>5kg)	1.628 (1.107, 2.396)	**0.013**	-	
Artesunate	2.480 (1.109, 5.547)	**0.027**	30.451 (9.298, 99.722)	**<0.001**
Gentamicin	4.007 (2.608, 6.154)	**<0.001**	1.941 (1.217, 3.093)	**0.005**
Ceftazidime	4.313 (1.471, 12.650)	**0.008**	-	
Flucloxacillin	2.784 (0.251, 30.935)	0.405	-	
Ceftriaxone	2.331 (1.407, 3.863)	**0.001**	-	
Benzylpenicillin	1.412 (0.882, 2.261)	0.151	-	
Antimicrobial class	0.903 (0.644, 1.265s)	0.552	18.559 (7.345, 46.894)	**<0.001**

3.6.1.1 Association between type of infection and under-dosing

Children who had infections were under-dosed (cOR 4.463, 95% CI: 1.638, 12.160). Patients with an infection were 4.5 times as likely to be under-dosed as compared to those patients without an infection. About 67% of the patients who were admitted due to an infection also had fever as one of the presenting symptoms, experienced under-dosing.

On bivariable regression analysis, there was a statistically significant association between sepsis and the occurrence of under-

dosing errors (cOR 6.6; 95% CI 2.6-16.6, p=<0.001) and on multivariable analysis it was still highly statistically significant (aOR 4.5; 95% CI 1.6-12.2, p=0.003).

3.6.1.2 Association between the type of drug, frequency of administration and under-dosing of antimicrobials

On multivariable analysis of factors leading to under-dosing, it was noted that children receiving artesunate were 30.5 times likely to be under-dosed (cOR=30.5: 95% CI: 9.3, 99.7, p=<0.001), as compared to those with the other antimicrobials. Those who were on antibacterials were 18.6 times likely to experience these errors as compared to other classes of antimicrobial (OR 18.6: 95% CI 7.3-46.9, p=<0.001).

Patients who were on antibacterials were nine times more likely to experience under-dosing errors (cOR 9.076, 95% CI: 5.107, 16.132) compared to those on other classes of antimicrobials (antifungals, antiparasitics and antivirals). On the bi-variable analysis, artesunate, ceftriaxone, ceftazidime, and gentamicin were the most likely to be under-dosed. Benzyl penicillin and flucloxacillin were not likely to be under-dosed yet these two antibiotics had a high frequency of administration. On adjusting for confounding, gentamicin and artesunate were the two drugs that remained most likely to be under-dosed.

The prevalence of under-dosing errors in pediatric patients was more than a third in children who received drugs once a day (35.5%). Patients who received antimicrobials once a day was 0.5 times less likely to be under-dosed as compared to all other dosing frequencies (cOR 0.524, 95% CI: 0.205, 1.340).

3.6.1.3 Association between anthropometric measures and under-dosing of antimicrobials

Weight was a very significant predictor of being under-dosed (cOR 1.628, 95% CI 1.107, 2.396). The median weight for patients who were under-dosed was 6.32 kg. Generally, patients who weighed less than 5kgs were 1.6 times more likely to be under-dosed than patients who weighed more than 5kgs.

Patients who were under-dosed had a median height of 63cm. The prevalence of under-dosing was generally higher in taller patients (cOR 1.724, 95% CI 1.048, 2.839). Patients who were taller than 47cm were 1.7 times as likely to be under-dosed compared to patients who were shorter than 47cm.

Patients with a Body Surface Area (BSA) of less than $0.2m^2$ had a higher prevalence of being under-dosed (cOR 1.787, 95% CI 1.076, 2.968). Patients with a $BSAm^2$ of less than $0.2m^2$ were 1.8 times as likely to be under-dosed compared to children who had a body surface area greater than $0.2m^2$. Patients who were under-dosed had a median age of nine months. Generally, younger patients with the age of less than six months were 0.7 times as likely to experience under-dosing errors compared to children older than six months of age (cOR 0.681, 95% CI 0.463, 1.004).

3.6.1.4 Effects of the ward of admission on prevalence of under-dosing

Patients in Room five were the most likely to receive an under-dose. This ward was the furthest from the nursing station and it had older stable patients. Patients in ward five were almost twice as likely to be under-dosed compared to patients in all other wards (cOR 1.95, 95% CI 1.032, 3.692). The prevalence of dosing errors in ward five was 25% of all prescription episodes compared to a prevalence of 14.6% in the rest of the pediatric wards.

3.6.2 Risk Factors for Overdosing

On analyzing and comparing the distribution of variables across those who experienced overdosing errors and those who did not, there was a statistically significant difference for the variables weight, height, body surface area, age, ward admitted in, frequency of dosing, diagnosis and the antimicrobial class. There were no statistical significant association between gender, elevated white blood cells,

creatinine levels and fever status. The findings are shown in Table 6.

Table 6: Risk factors for overdosing errors in pediatric patients

Variable	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Sepsis	0.294 (0.039, 2.221)	0.235	0.106 (0.013, 0.832)	**0.033**
Malaria	1.178 (0.440, 3.158)	0.745	-	
Meningitis	1.051 (0.457, 2.414)	0.908	-	
Pneumonia	2.515 (1.546, 4.093)	**<0.001**	-	
Diarrhea	1.568 (0.781, 3.149)	0.206	-	
BSA (m^2)	0.635 (0.429, 0.942)	**0.024**	-	
Dosing frequency	1.374 (0.891, 2.120)	0.15	2.967 (1.740, 5.059)	**<0.001**
Ward 2	0.751 (0.454, 1.240)	0.263	-	
Age (months)	0.714 (0.486, 1.049)	0.086	-	
Height	0.700 (0.480, 1.020)	0.063	-	
Weight (>5kg)	1.438 (0.978, 2.113)	0.064	-	
Artesunate	2.407 (1.077, 5.382)	**0.032**	28.701 (1.950, 422.712)	**0.014**
Gentamicin	1.803 (1.138, 2.857)	**0.012**	-	
Ceftazidime	0.410 (0.531, 3.161)	0.392	-	
Flucloxacillin	2.707 (0.244, 30.075)	0.418	-	
Ceftriaxone	1.709 (1.008, 2.897)	**0.047**	0.367 (0.198, 0.683)	**0.001**
Benzylpenicllin	1.443 (0.907, 2.297)	0.122	0.239 (0.131, 0.436)	**< 0.001**
Antimicrobial class	12.498 (6.619, 23.601)	**<0.001**	0.129 (0.035, 0.481)	**0.002**

BSA: Body surface area

3.6.2.1 Types of antimicrobial and frequency of administration as risk factors for overdosing

Children who were on antibacterial drugs were overdosed. Patients who were on this class of antimicrobials were 12.5 times as likely to experience overdosing errors (cOR 12.5, 95% CI: 6.62, 23.6) compared to other classes of antimicrobials (antifungals, antiparasitics and antivirals). On the variable analysis, benzyl penicillin and ceftriaxone were the most likely to be overdosed. Artesunate, ceftazidime, flucloxacillin and gentamicin were not likely to be under-dosed yet these antibiotics had a high frequency of administration. On adjusting for confounding, benzyl penicillin and ceftriaxone were the two drugs that remained most likely to be overdosed.

In bivariable analysis, the type of antimicrobial had a significant association with the occurrence of overdosing errors (cOR 12.5: 95% CI 6.62-23.6, P=<0.001) and on multivariate analysis it was still highly statistically significant (OR 0.13, 95% CI 0.04-0.48, P=0.003).

It was noted that children receiving artesunate were 28.7 times more likely to be overdosed (cOR 28.7: 95% CI: 1.95, 422.7, p=<0.001), as compared to those with the other antimicrobials. The dosing frequency was a major determinant of overdoses. Those who received drugs once a day were three times as likely to experience these errors as compared to other frequencies (OR 2.97: 95% CI 1.74-5.06, p=<0.001). The antimicrobial class (p=0.002), benzyl penicillin (p= <0.001), ceftriaxone (p=0.001) and sepsis (p=0.033) were statistically significant predictors of overdosing errors as well.

The occurrence of overdosing errors in pediatric patients was approximately a third of that of children who received drugs once a day (30.1%). Patients who received antimicrobials once a day was 1.4 times more likely to experience these errors as compared to all other dosing frequencies (cOR 1.37, 95% CI: 0.89, 2.12).

3.6.2.2 Effects of anthropometric measures on overdosing errors

Children who were overdosed had a median weight of 5.25 kg. Those less than 5.25kg were 1.4 times more prone to experiencing an overdose than the heavier patients (cOR 1.44, 95% CI 0.98, 2.11). Patients who were overdosed had a median height of 56cm. The prevalence of over-dosing among shorter patients was 18.5% (cOR 0.70, 95% CI: 0.48, 1.02). Patients who were less than 56cm in height were 0.7 times as likely to be overdosed as compared to taller patients.

The prevalence of overdosing errors was higher (19.6%) in children who had a median age of nine months. Generally, younger patients (less than seven months old) were 0.7 times as likely to experience overdosing compared to children over seven months of age (cOR 0.71, 95% CI: 0.49, 1.02).

Patients with a body surface area of less than $0.4m^2$ had a higher prevalence (18.2%) of being overdosed (cOR 0.64, 95% CI: 0.43, 0.94). Patients with a BSA (m^2) of less than $0.4m^2$ were 0.6 times as likely to experience overdosing compared to children with a body surface area greater than $0.2m^2$.

3.6.2.3 Effects of the ward of admission on prevalence of overdosing

Acute room (ward one) was the closest to the nursing station and it had critically sick children. Patients in room one were 0.8 times as likely to be overdosed compared to patients in all other wards (cOR 0.751, 95% CI: 0.45, 1.24). The prevalence of overdosing errors in ward one was 17.8% of all prescription episodes compared to a prevalence of 12.8% in the rest of the pediatric wards.

4.0 DISCUSSION

This study sought to measure the prevalence of prescription errors amongst children admitted in a resource limited setting. As reported on studies in Mbagathi District Hospital and other public hospitals, the age and gender distribution conformed to that reported in other studies. However, neonates were under-represented because the facility does not have a neonatal intensive care unit (NICU). For this reason, very low birth weight children were not treated here but referred to a level five or level six facility. Children over 5 years old were also under-represented because they were generally viewed as healthier and less susceptible to infections. The pattern of infections conformed to the national trend where pneumonia, acute diarrheal disease, malaria and neonatal sepsis are the major causes of infections in pediatric patients. [10,11]

Incomplete prescriptions accounted for close to half of the prevalence 811 (49.3%) of prescription errors which was in line with studies carried out before. Studies in Kenya and other countries have shown that, incomplete prescriptions are a common prescribing error. In a study by Mulwa et al on the patterns of prescribing practices at Makueni County Referral Hospital, the overall prevalence of incomplete prescribing errors was 54% with most prescriptions lacking the diagnosis. [12] In another study by Khaemba et al, missing information was significantly lower and accounted for 234 (22.8%) of all prescription errors. [13] The missing information included age, gender, name of the patient, prescriber's name date of prescription, name of the drug, drug formulation and the amount, frequency, strength, route and duration of administration. Another study by Hawaze et al in a teaching and referral hospital in Addis Ababa, missing information accounted for 14476 (63.5%) of all prescribing errors. [14,15] The prevalence of prescription errors was 39.4% with missing information being the most prevalent type (49.3%), followed by dosing errors (19.9%) then indication (8.6%) and documentation errors (8.3%) in this study.

According to the National Coordinating Council for Medication Error Reporting and Prevention [26] all prescriptions are required to clearly include the important information on the prescription or medication order such as dose, dosage form, frequency, duration and route of administration, the age and, when appropriate, height and weight of the patient. However, when prescriptions are incomplete, it may cause serious risks to patient safety. In this study, very few prescriptions analyzed contained the correct and complete specifications, which are paramount to treatment success. The use of brand names can also lead to a series of prescription errors especially in the lookalike sound alike drugs.

In the parsimonious model, the overall predictor variables for dosing errors identified included the antimicrobial class, sepsis, gentamicin, artesunate, ceftriaxone, benzyl penicillin, weight, frequency, ward 5 and basal surface area. On the multivariable regression analysis, children younger than nine months (OR 0.76, 95% CI: 0.49, 1.20) and had a height less than 56cm (OR 1.22, 95% CI: 0.32, 4.66), weight less than 5.5kg (OR 1.534, 95% CI: 0.978, 2.408) and body surface area less than $0.4m^2$ (OR 1.777, 95% CI: 1.028, 3.073) were more likely to experience more dosing errors. According to Anderson et al, pediatric dosing cannot be scaled down from an adult by weight. [15] Such practice could result to sub-optimum doses in children because drug elimination does not change in direct proportion to weight, and very large doses for neonates with immature drug elimination pathways. [15] According to the British National Formulary and other reference books, it is recommended that drug dosages for children be calculated according to body surface area (BSA). However, there are many drug dosage rules that have been developed, based on the age, weight and surface area but none has been simple and accurate enough for routine use. [16] The BSA priciple has been in existence for many years but there is no consistency across guidelines on use BSA to compute doses. Similarly, having accurate current weight measurements are essential for growth monitoring and drug dose determination

Pediatric patients in room five were 2.9 times as likely to experience under-dosing errors (OR 2.867, 95% CI: 1.379, 5.920) as compared to the other wards in multivariable analysis. This was consistent to the fact that, the further the room was from the nursing station, the higher the prevalence of prescription errors were likely to be. Children who were in room five which was furthest from the nursing station were much older and stable. For these reasons, the prescribers seemed to pay less attention to these patients and concentrated on the more critical patients. Patients in these wards could have been neglected because of a heavy workload and the general assumption of children being well. According to Zahavy et al, paying attention to the location of the ward, the workload and prescription practices should always be observed. [17,18] A pharmacist should always go around, to monitor and evaluate each prescription and to facilitate learning from the errors noted.

The type of infection was a significant risk of prescription errors. Of concern was sepsis, where patients who were treated for this infection were 4.6 times as likely to be dosed wrongly (OR 4.569, 95% CI: 1.651, 12.992). The type of antimicrobial class was a significant predictor for prescription errors.

Patients who were on antibacterials were 18.7 times as likely (OR 18.688, 95% CI: 7.380, 47.375) to experience these errors compared to the other classes of antimicrobials. However, it was noted that, despite well-defined guidelines on the rational use of antimicrobials being available, inappropriate prescribing patterns were noted as most children were started on antimicrobials empirically before laboratory confirmatory tests were done. According to Le Doare et al, there is great and urgent need to enhance the antimicrobial quality of prescribing worldwide, with greater need in resource-poor settings. This is so with regard to the growing global health priority in Antimicrobial resistance (AMR) threat. [19] According to the World Health Organization (WHO), approximately 50% of all medicines are prescribed or dispensed inappropriately and half of all the patients incorrectly take their medicines.

Patients who were being treated with benzyl penicillin, ceftriaxone, gentamicin and artesunate, were 0.2, 0.4, 1.9 and 30.5 times likely respectively to be dosed wrongly compared to patients not on these agents. Benzyl penicillin, gentamicin and ceftriaxone were the most empirically prescribed antimicrobials. According to Cousins et al of the Academic Division of Child Health, University of Nottingham,

Derbyshire children's hospital, there were about 33.3% overdose incidences of benzyl penicillin that was injected spinally. [20] In a study by Berhe et al, therapy using ceftriaxone was inappropriately prescribed in 62.4% of the cases [21] and in another study by Patel et al, there was a 7.9% prevalence of dosing errors due to ceftriaxone. [22] A study by Brasseur et al to determine the dosing accuracy and the consequential effects of artesunate in treatment of falciparum malaria in Senegal, there was a 30.6% prevalence of dosing errors. [23]

The dose frequency was also a major risk for patients who had prescription errors with patients dosed once daily being 3 times as likely to experience dosing errors (OR 2.967, 95% CI: 1.74, 5.059). In a study to determine the errors and omissions in hospital prescriptions by Calligaris et al, there was a 36.3% prevalence of wrong frequency errors. [24] In another study by Libsy et al, to investigate the type, frequency and the consequences of medication errors in the medication process, the prevalence of errors due to dosing frequency were 29.4% of all prescription errors that were noted. [25]

A number of factors predisposed pediatric patients to prescription errors as compared to others. Kaushal et al [27] attributed increases incidences of medication errors in children to formulations not suitable for neonate dosing. According to Manley et al., [28] the consequences of a poor workplace culture, such as a lack of communication and teamwork, have a direct influence on medication administration; for example, double-checking as a safety initiative will only succeed with effective communication and a strong sense of teamwork. Ivanovska et al [29] reported considerable degree of variation in current oral pediatric liquid formulations posing a risk of dosing errors.

The main strength of this study is that, being a prospective hospital-based cross sectional study data was collected in real time. The limitations of this study included incompleteness of medical records, which posed a big challenge despite having measures in place during data collection to ensure a near complete data set as possible. Assessment of the extent of prescription errors was sometimes subjective despite attempts to minimize it. There was also the risk of information bias (specifically reporting bias) because, obtaining data from the respondents may have not have been very reliable given that not all give a true response to some of the questions that sought to identify some valuable information.

CONCLUSION

There was a very high prevalence of various prescribing errors. Errors were more likely to occur for selected medicines and patients who were very ill. Interventions such as clinical pharmacists in the wards are required to minimise these errors.

Data availability

The primary data gathered by the authors and which supports the findings of this study are available from the corresponding author upon request

Conflicts of Interest

The authors declare that there are no conflicts of interest

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