Niger J Paediatr 2023; 50 (3): 129 – 135

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The global point prevalence survey of antimicrobial consumption and resistance (Global-PPS): First results of antimicrobial prescribing in a children hospital in Nigeria

DOI:http://dx.doi.org/10.4314/njp.v50i3.1

Accepted: 4th August 2023

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Abstract: *Background:* Antimicrobial stewardship is vital for our hospital practice but it requires a knowledge of antibiotic prescribing practices, which is currently lacking. This survey aimed to assess the antimicrobial prescribing practices in our hospital.

Method: To obtain baseline information on antimicrobial prescribing practices, a uniform and standardized method for surveillance of antibiotic use in hospitals was employed. A point prevalence survey (PPS) was conducted in all the wards of the Massey Street Children's hospital in June 2019. The PPS included all inpatients receiving an antimicrobial on the day of survey. Data collected included age, gender, antimicrobial agents, microbiological data, and compliance to guidelines, documentation of reasons and stop/ review date of prescription. The denominator was the number of eligible patients. A web-based application developed by the University of Antwerp was used for data-entry, validation and reporting.

Results: Sixty-seven children were eligible, of which 62 (92%) received 128 antimicrobials. Fifty-seven (85%) were on multiple antimicrobial therapies, and route of administration was parenteral in 86%. All prescriptions were empiric. Reasons for prescribing were documented in 121(94.5%) therapies in case notes; Stop/ review dates were not documented in 126(98.4%). The most frequently prescribed antibiotics were cefuroxime (18%), Ampicillin-sulbactam (15%) and gentamicin (12%). Antibiotic guidelines were not available. Most common diagnoses were sepsis (42%), pneumonia (15%) and malaria (9%).

Conclusion: This survey revealed very high antimicrobial prescribing rates in the hospital and the need to assess its appropriateness. We disclosed areas to improve antibiotic prescribing: antibiotic prescribing according to guidelines and low reporting of a stop/review date. There is a need to create awareness for evidence based antibiotic guidelines.

Keywords: Antimicrobial, Stewardship, Resistance, Children, Global-PPS

Introduction

Rational prescribing of antimicrobials is a major target to control inappropriate antimicrobial use and will help in the tackling of antimicrobial resistance.[1] This can be achieved with the establishment of an antimicrobial stewardship programme.[2]

According to the World Health Organization (WHO), antimicrobials would be used in a rational manner if patients receive the right antibiotics at appropriate dosefor the duration necessary, and at the least cost to them. [1] Inappropriate uses of antimicrobials include overuse, under-use, inadequate dosage, and misuse for non-bacterial infection, excess use of intravenous drugs instead of oral formulas as well as failure to prescribe according to antibiotics guidelines.

[1,3,5] In Africa, there is easy accessibility to antibiotics; from the streets, over the counter purchase as well as irrational prescribing in the hospital, thisencourages misuse, overuse/ excessive use of antimicrobial.[6,7] The higher the health challenges we face in African countries the higher the rates of exposure to antimicrobials especially among children.[8] As antibiotics use soars high so also the rate of antimicrobialresistance deepens. Antimicrobial resistance has been declared a global threat.[9-11] It substantially causes dramatic increase in already –rising healthcare costs and increases patients' morbidity and mortality.[12] Several pathogens are developing resistant strains and most hospitals heighten transmission of highly resistant pathogens like Methicillin Resistant *Staphylococcus aureus* (MRSA), Extended Spectrum Beta Lactamase (ESBL) producing Gram negative bacilli, Carbapenem Resistant Enterobacteriaceae (CRE), and most importantly, pathogens that are resistant to last line antimicrobials [13] World Health Organization has identified antimicrobial resistance (AMR) as a major health priority and proposed active initiatives and programs to decrease AMR in all healthcare settings.[14] Antimicrobial stewardship entails diverse interventions aimed at reducing inappropriate antimicrobial use while optimizing antimicrobial drug selection, dosing, route and duration of therapy to maximize clinical cure, prevent infection and limit unintended consequences such as the emergence of resistance, adverse drug events and the selection of pathogenic organisms.[15] Antimicrobial stewardship is vital for our hospital practice but it requires a knowledge of antibiotic prescribing practices, which is currently lacking. To improve antimicrobial prescribing practices in the hospital, a set of quality indicators were employed to identify primary areas of target to enhance rational antimicrobial use[16,17]. This survey aimed to assess antimicrobial prescribing practices in our hospital.

Materials and Methods

Ethics

The Global-PPS was considered exempt from ethical review as a quality assurance project, permission was however gotten from the hospital management.

Study Location

Massey Street Children's Hospital (MSCH) is a paediatrics specialist hospital owned by Lagos State government created in 1962 and serves as children's referral hospital. It has a significant heritage as the birthplace of many prominent Lagosians.The 76 bedded Neonatal and Paediatrics Unit is located on the Lagos Island in Lagos State has been providing child services for over 50 years and admits approximately 1500 children annually. This hospital is being managed by peadiatrics health force comprises; 4 consultants; 1 senior registrar;4 registrars and many staff nurses.

Study Design

This study was part of global point prevalence survey (Global-PPS) of antimicrobial consumption and resistance surveillance among in-patients in Nigeria. This aims to monitor rates of antimicrobial prescribing in hospitalised patients and also to determine the global variation in antibiotic prescribing in hospitalised patients across all continents using targeted qualities indicators.
A point prevalence survey (PPS) was conducted within two weeks in all the hospital wards in June 2019. It was carried out in all the seven wards which comprise three neonatal wards, three Paediatric wards, and one infectious disease ward of the hospital to obtain baseline information on antimicrobial prescribing practices. A uniform and standardized method [16] for surveillance of antibiotic use in hospitals was employed using global - PPS tools www.global-PPS.com. All inpatients admitted on a ward at 8 o'clock in the morning on the day of survey were counted in the denominator. All inpatients "on antimicrobial agents" at 8 o'clock in the morning on the day of survey were included in the numerator.

Patients already discharged before 8 o'clock and/or patients admitted after the commencement of the survey were not included and all-day cases were excluded. Essentially the data collected for the PPS were: Number of admitted patients and number of total available beds both occupied and empty beds in each ward. Patients' age in days, months or years and gender as well as the antimicrobial agents, their dose per administration, number of doses per day, and route of administration were included. Indication for therapy (community acquired infection, hospital acquired infection, or prophylaxis). Documentation of reasons for therapy and stop/review date of prescription were equally collected. Information about the anatomical site of infection and the target for prophylaxis according to the list of reasons for therapeutic or prophylactic use was also collected. All these serves as quality indicators for antimicrobial therapy. The choices of treatment based on microbiological investigations werealsonoted. Data were primarily collected by trained clinical microbiologist using established ward data form and patients data form.

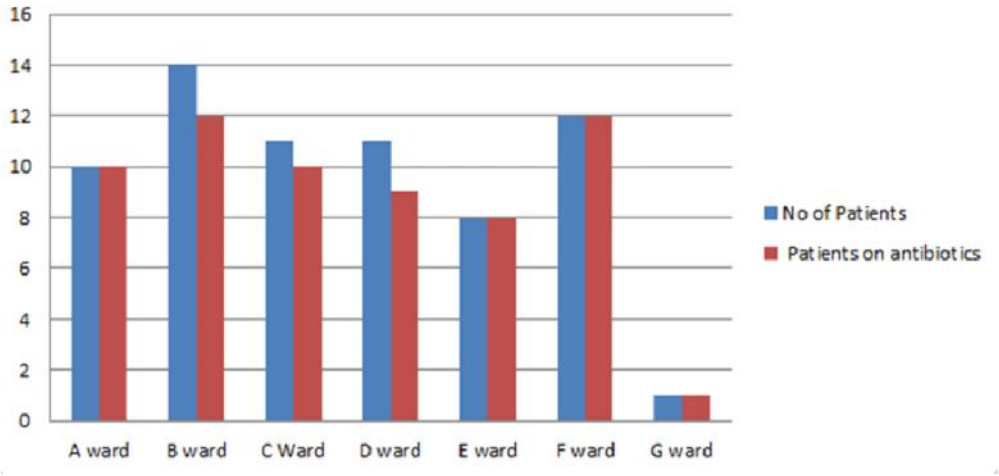
A web-based application was used for data entry, validation and reporting.URL: http:// app.globalpps.uantwerpen.be/globalpps_webpps/
Patients' data were entered into the Point Prevalence Survey program anonymously. Every patient record was given a unique not identifiable survey number. This number was automatically generated by Global-PPS tool. This number identifies uniquely the patient in the GLOBAL-PPS database. The Point Prevalence Survey

was a completely anonymous audit of local antibiotic prescribing practices. Patients' characteristics were analysed using descriptive statistics while the proportions of antimicrobial use were presented as prevalence rates.

Results

Sixty-seven children were eligible for this survey (see figure1for patients' distribution), of which 62 (92.5%) received 128 antimicrobials. The highest recorded prevalence was in general Paediatric and Neonatal medical wards (100%/ward) (Table1). Fifty-seven patients (85%) were on multiple antimicrobial therapies, and route of administration was parenteral in 86% (Table 2). All prescriptions were empiric. Biomarkers were not employed to initiate or monitor therapy. Most of the prescriptions (n=95; 74.2%) as counted at antimicrobial level were issued for community acquired infection, 18 (14.1%) were for healthcare associated infections. Eight children were on 14 (11.7%) antimicrobials for prophylaxis. Reasons for prescribing were documented for 121 (94.5%) prescriptions in the case notes; Stop/review dates were not documented for all except 2 prescriptions (n=126; 98.4%) (Table 2). Antibiotic guidelines were not available. The most frequently prescribed antibiotics were cefuroxime (18%), Ampicillin-sulbactam (15%) and, gentamicin (12%) (Figure3). Most common diagnoses were sepsis (42%), pneumonia (15%), and malaria (9%) (Table 3).

Fig 1: Patients distribution per ward



A ward = Neonatal ward; B ward = Neonatal ward;
C ward = Neonatal ward; D ward = General Paediatric Medical ward; E ward = General Paediatric Medical ward; F ward = General Paediatric Medical ward; G ward = Infectious disease ward

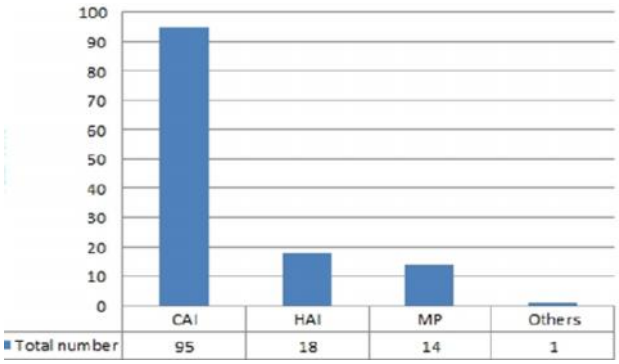
Table 1: Antimicrobial Prevalence rates by ward's Activity

Wards	A	B	C	D	E	F	G	Total
Total number of patients	10	14	11	11	08	12	01	67
Patients on antibiotic treatment	10	12	10	09	08	12	01	62
Prevalence of antibiotic use %	100	85.7	90.9	81.8	100	100	100	92.5

Table 2: Summary of quality indicators for antimicrobials use

Indicator	A ward	B ward	C ward	D ward	E ward	F ward	G ward	Total
Total prescription	18	26	20	22	15	25	02	128
Reason in note (%)	17(94)	25(98)	20(100)	22(100)	14(93)	22(88)	1(50)	121(94.5)
IV therapies (%)	18(100)	24(92.5)	18(90.0)	14(63.6)	14(93.3)	21(84.0)	2(100)	111(86.7)
Stop/Review date (%)	-	-	-	-	-	2(8)	-	-

Fig 2: Indications for Antimicrobial use



CAI= Community Acquired Infection; HAI= Healthcare Associated Infection;MP=Medical Prophylaxis; others= Motility drug.

Fig 3: Most common antibiotics prescribed for therapeutic use

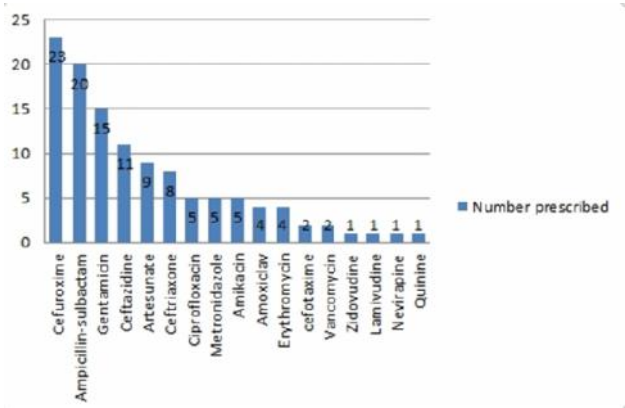


Fig 4: Overall proportion of antimicrobial class use

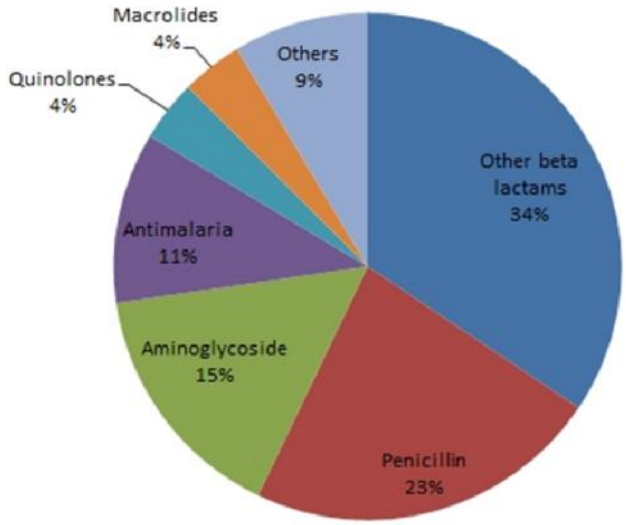


Table 3: Most common diagnoses treated with therapeutic antimicrobials

Diagnosis	N	n	n%
Sepsis	24	50	43.9
Pneumonia	10	20	17.5
Malaria	3	4	3.50
Sepsis and Malaria	4	12	10.5
Gastroenteritis	4	8	7.0
Gastroenteritis and Malaria	1	3	2.6
CNS Infection	3	5	4.4
CNS Infection and Malaria	2	5	4.4
Bone and joint infection	1	1	0.9
Intra-abdominal abscess	1	1	0.9
URTI and Malaria	1	2	0.9
Others	2	3	2.6
Total	53	114	100

N= Number of treated patients; n= Number of antimicrobial therapy

Discussion

Antimicrobials were prescribed at very high rates across the wards in the children's hospital of study, mostly for common childhood infections such as sepsis, pneumonia and malaria among others. These are the most commonly found infections in developing countries. This information is thus a useful and required content for the urgently needed antibiotic guidelines. However, in about 1% of cases, antibiotic therapy was prescribed for upper respiratory tract infections which might not necessarily need antibiotic therapy. Also worthy of note is the discrepancy between percentages of antimalarial prescribed and diagnosis of malaria, underscoring a need for policy and guidelines on diagnosis and testing. Similar needs were documented in other part of the country and continent.[4, 5, 15-19] A study done on the adherence to treatment guidelines for uncomplicated malaria in two public health facilities in Nigeria showed that there exists a significant scope for improved diagnosis and rational drug use, to enhance the accuracy of treatment and to reduce risks of adverse drug reactions, all in line with the goals of 'test and treat' policy of malaria case management.[20]

Quality indicators for antimicrobial use revealed problem areas of antibiotic misuse in this study. Of note was the observation that all antibiotics were prescribed empirically.Empiric therapy is generally considered as treatment based on clinical judgment or presentation of an infection without a definitive microbiology investigation result which is necessary to obtain an accurate infectious diseases diagnosis.[21] It is therefore not surprising that the most commonly prescribed antibiotics were broad spectrum antibiotics. Use and dominance of broad-spectrum antibiotics has been linked to poor prescribing practices [16] and excessive usage of such antibiotics found to be contributory to early

development of AMR.[16,21-26] To guide empiric therapy, the hospital needs to develop antibiotic guidelines and rely on it for appropriate choice of antibiotics.

Microbiology laboratory plays a great role in early detection and surveillance of multi-drug resistant organisms from routine cultures.[27-30] Clinicians' reliability on clinical diagnosis of infections alone can lead to inappropriate use, which may lead to unnecessary use orpoor choices of antibiotics, and also enhance the development of antimicrobial resistance in the hospital setting[6, 21-26,28]. It should be noted that properly diagnosed infections and appropriate antibiotic use will improve therapeutic outcome and quality of care, and delay development of multi-drug resistant organisms. [6,28,29]

Empiric therapy was compounded by prophylactic use of multiple antibiotics in 11.7% of prescriptions. Unwarranted use of multiple antibiotics for prophylaxis is not encouraged because it could hasten emergence of antimicrobial resistance.[21-26,28] This calls for development of appropriate evidence-based guidelines for medical prophylaxis in this category of patients. More so, it is well recognised that antibiotic combinations can provide synergism and a larger spectrum of activity[19,31] It is well known that biomarkers can be employed as a point of care test and as well as monitor responses to therapy yet they were never employed in this study. Thus, in addition to non-use of the microbiology laboratory, most therapies may be considered irrational because they lack the fundamental basis for antibiotic use.[21,23-26,31] Many cases of 'suspected' or 'at risk of sepsis' (42.97%) were not culture proven nor had the provisional diagnosis supported by biomarkers, which could have been used to guide the severity of symptoms, initiate or stop therapy [24,31].

Quality indicators also revealed tendency for prolonged duration of antibiotic therapy in most cases.[19] In order to prevent unnecessary prolonged antimicrobial therapeutic use, the hospital could develop strategies to encourage the notification of a stop or review date for every antimicrobial prescribed. All prescribed antimicrobial agents should have selected intended stop date to prevent patients from receiving unnecessary treatment which can leads to selection of resistance organisms, increase in cost of treatment as well as increase the possibility of developing illnesses associated with prolong antibiotic use such as *Clostridium difficle*[32]

Most therapies were initiated by the parenteral route and still continued as intravenous therapy. Parenteral therapy is an acceptable option for neonates, when older children cannot tolerate orally or when best option antimicrobial agents can only be administered intravenously.[33] However prolonged intravenous therapy can increase the duration of hospital stay and a potential risk of acquiring healthcare associated infections through the intravenous access[31,33]. Policy and guidelines for intravenous to oral switch policy is needful so the necessary switch is routinely done as early as possible while educating prescribers makes it achievable.[33]

Essentially, rational use of antimicrobials entails the use of an appropriate drug in the accurate dosage, and for the appropriate duration of treatment necessary to achieve a clinical cure, reduce the length of hospital stay as well as prevent the emergence of antimicrobial resistance[1,34]. Implementing antimicrobial guidelines and policies in the hospital would help to achieve this. [35] Developing antimicrobial guidelines for the hospital should be based on standard evidence-based results as obtainable in the region and in the hospital. [34] Therefore, Microbiology laboratory capacity to identify various pathogens and their susceptibility patterns is essential in establishing our antimicrobial guidelines and optimising antimicrobial use.

Antimicrobial stewardship program (ASP) in all healthcare institutions is a key intervention to reduce antimicrobial consumption in our hospitals and likewise a means of tackling resistance globally.[14] This initial PPS has given us the baseline information needed to plan and initiate an antimicrobial stewardship program in the hospital.

Conclusion

The hospital needs to develop evidence based antibiotic therapy to inform appropriate empiric prescribing of antibiotics. There is also need to invest in a clinical microbiology laboratory in order to encourage targeted therapy. There may be room for low hanging fruit such as intravenous to per oral switch policy, documentation of stop/review dates, use of biomarkers and antimicrobial prescribing rates. All activities can be ensured by an appropriately constituted antimicrobial stewardship committee.

Limitation

This study has limitation as it involves only one children hospital, therefore the result of the PPS cannot be extrapolated to other Paediatrics hospitals or units in other centres. However, the findings from this survey especially in the area of lack of functioning laboratory has been an eye opener to policymakers and others involved in management to identify areas that needs to be strengthened to support antimicrobial stewardship as well as to prevent emergence of antimicrobial resistance and inappropriate use of antimicrobials.

Conflict of interest: None
Funding: None

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