Antimicrobial use among hospitalized patients: A multi-center, point prevalence survey across public healthcare facilities, Osun State, Nigeria

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Abstract

Introduction **In order to inform sub-national action plan for control of antimicrobial resistance (AMR) and benchmark interventions to improve antibiotic use, it is essential to define situations on antibiotic use using standardized tools. We sought to assess quality of antimicrobial prescription across all government healthcare facilities with capacities for in-patient care in the first of the 36 states in Nigeria as part of ongoing state-wide situation analysis on AMR.**

Methods **A survey was conducted between 10-27 June 2019 using the *WHO methodology for point prevalence survey on antibiotic use in hospitals.* Data was collected from hospital administrators and records of hospitalized patients. Data analysis was done using Microsoft Excel 2010 (Redmond Washington).**

Results **Prevalence of antibiotic use amongst all 321 included patients was 76.6% (246/321). Of all indications recorded, the highest was surgical prophylaxis (96/260, 36.9%) for which there were multiple doses beyond 24 hours in almost all cases (91/96, 94.8%). The largest volume of prescribing took place in the surgical wards, and the most common prescriptions were metronidazole (142/564, 25.2%), cefuroxime (104/564, 18.4%), and ceftriaxone (77/564, 13.7%). Overall, 46.3% of the antibiotics used belong to Access group, 53.5% to watch and only 0.2% to Reserve. Treatment in almost all instances 544/563 (96.6%) was empiric.**

Conclusions **The majority of patients received multiple antibiotics mostly without compliance to guidelines. There was low prescribing of Access antibiotics and excessive use of antibiotics in the Watch group. Antibiotics were used most commonly for surgical prophylaxis but inappropriately. Inappropriate use of antibiotics in this study underscores the crucial need for an action plan incorporating antimicrobial stewardship.**

Keywords **Antimicrobial, stewardship, prescribing, Osun state**

Introduction

The discovery of antibiotics brought unprecedented revolutions to the practice of modern medicine including cancer chemotherapy, surgery and organ transplantations; but these gains are being challenged by emergence and global spread of resistance in microorganisms as agents of infectious diseases. Antimicrobial resistance (AMR) has become a global threat not only to effective healthcare delivery, but also to sustainable development and economic prosperity. The threat of AMR is heightened by dwindling antibiotic production pipelines leaving as options last-line drugs that are not only inaccessible but also toxic to vital organs in the

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human body. Globally, an estimated 700,000 people die annually from drug-resistant bacterial infections, with a projection of 10 million deaths by 2050 and a cost of $100 trillion to the global economy if effective interventions are not instituted.[1] Of the 10 million projected deaths by 2050, 4.1 million will be in Africa. AMR is a complex problem that transcends every border known to man: geographic, economic social and political, and it requires coordinated, multi-sectoral, whole-society engagements to combat. The World Health Organization (WHO) developed and adopted the global action plan (GAP) for control of AMR, and this was endorsed by the Food and Agriculture Organization as well as the World Organization for Animal Health with a political declaration by the United Nations General assembly.[2,3] In 2017, Nigeria began its national response to the threat of AMR by conducting a situation analysis on AMR, that informed and guided its 2017-2022 strategic national action plan (NAP) as a blueprint of interventions to mitigate AMR in the country.[4]

Leading drivers of AMR are overuse and misuse of antimicrobials, making the optimization of use of antimicrobial medicines to be pivotal in reducing the burden of AMR. Optimization of antimicrobial use as a core strategic objective of the GAP to mitigate AMR[5] entails coordinated interventions that promote responsible use of antimicrobial medicines in a way that prolongs their useful life and ensures sustainable access for effective prevention and treatment of infections.

Nigeria, in its 5-year Action Plan on AMR, identified interventions to ensure proper antimicrobial use and reduce AMR in the country. The National Action Plan (NAP) on AMR, 2017-2022, was developed to address priority gaps identified from situation analyses of antimicrobial use and resistance in Nigeria. The NAP included governance structure for control of AMR with 5 focus areas: increasing awareness and knowledge on AMR and related topics, one health AMR surveillance and research, infection prevention and control in the tripartite sector, promoting rational access to antibiotics and antimicrobial stewardship, and investing in research to quantify the cost of resistance and develop new antimicrobials and diagnostics. However, in order to achieve widespread implementation and make national efforts actionable, the country also realized the need to unbundle and decentralize activities to its federating States, to ensure a practical approach of achieving set goals for AMR response. This point prevalence survey on antimicrobial use (AMU) in healthcare facilities is part of a sub-national response, conducting a situation analysis on antimicrobial use and resistance to inform development of the first State Action Plan (SAP) on AMR. Previous surveys of AMU in Nigeria have described use at single or multiple healthcare institutions in different geopolitical units, but this was the first sub-national, coordinated initiative, defining antimicrobial use in all public healthcare facilities in one of the 36 Federating States of Nigeria. The present survey employed the recently developed tool by WHO[6] to determine the prevalence of antibiotic use and to assess the quality of antimicrobial prescription across government (public) healthcare facilities that provide in-patient care in Osun state, South-west Nigeria.

Methods

Study design and settings

This was a cross-sectional descriptive multicenter survey involving all public (government-owned) acute care hospitals in Osun

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State, conducted between 10-27 June 2019. Osun state, located in South-west, is one of Nigeria's 36 states. Healthcare as representative of the country is organized into three levels. Primary care includes general preventive, curative and pre-referral care. Secondary care services are provided at general hospitals and include general and specialized medical services as well as surgery, pediatrics, obstetrics and gynecology. Tertiary care are the highest services provided at teaching/specialist hospitals with highly differentiated clinical services by function. Guidance for the survey was by the state coordinator trained in point prevalence survey methodology, who constituted the investigator team including clinical microbiologists and data managers. Organization of the survey included a preparatory phase of ethical clearance, survey design, identification of included facilities and availability of forms for data collection. A pilot study aimed at reducing auditor bias was conducted, by reviewing clinical notes of 10 patients, before the full survey in one of the hospitals to agree on data extraction procedure and to ensure validity. The final survey included all public healthcare facilities meeting the inclusion criterion of current in-patient admissions spanning nine public healthcare facilities (four teaching/specialist and five secondary hospitals) with a total of 64 wards, 1181 hospital beds capacity (mean 131 beds, range 14-398 beds) and 17406 admissions in the preceding year, 2018.

Inclusion and exclusion criteria

All public hospitals that provided acute care services were included in the study. Other criteria for inclusion: all wards with acute care in-patients, all patients hospitalized as in-patients at or before 8.00 a.m. on the day of survey, and all neonates born before 8.00 a.m. on the day of the survey, counted separately from their mother (i.e., mother and baby were counted as two different patients). All patients meeting the eligibility criteria were included in the survey irrespective of whether they were receiving antibiotic treatment or not. Non-acute care facilities (including rehabilitation centers, or psychiatric centers), emergency departments (except for wards attached to those departments), day surgery wards and daycare wards were excluded. Patients from outpatient clinics, day surgery/day treatment, emergency rooms or discharged patients were also excluded. All antibiotics administered orally, parenterally or by rectal route or inhalation and ongoing at 8.00 a.m. on the day of the survey were included in the survey. Topical antibiotics, eye drops, ear drops and vaginal suppositories were excluded. Antibiotic therapy initiated after 8.00 a.m. or that was stopped before 8.00 a.m. on the day of the survey were excluded. Approval (LTH/EC/2019/06/421) for survey was sought and obtained from the research ethics committee of the Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Osun State, Nigeria. Written informed consent was obtained from patients or their parents/guardians for those within a pediatric age group.

Data collection

The survey was conducted using the protocol *WHO Methodology for Point Prevalence Survey on Antibiotic Use in Hospitals*.[6] Data collection was performed by resident doctors in the department of Medical Microbiology and Parasitology. We collected basic information relevant for treatment and management of infectious diseases from hospital administrators, medical records and associated documentation of in-patients. Following the pilot survey, we used standardized paper forms from the WHO protocol to collect data at different levels i.e., hospitals, wards, patients, indications for use and antibiotics.

Data analysis

Data collected using different paper forms were entered into Microsoft Excel 2010 (Redmond Washington). The data was anonymized and analyzed using descriptive statistics. Patients' ages were expressed as median and interquartile range while categorical variables were expressed as percentages. Antimicrobial prescribing rate was expressed as a percentage of patients on antimicrobials, or as a percentage of all antibiotic prescriptions (proportional use). Antibiotic prescribing was categorized according to specialty wards, indications and WHO AWaRe (Access, Watch, Reserve) three stewardship groups of antibiotics.[7] The Access group consists of antibiotics that are first or second choice empiric treatment options for infectious syndromes. The Watch group includes agents with high resistance potential, including those listed as highest priority antibiotics among the Critically Important Antimicrobials for Human Medicine[8] that should be prioritized as targets of local and national antimicrobial stewardship programs and monitoring. The Reserve group antibiotics are last resort options for treatment of confirmed or suspected infections due to multidrug-resistant organisms and should be prioritized as targets for national and international antimicrobial stewardship programs including regular monitoring of use.

Results

Demographical and clinical characteristics of patients

Of all 61 public healthcare facilities eligible to provide in-patient care in Osun State, only nine (four teaching/specialist and five secondary hospitals) provided in-patients care during the period of the survey. Across the nine facilities, there were 341 eligible patients among which 321 (94.1%) were recruited including 179 (55.8%) females and 142 (44.2%) males. The patients were mostly adults (226; 70.4%) with age range of 19-90 years and median age of 40 years (IQR 30-59 years). There were 53 children with age range of 13 months-18 years, median age of 7 years (IQR 3.5-7.5 years); 15 infants with age range 1-12 months and median age of six months (IQR 2-10 months); and 27 neonates, age range 1-26 days with median age of 6 days (IQR 4-14 days). Table 1 includes different diagnoses in the study participants. The most common infectious diseases diagnosed were clinical sepsis (25; 10%), skin and soft tissue infections (20; 8%), respiratory tract infections (18; 7.2%), and gastrointestinal tract infection (15; 6%). However, there were 146 (58.4%) patients in whom antibiotic use was for undefined diagnoses or reason other than specific directed treatment. Finally, 29.5% (87/295) of patients had had surgery in the current admission (Table 1).

Bacteriological profiles

Of the 246 patients on antibiotics, 47 samples had been taken from 38 patients (15.4%) with wound (20; 42.6%), blood (9; 19.1%) and sterile fluid (9; 19.1%) being the most common. Overall, 27 (57.4%) of the cultures were positive, with Enterobacteriaceae (19; 50%) being the majority of isolates. Among the 37 isolates in record, 14 (37.8) were resistant to third generation cephalosporins and five (13.3%) were methicillin-resistant *Staphylococcus aureus* (MRSA) (Table 1).

Prevalence and indication for antibiotic use in patients

Prevalence of antibiotic use among hospitalized patients in public hospitals in Osun State was 76.6% (246/321) and ranged between 72-90.7% among age categories. All patients, except for 58 (23.6%) that had antibiotics, used a minimum of two different antibiotics. There were a total of 564 antibiotic prescriptions, with antibiotic prescribing ratio of 1.8. In almost all cases, use of antibiotics was empiric (544/564, 96.5%) and the predominant route of administration was parenteral (504; 89.9%) with switch to oral route only in 19.9% of patients. Antibiotics were prescribed mainly by specialist physicians (497; 88.1%) and compliance to treatment guidelines was noted in 39.4% of patients (Table 2).

The most common antibiotic class used was cephalosporins (211, 37.4%) with cefuroxime (104; 18.4%) and ceftriaxone (77; 13.7%) being the highest used in the class. Other commonly prescribed antibiotics were metronidazole (142; 25.2%), ciprofloxacin (60; 10.6%), and gentamicin (59; 10.5%) (Table 3).

There were 260 recorded indications for antibiotic use which included community acquired infection (76; 29.2%) and surgical prophylaxis (96; 36.9%) which was for more than 24 hours in almost all (91/96, 94.8%) cases (Table 2).

Antibiotic prescribing across specialty wards

The largest volume of antibiotic prescribing was done in the surgical wards (129; 22.9%) and

Table 1. Demographical, clinical and bacteriological profiles of patients (N is the total number recorded for each variable)

Sociodemographic and clinical characteristics		n	%
Gender (N=321)	Male	142	43.9
	Female	179	56.1
Surgery since admission (N=295):	Yes	87	29.5
	No	208	70.5
Diagnoses (N=250):	Skin and soft tissue infection	20	8.0
	Bone and joint infection	1	0.4
	Central nervous system infection	2	0.8
	Ear, nose and throat infection	2	0.8
	Eye infection	2	0.8
	Respiratory tract infection	18	7.2
	Cardiovascular system infection	2	0.8
	Gastrointestinal tract infection	15	6.0
	Urinary tract infection	6	2.4
	Obstetrics and gynecological infection	9	3.6
	Clinical sepsis	25	10.0
	Systemic inflammatory response syndrome (SIRS)	2	0.8
	Undefined (site with no systemic inflammation)	33	13.2
	For use other than treatment	113	45.2
Culture sample taking (N=260)	Yes	38	14.6
	No	222	85.4
Specimens collected (N=47)[a]	Sputum and respiratory specimen	2	4.3
	Blood	9	19.1
	Sterile fluid	9	19.1
	Wound	20	42.6
	Urine	6	12.8
	Others	1	2.1
Culture results (N=47):	Positive	27	57.4
	Negative	20	42.6
Bacterial isolated from specimens (N=38)[b]	*Pseudomonas aeruginosa*	7	18.4
	Enterobacteriaceae*	19	50.0
	Staphylococcus aureus	12	31.6
Resistant phenotypes (N=37)	Resistance to third generation cephalosporins	14	37.8
	Carbapenem-resistant	3	8.1
	Methicillin-resistant *S. aureus*	5	13.5
	Unknown	15	40.5

*Enterobacteriaceae: *Klebsiella* spp. - 14, *Proteus* spp, - 3, *Escherichia coli* - 2;.
[a]47 specimens were collected from 38 patients.
[b]38 bacteria were from 27 specimens with positive culture.

Table 2. Prevalence and indication for antibiotic use in patients (N is the total number recorded for each variable)

Antibiotic use		N	%
Patients on antibiotics (N=321):	Yes	246	76.6
	No	75	23.4
Number of antibiotics used per patient (N=246)[a]:	1	58	23.6
	2	111	45.1
	3	46	18.7
	4	18	7.3
	≥5	13	5.3
Indication type (N=260):	Community-acquired infection	76	29.2
	Hospital-acquired infection	23	8.8
	Surgical prophylaxis	96	36.9
	Medical prophylaxis	29	11.2
	Others	36	13.8
Surgical prophylaxis duration (N=96):	SP1	1	1.0
	SP2	4	4.2
	SP3	91	94.8
Antibiotic administration route (N=564):	Parenteral	504	89.4
	Oral	55	9.8
	Inhalation	5	0.9
Antibiotic switch from parenteral to oral (498):	Yes	99	19.9
	No	399	80.1
Prescriber type (N=564):	Specialist physicians	497	88.1
	Non-specialist physician	67	11.9
Missed doses of antibiotics (N=534):	None	432	80.9
	1	25	4.7
	2	22	4.1
	≥3	55	10.3
Reasons for missed doses (102):	Patient could not purchase	96	94.1
	Other reasons	2	2.0
	Multiple reasons	4	3.9
Guidelines compliance (561):	Yes	221	39.4
	No	201	35.8
	Not assessable	139	24.8
Treatment type:	Empiric	544	96.6
	Directed	19	3.4

[a]246 patients used a total of 564 antibiotics.

SP1: if one dose was administrated to the patient; SP2: if multiple doses were administered to the patient within 24 hours; SP3: if multiple doses were administered to the patient for a duration extending 24 hours.

Table 3. Antibiotic prescribing across specialty wards

Antibiotics	Total wards, N (%)	AMW, n (%)	SW, n (%)	CW, n (%)	Ortho, n (%)	NNW/NICU, n (%)	Gyn, n (%)	ANW, n (%)	PNW, n (%)	MHW, n (%)	Ad ICU, n (%)	Burn, n (%)
Amikacin	1 (0.2)				1 (1.9)							
Gentamicin	59 (10.5)	5 (4.6)	8 (6.2)	10 (16.7)	5 (9.6)	22 (28.6)	3 (7.9)		4 (6.0)			2 (10.5)
Amoxicillin	7 (1.2)	1 (0.9)	2 (1.6)	1 (1.7)			2 (5.3)		1 (1.5)			
Amoxicillin/ clavulanate	30 (5.3)	14 (13.0)	3 (2.3)	3 (5.0)		1 (1.3)	3 (7.9)		4 (6.0)			2 (10.5)
Ampicillin	10 (1.8)					8 (10.4)		1 (20.0)	1 (1.5)			
Ampicillin/ cloxacillin	6 (1.1)		3 (2.3)	1 (1.7)					2 (3.0)			
Penicillin	2 (0.4)	1 (0.9)				1 (1.3)						
Cefuroxime	104 (18.4)	6 (5.6)	27 (20.9)	22 (36.7)	17 (32.7)	8 (10.4)	3 (7.9)	2 (40.0)	16 (23.9)			3 (15.8)
Cefixime	7 (1.2)	1 (0.9)	3 (2.3)						2 (3.0)			1 (5.3)
Cefixime/ clavulanate	1 (0.2)						1 (2.6)					
Cefotaxime	2 (0.4)		1 (0.8)								1 (20.0)	
Ceftriaxone	77 (13.7)	19 (17.6)	15 (11.6)	9 (15.0)	1 (1.9)	14 (18.2)	7 (18.4)		8 (11.9)		1 (20.0)	3 (15.8)
Ceftriaxone/ sulbactam	2 (0.4)		1 (0.8)				1 (2.6)					
Ceftazidime	12 (2.1)	2 (1.9)	4 (3.1)	2 (3.3)		3 (3.9)						1 (5.3)
Cefpodoxime	5 (0.9)		1 (0.8)	2 (3.3)					1 (1.5)	1 (25.0)		
Cefepime	1 (0.2)	1 (0.9)										
Azithromycin	7 (1.2)	5 (4.6)		1(1.7)	1 (1.9)							
Erythromycin	3 (0.5)	2 (1.9)	1 (0.8)									
Clarithromycin	3 (0.5)	2 (1.9)					1 (2.6)					
Ciprofloxacin	60 (10.6)	13 (12.0)	15 (11.6)	3 (5.0)	10 (19.2)	10 (13.0)	4 (10.5)		1 (1.5)	1 (25.0)	1 (20.0)	2 (10.5)
Levofloxacin	4 (0.7)	2 (1.9)	2 (1.6)									
Clindamycin	2 (0.4)		1 (0.8)		1 (1.9)							
Imipenem	1 (0.2)											1 (5.3)
Meropenem	4 (0.7)	1 (0.9)	2 (1.6)			1 (1.3)						
Metronidazole	142 (25.2)	30 (27.8)	40 (31.0)	5 (8.3)	15 (28.8)	4 (5.2)	13 (34.2)	2 (40.0)	26 (38.8)	2 (50.0)	2 (40.0)	3 (15.8)
Nitrofurantoin	2 (0.4)	1 (0.9)							1 (1.5)			
Doxycycline	1 (0.2)											1 (5.3)
Trimethoprim/ sulfamethoxazole	1 (0.2)	1 (0.9)										
Vancomycin	8 (1.4)	1 (0.93)		1 (1.7)	1 (1.9)	5 (6.5)						
Total	564	108 (19.1)	129 (22.9)	60 (10.6)	52 (9.2)	77 (13.7)	38 (6.7)	5 (0.9)	67 (11.9)	4 (0.7)	5 (0.9)	19 (3.4)

Ad ICU – adult intensive care unit; **AMW** – adult medical ward; **ANW** – antenatal ward; **Burns** – burns ward; **CW** – children ward; **Gyn** – gynaecology ward; **MHW** – mental health ward; **NICU** – neonatal intensive care unit; **NNW** – neonatal ward; **Ortho** – orthopaedic ward; **PNW** – postnatal ward; **SW** – surgical ward.

this was followed closely by adult medical wards (108; 19.1%). Metronidazole, cefuroxime, ceftriaxone and ciprofloxacin were predominantly prescribed in surgical wards constituting 75.2% (n=97) of the total antibiotic use. Likewise, for adult medical wards, metronidazole, ceftriaxone, amoxicillin-clavulanate, and ciprofloxacin were the most prescribed (76; 70.4%). The largest proportions of gentamicin (22; 37.3%), ampicillin (8; 80%), and vancomycin (5; 62.5%) prescribed were in the neonatal wards (Table 3).

Antibiotic prescribing according to indications

Antibiotic use was mainly for surgical prophylaxis (204; 36.2%) and community acquired infections (169; 30%). Other indications for antibiotic use included medical prophylaxis (68; 12.1%) and hospital-acquired infection (42; 7.4%) (Table 4).

Antibiotic prescribing according to WHO AWaRe classification

Antibiotics used amongst hospitalized patients were analysed following the recent WHO AWaRe categorization into Access, Watch and Reserve categories to inform antimicrobial stewardship interventions. All 564 antibiotics prescribed grouped into Access (46.3%, n=261), Watch (53.5%, n=302) and Reserve (0.2%, n=1) (Table 5).

Discussion

Our survey showed very low healthcare-seeking behavior and hospitalizations in government-owned facilities with patients admission only in nine (14.8%) of all 61 eligible healthcare facilities and bed occupancy 341 at the time of survey. This is a possible reflection of the predominant role of the private sector in Nigeria's health system as well as the effect of out-of-pocket (OOP) payments for healthcare. OOP spending is not reimbursed by a health insurance company and accounts for about 70% of healthcare payments in Nigeria, with the country having one of the highest rates in the world.[9] Although the National Health Insurance Scheme had been established under Act 35 of 1999 and it became operational in 2005, optimal coverage is yet to be achieved. Osun State, Nigeria has become the first beneficiary of a World Bank-assisted health-financing project, tagged Osun Health Insurance Scheme (O-HIS); it is hoped that its effect will soon be seen in enhancing healthcare seeking behavior as well as health service provision within this southwest Nigeria State. Beyond health financing, the need for manpower deployment to provide services in all existing healthcare facilities within the State is brought to the fore by our survey. To our knowledge, it is the first Nigeria state-wide survey on antimicrobial prescribing and presents a sub-national initiative to inform development of a State Action Plan on AMR and benchmark interventions to improve use.

The prevalence of antibiotic use in this study was 76.6%, a rate that is comparable with what was reported in Northern Nigeria[10] and South East Nigeria.[11] Prevalence of antimicrobial use varies considerably in healthcare facilities world over; it tends to be high in low- and middle-income countries in Africa and Asia.[12,13] This is because of uncontrolled, excessive antimicrobial prescribing where antibiotics have largely become a 'quick fix' for care, productivity, hygiene and inequality[14] as well as institutional antimicrobial stewardship mostly either not in place or limited.[15] On the other hand, hospitals in developed countries including Belgium and Canada reported antimicrobial use rates of 25.9%, 27.1% and 34% respectively.[16,17] Also noted in this study, there was higher antimicrobial use in pediatric age groups than in adults, a finding buttressed by that of a survey of antimicrobial use among hospitalized children in six hospitals in Asia.[18] Excessive use of antimicrobials among patients of pediatric age groups is due to high frequency of infection because their immune system is not fully-developed, and possibilities of symptoms and signs of other clinical conditions mimicking an ongoing infection.

Antibiotic use remains essentially empiric in almost all the patients in the present survey. Similar high rates of empiric prescribing are reported in some other low- and middle income countries (LMICs), including a rate of 82.6% in a

Table 4. Antibiotic prescribing according to indications

Antibiotics	CAI, n (%)	HAI, n (%)	SP, n (%)	MP, n (%)	Others, n (%)
Amikacin	1 (0.6)				
Gentamicin	19 (11.2)	6 (14.3)	14 (6.9)	15 (22.1)	3 (4.7)
Amoxicillin	3 (1.8)		1 (0.5)	1 (1.5)	2 (3.1)
Amoxicillin/clavulanate	12 (7.1)	4 (9.5)	7 (3.4)	2 (2.9)	4 (6.3)
Ampicillin	1 (0.6)			8 (11.8)	1 (1.6)
Ampicillin/cloxacillin	1 (0.6)	2 (4.8)	2 (1.0)		1 (1.6)
Penicillin	1 (0.6)				1 (1.6)
Cefuroxime	27 (16.0)	5 (11.9)	52 (50)	5 (7.4)	13 (20.3)
Cefixime	3 (1.8)	2 (4.8)	1 (0.5)		1 (1.6)
Cefixime/clavulanate	1 (0.6)				
Cefotaxime			2 (1.0)		
Ceftriaxone	26 (15.4)	3 (7.1)	25 (12.6)	11 (16.2)	11 (17.2)
Ceftriaxone/sulbactam			2 (1.0)		
Ceftazidime	2 (1.2)	3 (7.1)	3 (1.5)	3 (4.4)	1 (1.6)
Cefpodoxime	1 (0.6)	2 (4.8)	1 (0.5)		1 (1.6)
Cefepime	1 (0.6)				
Azithromycin	5 (3.0)				2 (3.1)
Erythromycin	3 (1.8)				
Clarithromycin	3 (1.8)				
Ciprofloxacin	13 (7.7)	4 (9.5)	22 (10.8)	12 (17.6)	6 (9.4)
Levofloxacin	1 (0.6)		2 (1.0)		1 (1.6)
Clindamycin	1 (0.6)		1 (0.5)		
Imipenem		1 (2.4)			
Meropenem	1 (0.6)	1 (2.4)	1 (0.5)	1 (1.5)	
Metronidazole	36 (21.3)	7 (16.7)	68 (33.3)	7 (10.2)	16 (25.0)
Nitrofurantoin	2 (1.2)				
Doxycycline		1 (2.4)			
Trimethoprim/sulfamethoxazole	1 (0.6)				
Vancomycin	4 (2.4)	1 (2.4)		3 (4.4)	
Total	169 (30.0)	42 (7.4)	204 (36.2)	68 (12.1)	64 (11.3)

CAI – community-acquired infection; **HAI** – healthcare-associated infection; **MP** – medical prophylaxis; **SP** – surgical prophylaxis.

Table 5. Antibiotic prescribing according to WHO AWaRe classification

Wards (N)	Access, n (%)	Watch, n (%)	Reserve, n (%)
Adult medical (108)	52 (48.1)	55 (50.9)	1 (0.9)
Surgical (129)	53 (41.1)	76 (58.9)	0 (0.0)
Children (60)	19 (31.7)	41 (68.3)	0 (0.0)
Orthopedic (52)	21 (40.4)	31 (59.6)	0 (0.0)
Neonatal (77)	36 (46.8)	41 (53.2)	0 (0.0)
Gynecology (38)	21 (55.3)	17 (44.7)	0 (0.0)
Postnatal (67)	36 (53.7)	31 (46.3)	0 (0.0)
Burns (19)	8 (42.1)	11 (57.9)	0 (0.0)
Antenatal (5)	3 (60.0)	2 (40.0)	0 (0.0)
Mental health (4)	2 (50.0)	2 (50.0)	0 (0.0)
Adult ICU (5)	2 (40.0)	3 (60.0)	0 (0.0)
Total (564)	261 (46.3)	302 (53.5)	1 (0.2)

532 bedded teaching hospital in Kenya[19] and 96.2% from a point prevalence survey involving 13 hospitals also in Pakistan.[20] Hospitals in industrialized countries engage in modest empiric therapy, for example empiric antibiotic treatment rates reported in Canada and Romania were 40.4% and 50.6% respectively.[17,21] Reliance on empiric antibiotic use in LMICs is a reflection of poor and insufficient diagnostic microbiology capacity that is prevalent.[22] This is also the case in this survey in which culture was carried out only in 38 (15.4%) of 246 patients on antibiotics. Hospitals in well-resourced countries with good laboratory infrastructures tend to have good antimicrobial resistance surveillance systems that inform patients' management leading to lower rates of empiric antibiotic prescribing. This is typified in a global point prevalence survey carried out among hospitalized patients in 110 Belgian acute care facilities in 2017 in which as high as 38% of therapeutic antimicrobial prescribing was guided by microbiology results.[16] It is expected that the narrative about poor diagnostic capacity in many LMICs will change with present global attention and support for improving AMR surveillance. The UK Fleming Fund is providing support for 24 countries in LMICs in Africa and Asia including Nigeria. In Nigeria, two of the 10 human health institutions being supported on the Fleming Fund country grant with upgrade in diagnostic capacity are in Osun State and should soon result in availability and increase in quality-assured surveillance data to guide use and prescribing of antimicrobials. Prescribing was carried out by specialist physicians in 88% of times, a reflection that 92.8% (298/321) of patients seen were in specialist hospitals. The high level of parenteral therapy route (89.9%) found in this study could be explained by the fact that a large number of patients in this environment are faced with poverty and have poor health-seeking behaviour[23] manifesting in late presentation to healthcare facilities often with severe and overwhelming infections, treatment of which is unavoidably parenteral. Parenteral to oral switch was noted in 19.9% of patients while compliance to treatment guidelines was ensured only in 39% of patients; these rates are considered to be low as consequences of poor institutional antimicrobial stewardship in Nigeria.[24]

Antibiotic use in this study was commonly indicated for surgical prophylaxis (36.9%) and community acquired infection (CAI) (29.2%), justifying the large antibiotics volume used in surgical and adult medical wards; this finding is similar to what was documented from other surveys in Africa[25,26] and attributed to the fact that the vast majority of hospitalized patients either presented with CAI or were surgical patients. Similar to what was noted by Horumpende et al. in Northeast Tanzania[25] and Saleem et al. in Pakistan,[20] antibiotics for surgical prophylaxis in this survey were inappropriately used for longer than 24 hours in almost all (94.8%) cases, which is a pointer to either lack of antibiotic treatment guidelines or poor adherence to it in surgical subspecialties. In hospitals in more civilized climes, surgical prophylaxis was more appropriately carried out.[16-18] This study also agrees with reports from point prevalence surveys of patients in healthcare facilities in Korle-Bu Ghana and Punjab Pakistan[20,26] that metronidazole was the most common agent used for surgical prophylaxis, and this is essentially due to the need for prevention of anaerobic infection in surgical patients. Antibiotic use in 13.3% of surveyed patients was inappropriate for an undefined diagnosis in which there was no systemic inflammation. The survey in Ghana also reported use of antibiotics for undefined indication in 16% of patients, emphasizing that inappropriate use of antimicrobials is a common event in sub-Saharan Africa.[26]

Among a total of 564 antibiotic prescriptions, the majority of patients received multiple antibiotics with an overall antibiotic-patient prescribing ratio of 2.3. Prescribing more than one antibiotic per patient is a common practice across many hospitals in the continent.[19,26] Deployment of multiple antimicrobial therapies to tackle clinical infection is a make-up for markedly low targeted therapy caused by low level of microbiologic culture in our environment.

Similar to findings from this survey, hospitals in several developing countries show high preference for metronidazole and cephalosporin particularly ceftriaxone[13,19,26] because of almost absolute reliance on empiric treatment requiring broad microbiologic coverage both in terms of bacterial and resistance spectra as well as lack of anaerobic culture. Prescribing patterns are diverse in hospitals across regions and they are largely determined by local antibiogram as well as patient factors; for example, this survey and others elsewhere in Nigeria and Kenya[10,19] noted the preponderance of prescribing gentamicin in neonates. The strikingly high use of vancomycin in the neonatal age group in this study is justified by findings in a recent study (unpublished) of high prevalence of MRSA among neonates in our location. Furthermore, carbapenems only constituted 0.9% (n=5) of all antibiotics used in this survey, reflecting poor access to these drugs for treatment of multidrug-resistant infections. Barriers to antibiotic access, especially in developing countries, are poor affordability and low health funding as well as limitations to drug supply chains.[27]

Analysis of survey results showed that more than half (53.5%) of all antibiotics used by patients belonged to the Watch category, while only 46.3% belonged to the Access group. The current pattern of antibiotic use falls short of the WHO AWaRe categorization goal of having a minimum of 60% of national antibiotic consumption from the Access group. Alignment of countries with AWaRe categorization and reaching the threshold by 2023 will result in better use of antibiotics at reduced cost and improved access for achievement of the health-related targets of the Sustainable Development Goals.[28] To ensure alignment with WHO AWaRe categorizations, a number of context-specific interventions will be necessary; Nigeria and by extension, Osun State will need to incorporate AWaRe categorization into the National Essential Medicines List due for revision in 2021. This expectedly will impact procurement of antimicrobials such that consideration is given to purchase for use by the public healthcare system and healthcare facilities in lines with the AWaRe list. Likewise, it will be essential to update the national standard treatment guidelines for treatment of infectious diseases with consideration of the AWaRe list. Although pharmaceutical enforcement against over-the-counter sales of drugs is a current challenging issue, the priority of such enforcement mechanisms needs to focus on the Watch and Reserve groups of antibiotics. Furthermore, pre-service and in-service healthcare professionals' education curriculum needs to include AWaRe as a way to impact prescription-based practices and OTC sales of antibiotics. Periodic survey of antibiotic use at the national and sub-national levels should regularly assess alignment with AWaRe to target attainment of minimum of 60% of consumption from the Access group.

Conclusions

Our survey was limited by the relatively low number of hospitalized patients resulting from very low patronage in government-owned healthcare facilities also due to prevalent medicines stock-out despite free healthcare program in the State. However, the number of available patients surveyed did not invalidate the findings from the study. Antibiotic prescribing in almost all cases was empiric due to low microbiological culture rate with poor compliance to guidelines. The most common indications for antibiotic use were community-acquired infections and surgical prophylaxis, which was received for longer than 24 hours in almost all patients, with use for undefined indications in a considerable number of patients. Metronidazole, cefuroxime and ceftriaxone constituted 57% of the total antibiotic use, mostly through parenteral routes. Prescribing patterns have yet to meet the goal of the WHO AWaRe antibiotic categorization with Access drugs falling short of the 60% target. The survey has identified specific entry points for state-wide improvement of use of antimicrobial medicines.

Authors' contributions statement: AOA1 conceptualized and coordinated the study, AOA1 and AA2 carried out the study design, AOA1, AA2, AO4, AA5, AO6, OO7, OF8, and AA9 were involved with the data collection, AOA1, ATA2 and AAO carried out data entry and analysis, AOA1 and AA2 prepared the initial manuscript draft, AOA1, AA2, OH11 and WF12 revised the manuscript and prepared the final draft. All authors read and approved the final version of the manuscript.

Conflicts of interest: All authors – none to declare.

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