Inappropriate Use of Antibiotics and Their Predictors in Pediatric Patients Admitted at the Hospital Central De Nampula, Mozambique

Sancho Pedro Xavier (✉ s.xavier@unilurio.ac.mz)

Universidade Lurio <https://orcid.org/0000-0001-9493-4098>

Audêncio Victor

Universidade Federal da Bahia Instituto de Saude Coletiva

Graciano Cumaquela

Universidade Lurio Faculdade de Ciencias de Saude

Melsequisete Daniel Vasco

Universidade Federal da Bahia Instituto de Saude Coletiva

Osiyallê Rodrigues

Universidade Federal da Bahia Instituto de Saude Coletiva

Alexandre de Fátima Cobre

Universidade Federal do Parana

Research

Keywords: Pediatrics, Antibiotic prescription, Inappropriate use of antibiotics

Posted Date: August 18th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-786683/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

Antibiotics are synthetic or natural substances used to treat diseases of infectious origin. When used incorrectly, they can be a factor in the development of antimicrobial resistance, increased treatment time, costs, and mortality. The present study aimed to assess the pattern inappropriate use of antibiotics and their predictors in pediatric patients admitted to the Hospital Central de Nampula, Mozambique

Methods

A cross-sectional, retrospective study with a quantitative approach was conducted between January and July 2019. The population consisted of children aged 0 to 10 years hospitalized in the pediatric ward I. Binary logistic regression was used to determine risk factors for inappropriate use of antibiotics with 95% CI.

Results

The prevalence of antibiotic use among pediatric patients was 97.5%. Of the 464 antibiotics prescribed, 39.9% were for patients suffering from gastroenteritis, 21.8% and 9.1% Affected with pneumonia and malaria. Most antibiotics were for systemic use (95.9%, 445/464). Most (36.5%) of prescriptions had errors. Duration of treatment (74.6%) and dosage (25.4%) were the most frequent errors. Binary logistic regression analysis revealed that patients were prescribed with ≥ 3 antibiotics (OR = 2.920, 95% CI = 1.283–6.646, p-value = 0.011) and with a short hospitalization time (OR = 1.726, 95% CI = 1.040–2.864, p-value = 0.035) were more likely to experience some inappropriate use of antibiotics.

Conclusion

The study showed a higher prevalence of antibiotic use, however, a greater number of prescriptions contained errors. Errors related to dose and duration of treatment were the most common among pediatric patients. These results reveal a concern, since inappropriate and excessive use of antibiotics is a major factor for the development of antibiotic resistant microorganisms. Therefore, strategies concerning the use of antibiotics in order to reduce their inappropriate and excessive use are necessary.

Background

Antibiotics are drugs used to treat infectious diseases, which can be of natural or synthetic origin, with the ability to inhibit the proliferation or destroy microorganisms, and are the most used drugs in pediatric age, and play a vital role in the treatment of infectious diseases worldwide (1–3). Studies have shown that about 86% of hospitalized children received at least one antibiotic (4). Currently, these drugs are

overused inappropriately, putting users at risk, such as the development of microorganisms resistance and ineffective treatment (5). The worldwide excessive use of antibiotics in human medicine and agriculture results in the proliferation and dissemination of a multitude of antibiotic-resistant genes, which constitutes the biggest and main public health problem Globally (6–8). This practice of excessive and inappropriate use of antibiotics is the main cause of bacterial resistance globally, which is considered a major public health problem (9–11). The inappropriate use of antibiotics has been the most common mode of irrational use of these drugs worldwide and includes errors in prescription, administration, dosage and duplication of the same product (12). Some studies have shown that the percentage of Improper use of some antibiotics in hospitals ranges from 20–80% (13, 14). Moreover, patients with antibiotic resistant infections are more likely to experience ineffective treatment, recurrent infection, delayed recovery and even death (15). Therefore, about 6.5% of morbidity and mortality in hospital admissions is associated with inappropriate antibiotic prescription (16). In the United States and Canada, 30% – 50% of antibiotics are used incorrectly, similarly in some Asian and African nations, 50% of prescribed antibiotics are identified as inappropriate (17, 18). According to the World Health Organization (WHO), antimicrobial resistance among pathogens responsible for common infections is alarmingly high (19). The Centers for Disease Control and Prevention (CDC) estimates that in the United States of America, less than 2 million illnesses and about 2300 deaths are due to bacterial resistance to antibiotics. According to the WHO, 25,000 deaths per year are registered in European hospitals and 700,000 worldwide are associated with antibiotic resistance (20, 21). In Middle East regions, 90% of hospitalized newborns with sepsis had bacterial resistance to antibiotics (22). In sub-Saharan Africa, 66% of neonatal sepsis and meningitis are caused by antibiotic-resistant bacteria (23). It was predicted by European Commission (2018) that by 2050, antimicrobial resistance will be responsible for more deaths than cancerous diseases (24). A current, high-level report estimates that by 2050, 10 million people will die every year because of antimicrobial resistance unless there is global action against this problem (25). Reduce misuse is essential to reduce not only antibiotic resistance but adverse reactions as well (18). In this case, several actions are essential, resulting in a positive effect. These actions aim to reduce the complex consumption and use of broad-spectrum antibiotics. The use of antibiotics should be careful and limited to certain circumstances. Therefore, proper prescription is the main strategy to prevent the rapid growth of bacterial resistance to antibiotics (5, 22). Finally, having knowledge about the patterns of incorrect use of antibiotics and their risk factors in the pediatric population is essential to create programs, policies and actions related to the dispensing of these drugs in this population. Thus, the present study aimed to assess the pattern improper use of antibiotics and their predictors in pediatric patients admitted to the Nampula Central Hospital, Mozambique

Methods

Study design

A cross-sectional study with a quantitative approach was conducted in patients hospitalized at the Hospital Central de Nampula (HCN), Mozambique. Pediatrics I is a ward that welcomes patients with various pathologies, categorized into gastrointestinal, respiratory and general diseases. Clinical files and

medical prescriptions of hospitalized patients from January to July 2019 were used. In the clinical files, information was obtained on independent variables such as sex, age, medical diagnosis, treatment time, discharge, and information were obtained from the cardex on the prescribed antibiotics, dosage and route of administration. The survey was carried out in the year 2020.

Population and sample size

From January to July 2019, a total of 1745 patients were registered, the sample size was obtained, taking into account the exclusion and inclusion criteria. The sample consisted of 315 patients. The simple randomization technique was used, a technique that allows obtaining a representative sample size, where each element of the population has an equal chance of being selected to be part of the sample. The logbook was used to obtain the master list containing numbered population. From the master list, randomization was performed to select the research participants. All clinical files with the respective cardex of patients aged between 1 and 120 months, hospitalized in that ward during the period from January to July 2019 were included in the study. To obtain the sample size, a formula was used based on a known population, as illustrated below.

$$n = \frac{p(1 - p)Z^2N}{\epsilon^2(N - 1) + Z^2p(1 - p)}$$

Where: n: sample size; p: expected proportion (50%=0.5); Z: Normal distribution value for a given confidence level (95%) =1.96; N: population size (1745); ϵ : size of the confidence interval “margin of error” (5%=0.05) (26).

Study variables

The use of antibiotics was considered the dependent variable and considered as the study outcome variable, in which it was classified as dichotomous categorical. It was coded using code one (1) for misuse, which is inappropriate antibiotic use, and zero (0) for correct use, which is proper use. The variable of interest was code 1. The independent variables were sex, age, weight, medical diagnosis, outcome (discharge, dropout and death), prescribed antibiotics, dose, frequency, route of administration, duration of treatment and length of hospitalization, also considered as clinical predictors, were classified as numerical and categorical. The numerical ones were age, weight, number of antibiotics prescribed and duration of treatment. Categorical variables were gender, medical diagnosis, outcome, dosage, dose, route of administration and length of hospitalization. The variable age was also considered as categorical, where it was categorized into: child (1-3 years), infant (28 days- 12 months), preschool (3-5 years) and school (6 - 10 years). The variable weight was transformed into categorical: <10, 10 -18.9 and ≥ 19 . The dose was categorized into underdose and overdose, and duration of treatment was transformed into categorical, according to table 1. The variables used to predict the outcome of interest were age, weight, length of hospital stay and number of antibiotics prescribed.

Determining Prescription Errors

The antibiotics used were considered appropriate for the patient, if the dose present in the cardex (medical prescription) was in accordance with their respective weight. Antibiotics were considered inappropriate if the prescribed dose was lower or higher (dose error) than recommended by international guidelines and databases, classified overdose and underdose; association of antibiotics of the same class (irrational selection), wrong antibiotic prescription for the disease, dosage error, non-recommended route of administration, wrong duration of antibiotic use. Regarding the dose error, a significance level (error margin) of 10% was considered. Prescription doses with an error above 10% were considered overdose, while prescribed doses below 10% were considered underdose. To determine prescription errors, guidelines and international databases, WHO guidelines (27–30), British National Formulary (BNF) 2019 – 2020 were used (31,32). NICE (National Institute for Health and Care Excellence) was used as guidance (33–35), for both the dose and the dosage and indication of the antibiotic. The indicators used in this study to weight the appropriate or inappropriate use of antibiotics were antibiotic selection, dosage, antibiotic dose and amount of antibiotics prescribed per prescription and duration of treatment.

Data analysis

Descriptive analysis was applied to frequency distribution, measures of central tendency, and variables dispersion (standard deviation). Also, binary logistic regression was used to determine risk factors for inappropriate use (prescription errors) of antibiotics. The Odds Ratio (OR) was applied to determine the chances of inappropriate use of antibiotics occurring with a Confidence Interval (CI) of 95% and p - Value < 0.05 for statistically significant differences between the independent variables with the outcome of interest. To verify the collinearity analysis also was performed linear regression.

The analyses were performed in the Microsoft Excel 2019 and SPSS 25.0 software.

Results

Demographic and clinical features of patients

Of the 315 pediatric patients selected for the study, 63.2% were male. The majority (162; 51.4%) had an age between 1 and 3 years. The mean age in months was 30.44 (SD ± 26.07), 21 was the

median, being 5 months the minimum age and 120 months the maximum. Most pediatric patients (48.9%) weighed less than 10 kg. for the length of hospital stay (in days), 61.6% had a short hospital stay, with an average of 2.85 days, and 39.4% a long hospital stay, with an average of 8.99 days, where 39 days was the longest time (table 1). **Table 1.** Demographic and clinical characteristics of pediatric patients hospitalized in the Pediatrics I ward

Variables	(n=315)	%
Sex		
Male	199	63.2
Female	116	36.8
Age		
[13 years]	162	51.4
[28 days – 12 months]	74	23.5
[3–5 years]	41	13.0
[6 – 10 years]	38	12.1
Age in months	(mean ± SD) = 30.44 ± 26.07	
Weight (Kg)		
<10	154	48.9
10 - 18.9	136	43.2
≥19	25	7.9
Number of prescribed antibiotics		
1	187	60.9
2	90	29.3
≥3	30	9.7
Hospitalization time (days)		
Short [average = 2.85, range 0 - 4]	194	61.6
Long [average = 8.99, range 5 - 39]	121	38.4
Antibiotic treatment duration (days)		
0 – 5	382	82.3
6 – 8	40	8.6
9 – 14	22	4.7
≥15	20	4.3
Outcome		
Discharge	301	95.6
Abandonment	8	2.5

Description of used antibiotics

Of the 315 pediatric hospitalized patients, 307 were prescribed antibiotics. A total of 464 antibiotics were prescribed. The prevalence of antibiotic use during the study period was 97.5% (307/315). Most antibiotics (39.9%) were prescribed for patients suffering from gastroenteritis, 21.8% for pneumonia, while 9.1% for patients affected malaria (Table 2). Most antibiotics prescribed (445; 95.9%) were for systemic use, followed by oral use (17; 3.7%). As for oral antibiotics, 3.0% (n=14) were in suspension form and 0.6% (n=3) tablets.

Table 2 Distribution of antibiotics prescribed by diagnosis among patients

Diagnostic	(n= 464)	%	Diagnostic	n	%
Gastroenteritis	185	39.9	Asthma	7	1.5
Malaria	42	9.1	Tonsillitis	2	0.4
Convulsive Syndrome	34	7.3	hemangioma	3	0.6
Bronchopneumonia	101	21.8	Tumor	2	0.4
Hydrocephalitis	6	1.3	Infectious pyoderma	4	0.9
Anemia	12	2.6	Pains	1	0.2
Pharyngotonsillitis	7	1.5	Cerebral palsy	4	0.9
Typhoid fever	11	2.4	Heart disease	4	0.9
Burn	1	0.2	Splemegaly	1	0.2
Sepsis	16	3.4	Dermatitis	2	0.4
Epilepsy	6	1.3	Menychocephalitis	5	1.1
Trauma	1	0.2	Pharyngitis	3	0.6
Allergy	2	0.4	Laryngitis	1	0.2
Injuries	1	0.2			

Fig.1. Shows that the most used antibiotics were crystalline penicillin (155/464, 33.4%), ceftriaxone (95/464, 20.5%), co-trimoxazole (86/464, 18.5%), gentamicin (52/464, 11.2%) and ampicillin (43/464, 9.3%).

Description of antibiotic use errors

A total of 36.5% (112/307) of medical prescriptions had errors, that represents a total sum of 34.5% (160/464) of incorrectly prescribed antibiotics. 57.1% (64/112) of prescriptions had an error, while 27.7% (30/112), 11.6% (n=13/112), 3.6% (4/112) and 0.9% (1/112) had respectively two, three and four errors due to prescription. Higher error rates were detected in patients suffering from gastroenteritis (63; 39.4%), pneumonia (16.3%; 26/160), seizure syndrome 6.9%; (11/160), followed by sepsis (6.3%; 10/160) and malaria (5.6%; 9/160). Dosage 25.4% (47/185), duration of treatment 74.6% (138/185) and duplication of therapy (n=3/121; 2.5%) were the most frequent prescription errors. Regarding dosage errors, a proportion of 14.0% (26/185) of antibiotics had high doses, while 11.4% (21/185) had low doses. Most antibiotics 55.1% (102/185) had a short time of use, while 19.5% (36/141) had a long time.

Analysis to determine risk factors for inappropriate use of antibiotics

Binary logistic regression was applied to verify whether age, weight, number of antibiotics and length of hospital stay predict inappropriate use of antibiotics. The model containing age, number of antibiotics and length of hospital stay was significant ($X^2(1) = 13.937$; $p < 0.001$; R^2 Cox & Snell = 0.44). The chance of succeeding the inappropriate use of antibiotics was 2.920 times greater in pediatric patients with a prescription of ≥ 3 antibiotics per prescription (OR = 2.920, 95% CI = 1.283 - 6.646, p - value = .011) increasing by 192% chance in relation to patients prescribed an antibiotic by prescription. In patients with a short hospitalization time, the chance of succeeding the inappropriate use of antibiotics was 1.726 times higher (OR = 1.726, 95% CI = 1.040 - 2.864, p - value = .035) increasing in 72.6% of odds comparatively to patients with a long period of hospitalization (Table 3).

Table 3. Determination of risk factors for inappropriate use of antibiotics.

Variables	Clinical predictors	OR	(95% CI)	p – Value
Age	1 – 3 years			
	28 days – 12 months	0.824	0.418 – 1,622	0.575
	3 -5 years	1.26	0.582 – 2,746	0.553
	6 – 10 years	1.35	0.505 – 3,621	0.549
Weight (Kg)	<10			
	10 – 18,9	1.09	0.511 – 2.021	0.778
	≥19	1.49	0.416 – 5.345	0.539
Number of antibiotics per prescription	1			
	2	1.412	0.824- 2.419	0.209
	≥3	2.92	1.283 – 6.646	0.011*
Hospitalization time (days)	Short (<4)	1.72	1.040 – 2.864	0.035*
	Long (≥5)			

Note* showed to have statistical significance with p value less than or equal to 0.05 (95% CI)

Discussion

Antibiotics are the most commonly prescribed drugs, and their use in the pediatric population is a huge concern in some countries (36,37). Today, antibiotic resistance is one of the biggest serious public health problems that has grown through the excessive and inappropriate use of antibiotics, both in humans and animals (38).

Description of antibiotics used

Studies have shown that antibiotics are more used among pediatric patients. This study found a higher prevalence (97.5%) of using these medications. This prevalence converges with that found by Abubakar, in a hospital in Nigeria (80.1%) and by Monteiro LGS et al., in two hospitals (Central and Geral) in Maputo (97.6%) (39,40). Very low prevalence (43.5%) was found by Wai et al., in a tertiary hospital in Malaysia (41). In this study, gastroenteritis (39.9%), pneumonia (21.8%) and malaria (9.1%) were the diagnoses for which antibiotics were commonly prescribed. Chaw et al., in their research, similarly evidenced that antibiotics have been prescribed to patients suffering from pneumonia (37.1%), followed by sepsis (14.1%) (42). Whereas, Monteiro LGS et al., identified that 100% of antibiotics were more prescribed for patients suffering from pneumonia, fevers, sepsis and gastroenteritis, while 97.8% for patients suffering from malaria (40). Regarding the most used dosage form, the research revealed more prescriptions for systemic antibiotics (95.5%). Labi et al., found a convergent frequency (83.5%) (43). Monteiro LGS et al., noted a very low frequency (52.9%) that the most used antibiotics were systemic (52.9%) (40), while Mgbahurike et al. observed a very high rate of oral antibiotics (86.3%) (44). Regarding the most used antibiotics, this study observed that crystallized penicillin (33.4%), ceftriaxone (20.5%), cotrimoxazole (18.5%) and gentamicin (11.2%) were the most used antibiotics. Muslim and Meinisasti found a convergent frequency of gentamicin (34.9%) and a divergent frequency of ampicillin (34.3%) (45). Labi et al., found a higher rate of use of ceftriaxone (80.5%), followed by of gentamicin (76.5%) (42), while Chaw et al. identified ampicillin (19.5%), followed by gentamicin (14.5%) and ceftriaxone (12.8%) as the most common antibiotics used (42,43). These antibiotic prescribing rates are alarming, being extremely high than those recommended By WHO, which recommends that frequency of antibiotic use in hospitals should be 20.0-26.8%, while injectables (systemic or parenteral) should be 13.4–24.1 % (46). This high use of antibiotics may be due to the range age of patients and the severity of infections and their clinical conditions. It could also be because of the country's limited resources. However, when antibiotics are used unnecessarily and excessively, they can provide a means for the development of antibiotic-resistant microorganisms, which can lead to ineffective treatment, recurrent infections, increased treatment costs or even worse, mortality.

Description of antibiotic use errors

This research observed 36.5% of medical prescriptions containing errors, with a total of 34.5% of antibiotics being improper prescribed. Iftikhar et al., and Denny et al., observed convergent rates of 40.8% and 22.9% improper prescriptions, respectively (47,48). A survey by Santander et al. found a convergent rate of 51.9 % of improper medical prescriptions, Okello et al., (68.4%) (49,50). In this research, 57.1%, 27.7%, 11.6% and 3.6% of the prescriptions presented a, two, three and four errors respectively. Iftikhar et al. found that 47.2% of prescriptions had an error, while 21.7% and 30.9% respectively had two and three or more prescription errors (47). The errors detected in this research were related to dosage (25.4%) and duration of treatment (74.6%). Fekadu et al. observed dosage (low doses = 27.1%, high doses = 7.03%), dosage (low = 20.54%, high = 3.78%) and duration of use (short duration = 13.51%, prolonged = 0.54%) were the most common errors (51). Shiva et al., observed dosage errors in less than 7% and prolonged duration in 25.6% (52). Oguz et al., found that 55.69% of antibiotics were prescribed less than necessary, (25.88%), route of administration (16.08%) and dosage errors (2.67%) (53). These results are alarming,

since the inappropriate use of these drugs constitutes a main issue for the emergence, growth and dissemination of resistant microorganisms. Therefore, the high inappropriate use of antibiotics may be due to the careless or poor judgment of prescribers regarding the proper use (prescription) of these drugs, considering the characteristics of patients and guidelines.

Analysis to determine risk factors for inappropriate use of antibiotics

The study showed that patients prescribed ≥ 3 antibiotics per prescription are more likely (about 3 times more) to have some inappropriate use of antibiotics than those prescribed an antibiotic, and that patients with a short hospital stay have about 2 times more chances of experiencing some inappropriate use of antibiotics. Iftikhar et al., they found similar results that prescribing three antibiotics or more (OR = 1.7, 95% CI = 1.1–2.1, p-value = 0.020) is a greater risk factor for inappropriate use of antibiotics compared to patients prescribed one antibiotic by medical prescription and, in contrast, these authors found that long hospital stay (OR = 12.5, 95% CI = 10.1–17.6, p-value < 0.001) constitutes a risk factor for experiencing some incorrect use of antibiotics (47). Some reasons may lead prescribers to Recommend three or more antibiotics per prescription, such as an uncertain diagnosis due to the clinician's poor ability to differentiate viral from bacterial infections, non-compliance with guidelines, and poor practice of antibiotic prescribing principles. Meanwhile, the pressure exerted on physicians by family members and guardians of pediatric patients may be a reason for their short hospital stay. However, antibiotics are the widely prescribed therapeutic agents and their use in pediatrics is concern in some countries (54). Antimicrobial resistance is the biggest health problem especially in countries where resources are limited and levels of infectious diseases are high (42,55). The inappropriate use of this class of drugs is one of the major factors for the development of resistant microorganisms. Indeed, interventions on the use of these antibiotics in order to reduce their use taking into account this age group, consequently reducing antimicrobial resistance are necessary. These interventions aim to improve the appropriate use of antibiotics by promoting selection of the best therapeutic regimen, dose, duration of treatment and route of administration, obtaining better clinical results related to the use of antibiotics, reduction of adverse effects, such as toxicity or others, reduction of costs, and limit the selection of resistant microorganisms (54).

Conclusion

Antibiotic use among hospitalized pediatric patients was so prevalent. Most medical prescriptions were inappropriate, in which dosage and duration of treatment were the most frequent errors. Prescription of three or more antibiotics and short hospital stay were the risk factors for inappropriate use of these drugs. These results reveal a concern, as overuse and inappropriate use of antibiotics are a major factor in the development of antibiotic resistant microorganisms. Prioritizing the design and development of new antibacterial agents is not a great strategy to solve this major public health problem around the world, creating or improving policies, programs and methods on the use and dispensing of these drugs must be a priority. Multiple interventions, such as educating both health professionals and the general public about the rational use of antibiotics is essential, through lectures and poster distributions. It is

essential to have up-to-date, internal forms and guidelines on the most commonly used antibiotics, which can assist in decision-making on the need to use antibiotics according to the needs of each individual patient.

Abbreviations

BNF: British National Formulary; CDC: Centers for Disease Control and Prevention; SD: Standard Deviation; HCN: Nampula Central Hospital; IBM: International Business Machines corporation; CI: Confidence Interval; NICE: National Institute for Health and Care Excellence; OR: Odds Ratio; WHO: World Health Organization; SPSS: Statistical Package for the Social Sciences.

Declarations

Acknowledgements

The authors thank the coordination of the pharmacy course of the Universidade Lúrio, Faculdade de Ciências de Saúde for approving the accomplishment of the research. They thank the scientific management of the Hospital Central de Nampula and Pediatrics Ward I for approving and authorizing the authors to use the data from clinical files and medical prescriptions for the research. The classmates, Ananias Diego and Manuel Ofumane in data collection, the authors thank them all.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

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

Authors' contributions

All authors were involved in the conceptualization of the study, review and submission of the manuscript. OSA, SX and GC, was involved in data collection, database creation and data releases. AV and MD: translation of the manuscript into English. SX, AV and ALC: data analysis and interpretation. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This research was approved by the Scientific Committee of Universidade Lúrio, Faculdade de Ciências de Saude, Hospital Central de Nampula and Pediatrics Infirmary, where the data were collected. Approval

was obtained before the research was conducted. The data obtained in the clinical files and medical prescriptions were well kept in order to guarantee security and privacy.

Consent for publication

Not applicable.

Competing interests

The authors declare that there are no competing interests.

Author details

¹Departamento de Farmácia, Universidade Lúrio, Faculdade de Ciências de Saúde. Bairro do Marrere, R, nº4250;2,3-Nampula, Moçambique

²Instituto de Saúde Coletiva, Universidade Federal da Bahia, Brasil, Rua Basílio da Gama, s/nº Campus Universitário Canela. Salvador – BA Cep: 40.110-040, Brazil.

³Departamento de Farmácia, Universidade Federal do Parana, Avenida Prefeito Lothário Meissner, 632-Bairro Jardim Botânico – Curitiba Paraná. Brasil

References

1. Klepser ME, Altom A, MacCallum C, Nordquist E, Klepser DG. Description of the methods for describing and assessing the appropriateness of antibiotic prescribing and adherence to published treatment guidelines in an academic medical clinic. *Inov Pharm.* 2016;7(1):1–8.
2. Nicolini G, Sperotto F, Esposito S. Combating the rise of antibiotic resistance in children. *Minerva Pediatr.* 2014;66(1):31–9.
3. Flávio Danni Fuchs, Lenita Wannmacher. *Farmacologia clínica e terapêutica*. 5 ed. KOOGAN G, editor. Rio de Janeiro; 2017. 863 p.
4. Kebede HK, Gesesew HA, Woldehaimanot TE, Goro KK. Antimicrobial use in paediatric patients in a teaching hospital in Ethiopia. *PLoS One* [Internet]. 2017;2(3):e0173290. Available from: doi:10.1371/journal.pone.0173290
5. Santos RG, Jesus IS De. Prescrições de antimicrobianos De uso restrito de pacientes Internados em um hospital de ensino. 2016;8–12.
6. Andrade JV, Vasconcelos P, Campos J, Camur T. Antibiotic Prescribing in Ambulatory Care of Pediatric Patients with Respiratory Infections. 2019;32(2):101–10.
7. Arcenillas P, Xercavins M, March P, Martinez L, Madrdejós R, Badia C, et al. Assessment of Quality Indicators for Appropriate Antibiotic Use Paula. 2018;62(12):1–9.

8. Tyrrell C, Burgess CM, Brennan FP, Walsh F. Antibiotic resistance in grass and soil. 2019;(2):1–10. Available from: <https://doi.org/10.1042/BST20180552>
9. Tedijanto C, Grad YH, Lipsitch M. Potential impact of outpatient stewardship interventions on antibiotic exposures of common bacterial pathogens. 2020;1–12.
10. Lovegrove MC, Geller AI, Fleming-dutra KE, Shehab N, Sapiano MRP, Budnitz DS. US Emergency Department Visits for Adverse Drug Events From Antibiotics in Children , 2011 – 2015. 2019;8(2):2011–5.
11. Umar LW, Isah A, Musa S, Umar B. Prescribing Pattern and Antibiotic Use for Hospitalized Children in a Northern Nigerian Teaching Hospital. Nigeria; 2018.
12. Umar LW, Isah A, Musa S, Umar B. Prescribing Pattern and Antibiotic Use for Hospitalized Children in a Northern Nigerian Teaching Hospital. *Ann Afr Med*. 2018;17(1):26–32.
13. Koopmans LR, Finlayson H, Whitelaw A, Decloedt EH, Dramowski A. International Journal of Infectious Diseases Paediatric antimicrobial use at a South African hospital. *Int J Infect Dis* [Internet]. 2018;74:16–23. Available from: <https://doi.org/10.1016/j.ijid.2018.05.020>
14. Lam TP, Chan TH, Sun KS, Lam KF, Kwok KW, Ho PL. Antibiotic prescriptions by medical interns in Hong Kong: influence of the hospital settings and prescription culture. *Postgrad Med J* [Internet]. 2020;1–8. Available from: [doi:10.1136/postgradmedj-2020-138414](https://doi.org/10.1136/postgradmedj-2020-138414)
15. Aidara-Kane A, Angulo FJ, Conly JM, Minato Y, Silbergeld EK, McEwen SA, et al. World Health Organization (WHO) guidelines on use of medically important antimicrobials in food-producing animals. *Antimicrob Resist Infect Control*. 2018;7(7):1–8.
16. Dyar OJ, Huttner B, Schouten J, Pulcini C, on behalf of ESGAP. What is antimicrobial stewardship? *Clin Microbiol Infect*. 2017;23(11):793–8.
17. McCullough AR, Pollack AJ, Hansen MP, Glasziou PP, Looke DFM, Britt HC, et al. Antibiotics for acute respiratory infections in general practice: Comparison of prescribing rates with guideline recommendations. *Med J Aust*. 2017;207(2):65–9.
18. Fleming-dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, Jr TMF, et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. *JAMA* [Internet]. 2020;4027(17):1864–73. Available from: [doi: 10.1001/jama.2016.4151](https://doi.org/10.1001/jama.2016.4151) 1864
19. World Health Organization. Antimicrobial resistance: global report on surveillance. World Health Organization; 2014. xxii, 232 p.
20. Zhang Z, Hu Y, Zou G, Lin M, Zeng J, Deng S, et al. Antibiotic prescribing for upper respiratory infections among children in rural China : a cross- sectional study of outpatient prescriptions. *Glob Health Action* [Internet]. 2017;00(00):1–9. Available from: <http://dx.doi.org/10.1080/16549716.2017.1287334>
21. Ncube NBQ, Sc M, Solanki GC, Kredo T, Lalloo R, Town C, et al. Antibiotic prescription patterns of South African general medical practitioners for treatment of acute bronchitis. 2017;107(2):119–22.
22. Doare K Le, Barker CIS, Irwin A, Sharland M. Improving antibiotic prescribing for children in the resource-poor setting. *BrJ Clin Pharmacol*. 2014;79(3):446–55.

23. Okomo U, Akpalu ENK, Doare K Le, Roca A, Cousens S, Jarde A, et al. Aetiology of invasive bacterial infection and antimicrobial resistance in neonates in sub-Saharan Africa: a systematic review and meta-analysis in line with the STROBE-NI reporting guidelines. 2019;3099(19):1–16.
24. Zalewska M, Błazejewska A, Czapko A, Popowska M. Antibiotics and Antibiotic Resistance Genes in Animal Manure – Consequences of Its Application in Agriculture. *Front Microbiol.* 2021;12(616656):1–21.
25. Kraker MEA de, Stewardson AJ, Harbarth S. Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050? *PLoS Med* [Internet]. 2016;13(11):1–6. Available from: doi:10.1371/journal.pmed.1002184
26. Agranonik M, Hirakata VN. Cálculo de tamanho de amostra: proporções. *Rev HCPA.* 2011;31(3):2–8.
27. World Health Organization. Antibiotic Dosing for Children: Expert Recommendations For Children Ages 2 months to 12 years. 2017;1–6.
28. Lutsar I. WHO report on consensus guidance on pediatric dosing regimens for access antibiotics on the Essential Medicine List for children.
29. Fuchs A, Bielicki J, Mathur S, Sharland M, Van Den Anker JN. Reviewing the WHO guidelines for antibiotic use for sepsis in neonates and children. *Paediatr Int Child Health* [Internet]. 2018;38(51):S3–15. Available from: <http://doi.org/10.1080/20469047.2017.1408738>
30. Mathur S, Jackson C, Urus H, Ziarko I, Goodbun M, Hsia Y, et al. A comparison of five paediatric dosing guidelines for antibiotic. *Bull World Health Organ* [Internet]. 2020;98(6):406–12. Available from: <http://dx.doi.org/10.2471/BLT.19.234310>
31. British National Formulary. BNF for Children setember 2019 - 20. 2019. 1173 p.
32. British National Formulary. BNF for Children (BNFC). 2017. 1093 p.
33. National Institute for Health and Care Excellence. Summary of antimicrobial prescribing guidance – managing common infections. *Public Heal Engl.* 2020;(3):1–27.
34. National Institute for Health and Care Excellence. Pneumonia (community-acquired): antimicrobial prescribing. 2019;(9):1–3.
35. National Institute for Health and Care Excellence. Pneumonia (hospital-acquired): antimicrobial prescribing. 2019;(9):1–3.
36. World Health Organization (WHO). Global Report on Surveillance 2014. WHO 2014 AMR Rep [Internet]. 2014;2:1–8. Available from: http://www.who.int/drugresistance/documents/AMR_report_Web_slide_set.pdf
37. Buccellato E, Melis M, Biagi C, Donati M, Motola D. Use of Antibiotics in Pediatrics: 8-Years Survey in Italian Hospitals. *PLoS One* [Internet]. 2015;10(9):e0139097. Available from: 10.1371/journal.pone.0139097
38. Huttner A, Harbarth S, Carlet J, Cosgrove S, Goossens H, Holmes A, et al. Antimicrobial resistance: A global view from the 2013 World Healthcare-Associated Infections Forum. *Antimicrob Resist Infect Control.* 2013;2(1):1–13.

39. Abubakar U. Antibiotic use among hospitalized patients in northern Nigeria: a multicenter point-prevalence survey. *BMC Infect Dis.* 2020;20:1–9.
40. Monteiro LGS, Chaúque A, Barros MP, Irá TR. Determinants of antibiotic prescription in paediatric patients: The case of two hospitals in Maputo , Mozambique. 2017;11(3):109–11.
41. Wai D, Tham J, Abubakar U, Tangiisuran B. Prevalence and predictors of antibiotic use among children visiting the Emergency Department in a Tertiary Hospital in Malaysia. 2020;743–8.
42. Chaw PS, Schlinkmann KM, Raupach-rosin H, Karch A, Pletz MW, Huebner J, et al. Antibiotic use on paediatric inpatients in a teaching hospital in the Gambia, a retrospective study. *Antimicrob Resist Infect Control.* 2018;7:1–9.
43. Labi A, Obeng-nkrumah N, Sunkwa-mills G, Bediako-bowan A, Akufo C, Bjerrum S, et al. Antibiotic prescribing in paediatric inpatients in Ghana : a multi-centre point prevalence survey. 2018;1–9.
44. Mgbahurike AA, Ojiyi ID, Daniel V. Antibiotic Utilization Pattern in Pediatrics Unit South–South of Nigerian Teaching Hospital. 2020;8(2):337–42.
45. Muslim Z, Meinisasti R. Short Communications Rationality of Antibiotic Usage in Paediatrics in Bengkulu, Indonesia: Gyssens' Criteria and Type of Therapy Analysis. *Indian J Pharm Sci.* 2016;78(October):840–4.
46. Bilal AI, Osman ED, Mulugeta A. Assessment of medicines use pattern using World Health Organization ' s Prescribing, Patient Care and Health facility indicators in selected health facilities in eastern Ethiopia. *BMC Health Serv Res.* 2016;16(144):1–8.
47. Iftikhar S, Sarwar MR, Saqib A, Sarfraz M, Shoaib Q. Antibiotic Prescribing Practices and Errors among Hospitalized Pediatric Patients Suffering from Acute Respiratory Tract Infections : A Multicenter, Cross-Sectional Study in Pakistan. *www.mdpi.com/journal/medicina.* 2019;1–12.
48. Denny KJ, Gartside JG, Alcorn K, Cross JW, Maloney S, Keijzers G. Appropriateness of antibiotic prescribing in the Emergency Department. *J Antimicrob Chemother.* 2019;(November 2018):515–20.
49. Santander BC, Alonso EC, Carrión AS, Fuentes LM, Flores ID, Vargas JC. Adecuación de la prescripción de antimicrobianos en población pediátrica en un servicio de urgencias hospitalario. *analesdepediatria.* 2018;88(5):1–7.
50. Okello N, Oloro J, Kyakwera C, Kumbakumba E, Obua C. Antibiotic prescription practices among prescribers for children under five at public health centers III and IV in Mbarara district. *PLoS One [Internet].* 2020;15(12):e0243868. Available from: <http://dx.doi.org/10.1371/journal.pone.0243868>
51. Fekadu G, Sado E, Chennupati S V, Bayisa G. Evaluation of Antibiotics Use and Prescribing Error among Hospitalized Pediatric Patients in Nekemte Referral Hospital, Ethiopia. *J Appl Chem.* 2017;6(4):607–19.
52. Shiva F, Ghanaie R, Shirvani F, Armin S, Rafiei Tabatabaei S, Fahimzad SA, et al. Pattern of antibiotic usage in children hospitalized for common infectious diseases. *Arch Pediatr Infect Dis [Internet].* 2018;6(1):1–7. Available from: doi: 10.5812/pedinfect.34474
53. Oguz E, Bebitoglu BT, Nuhoğlu Ç, Çağ Y, Hodzic A, Temel F, et al. Evaluation of antibiotic use among hospitalized patients in a pediatric department of a training hospital in Turkey Running Head:

2017;1–18.

54. Quaak CH, Cové E, Driessen GJ. Trends in paediatric inpatient antibiotic therapy in a secondary care setting. Eur J Pediatr [Internet]. 2018;177:1271–8. Available from: <https://doi.org/10.1007/s00431-018-3185-z>
55. Mboya EA, Sanga LA, Ngocho JS. Irrational use of antibiotics in the Moshi Municipality Northern Tanzania: a cross sectional study. Pan Afr Med J [Internet]. 2018;31(165):1–10. Available from: [doi:10.11604/pamj.2018.31.165.15991](https://doi.org/10.11604/pamj.2018.31.165.15991)

Figures

Figure 1

Antibiotics prescribed among hospitalized pediatrics patients