

## **Antibiotic resistance and rational use of antibiotics – a point prevalence study carried out at a tertiary hospital in South-south Nigeria**

### **Abstract**

#### **Introduction**

The burden of antibiotic resistance in the hospitals and communities is progressively worsening hence the **critical** need to put into **practice** all the key components of rational use of antibiotics in our daily patient interactions. This paper aims to highlight the problem of antibiotic resistance, the importance of rational use of antibiotics and to show an on the spot sketch of the antibiotic use pattern among in-patients in the children wards in a tertiary hospital.

#### **Methodology**

A brief review of the existing literature on antibiotic resistance and the rational use of antibiotics was done. A one-day cross-sectional point prevalence study was conducted in the children wards in UPTH and all children receiving antibiotics on that day, identified. The information concerning antibiotic in use and antibiotic sensitivity pattern where culture results were done was obtained from the case notes and treatment charts of **in-patients** after obtaining consent from the patients/caregivers. **The** prevalence of antibiotic use was determined by dividing the number of inpatients on antibiotics at the time of the survey by the total number of patients on admission. Data were presented in percentages using pie and bar charts.

#### **Results**

There were a total of 40 children on admission in the paediatric wards with a Male: Female ratio of 1.2:1. 34 (85.0%) of the children on admission were receiving at least one antibiotic. The most common route of administration of the antibiotics was the intravenous route (94.1%). The five most commonly prescribed antibiotics in the children medical wards and the emergency ward were Ceftriaxone, Gentamycin, Cefuroxime, Metronidazole and Crystalline penicillin, while the five most common antibiotics prescribed in the special care baby unit were Gentamycin, Ceftazidime, Ceftriaxone, Metronidazole and Ofloxacin. Only 10 (29.4%) out of children receiving antibiotics had a microbiology culture result available, and 4 were receiving antibiotics in line with the culture sensitivity pattern. Two (5.9%) children had a multidrug-resistant infection.

## **Conclusion**

This study showed a high prevalence of antibiotic use among inpatients and low utilization of microbiology culture results in the choice of antibiotics in a tertiary hospital in South-south Nigeria. Antibiotic prescribing patterns among healthcare workers should be improved upon by training and retraining of personnel as well as strict adherence to antibiotic prescription guidelines.

## **Keywords**

Antibiotic resistance, rational use, antibiotics, stewardship, point-prevalence

## **Introduction**

In the words of William Osler, “*One of the first duties of the physician is to educate the masses not to take medicine.*” In other words, though medicines are useful for the treatment of disease, they should be taken following the prescription of a physician and this

prescription should be made only when it is completely necessary.<sup>1</sup> This is, however, not common practice today as in many developing countries, the control on antimicrobial drug administration is weak.<sup>2</sup> Unfortunately, antibiotics are often sold as over-the-counter drugs (OTC). Individuals, then indulge in self-medication, and more often than not, take antibiotics before presentation in the hospital.<sup>3</sup> These and many other laxities with the use of antibiotics has led to the development of drug resistance.<sup>2</sup>

Antibiotics are substances produced by micro-organisms that are antagonistic to the growth of life or other micro-organisms.<sup>4</sup> They are chemicals produced naturally, semi-synthetically or synthetically and function by inhibiting bacterial growth (bacteriostatic) or killing bacteria (bactericidal). They destroy the organism without harming the host.<sup>4,5</sup> They are one of the most commonly prescribed drugs today.<sup>6</sup> Their discovery has been hailed as one of the wonders of modern medicine. The emergence of antibiotic resistance has, however, become a major concern worldwide.<sup>7</sup>

Antibiotic resistance is the relative or complete lack of effect of an antibiotic against a previously susceptible microbe.<sup>8</sup> It occurs due to changes in the genetic material of the micro-organism, mutations in one or some of the genes or with a new gene, by "contamination" of the organism with plasmids, and other elements.<sup>8</sup> Mono-drug resistance refers to the resistance of a microbe to one drug while multi-drug resistance refers to the resistance of a microbe to more than one drug. Multi-drug resistant microbes pose a greater threat to public health as it is associated with increased morbidity and mortality.<sup>9</sup> Antibiotic resistance is of public health concern because it reduces the doctor's choice of treatment, it increases human pain and mortality and may even lead to medico-legal issues. Rational use of antibiotics has thus been proffered as a major weapon in this battle against resistant microbes.<sup>2</sup> The World Health Organization<sup>10</sup> defines rational use of medicine as requiring patients receive medications appropriate to their clinical needs, in doses that meet their

requirements, for an adequate period, and at the lowest cost to them and their community. Attendant effects of irrational use of antibiotics include ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and harm to the patient, higher cost of treatment and even death.<sup>1,11</sup>

Omoyibo et al,<sup>12</sup> in a study in a tertiary hospital in south-west Nigeria, showed that antibiotics prescribed more commonly had developed resistance more than those antibiotics used less frequently. Hence the onus is on the prescribing doctor to use certain antibiotics only when extremely necessary to avoid the development of resistance. Sadly, Enato and Uwaga<sup>13</sup> in a study in six hospitals/clinics and four community pharmacies in the University of Port Harcourt, Rivers state, found that 23% of the antibiotic prescriptions were inappropriate. Despite the huge burden of inappropriate prescriptions and antibiotic resistance, there is a dearth in research and availability data on this subject in resource-limited settings.<sup>1</sup> Hence this study set out to capture the antibiotics in use for the treatment for inpatients at a paediatric department in the University of Port Harcourt teaching hospital, Rivers state, Nigeria and the susceptibility pattern of culture results of same patients to buttress the value of culture results in patient care.

## **Subjects and methods**

### **Study Setting**

The University of Port Harcourt Teaching Hospital (UPTH) is one of the two tertiary health care facilities in Rivers State, Nigeria that provides medical care for its populace and that of the **neighbouring** states. The hospital has various departments including Paediatrics, Internal Medicine, Surgery, Obstetrics and Gynaecology, Psychiatry, Community Medicine, Oral and Maxillofacial Surgery and Restorative Dentistry. The Paediatric Department is well staffed with its components of nursing staff, house officers, medical officers, registrars and consultants. Patients are admitted through the children emergency ward. Neonates are

immediately transferred to the Special Care Baby Unit while children aged 2 months to 18 years are admitted into the children emergency ward where they spend a minimum of 24 hours, after which they are moved into the children medical wards 1 and 2 to be managed by medical teams consisting of unit consultants, residents and house officers. The study setting comprised three paediatric wards (Special Care Baby Unit, Children Medical Wards 1 and 2). Each of the three wards has an official bed capacity of 15-25.

This was a point prevalence study carried out using the medical records of patients on admission on the exact day the study was done (25<sup>th</sup> of April, 2019). It covered children from birth to 18 years admitted into the children emergency ward, medical ward and special care baby unit of UPTH. The process of medication ordering and administration is a handwritten system whereby doctors prescribe medicines and transcribe medication orders onto patients' treatment/administration charts. The prescribed intravenous antibiotics are dispensed to patients by house-officers (internship doctors). Nurses ensure patients to take their prescribed oral or topical medication, but directly administer intramuscular/injectable medicines and record this information (drug name, dose, route and time of administration) on patients' hospital medication administration charts. Only medical records of inpatients on admission before 8 am on the day of the study were included.

### **Data collection**

Data was collected by a team of five doctors, the principal investigator and four internship doctors. The four internship doctors were trained by the principal investigator on the study protocol in a brief training session five days before the day the actual survey was conducted. The brief training session introduced the team to the objectives of the study, the data collection tool as well as the methods of retrieving individual patient data from the case notes and treatment charts. A 1-day pilot point-prevalence survey was also done immediately after

the training session at a Surgery ward in the same hospital and minor corrections made to the study tool.

On the day of the actual study, data were collected between 8 am and 4 pm. Data collection from each paediatric ward was completed within 4 hours. Information retrieved include age, sex, ward, the total number of patients on admission, antibiotics being used, route of administration. Also, the presence of any microbial culture results and their drug sensitivity pattern was noted. The antibiotic in use by individual patients was compared with the antimicrobial suggested by the laboratory culture result for the patient who had available culture results.

**Sampling procedure:** After obtaining consent from the patient/patient caregivers and soliciting the support of the ward nurses, all case notes and treatment charts of the patients on admission in the ward by 8 am on the day of the study were assembled and the required information retrieved. Case notes of children on admission for less than 24 hours, those undergoing same-day treatment, as well as those who were discharged from the wards before the time of the survey were excluded. The information sought for include the types of medication the patient was receiving, the number and names of the antibiotics being used if any, the presence of any specimen **microbiological** culture and sensitivity results and whether or not the patient is receiving antibiotics in line with the culture sensitivity patterns. Data collection from each ward was completed within 4 hours.

**Analysis:** The results were expressed as percentages and displayed in bar and pie charts. The prevalence of antibiotic use was defined as a percentage of the total number of patients on a systemic antibiotic at the time of the survey against the number of patients on admission.

## **Results**

On the day of the survey, there were a total of 40 children on admission in the paediatric wards with a Male: Female ratio of 1.2:1. 34 (85.0%) of the children on admission were receiving at least one antibiotic. The majority of the children (44%) were receiving antibiotics for the treatment of sepsis while 2 (5.9%) children received antibiotics for infection prophylaxis. The most common route of administration of the antibiotics was the intravenous route (94.1%). Only 10 (29.4%) out of children receiving antibiotics had a microbiology culture result available, and 4 were receiving antibiotics in line with the culture sensitivity pattern, (Table 1). Two (5.9%) children had a multidrug-resistant infection.

**Table 1- Demographics and antibiotic use**

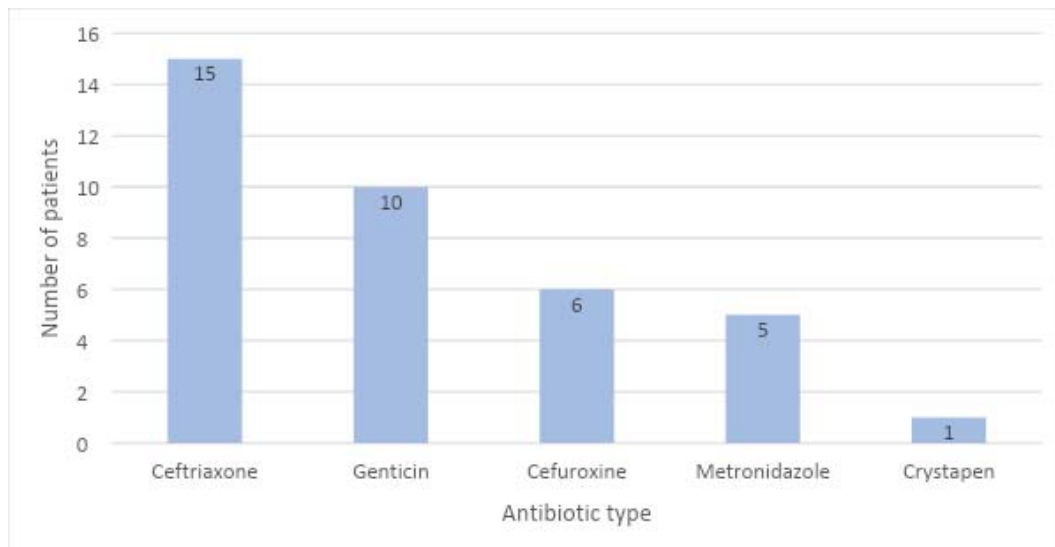
	<b>n(%)</b>	<b>Total (n=40)</b>
<b>Wards</b>		
Special care baby unit	18 (45.0)	
Emergency ward	7 (17.5)	
Children Medical ward 1	10 (25.0)	
Children medical ward 2	5 (12.5)	40 (100.0)
<b>Age</b>		
0-28 days	18 (45.0)	
2months- 5 years	6 (15.0)	
6 – 10 years	7 (17.5)	
11- 15 years	5 (12.5)	
15-18 years	4 (10.0)	40 (100.0)
<b>Sex</b>		
Male	22 (55.0)	
Female	18 (45.0)	40 (100.0)
<b>Receiving antibiotics</b>		
Yes	34 (85.0)	
No	6 (15.0)	40 (100.0)
<b>Indications for antibiotic use (n=34)</b>		
Sepsis	15 (44.1)	
Bronchopneumonia	7 (20.6)	
Meningitis	6 (17.6)	

Upper respiratory infections	4 (11.8)	
Infection prophylaxis	2 (5.9)	34 (100.0)
<b>Route of administration of antibiotics (n=34)</b>		
Intravenous route	32 (94.1)	
Oral route	2 (5.9)	
Intramuscular route	0 (0.0)	34 (100.0)
<b>Culture result available (n=34)</b>		
Yes	10 (29.4)	
No	24 (70.6)	34 (100.0)
<b>Receiving antibiotic in line with culture sensitivity pattern (n=10)</b>		
Yes	4 (40.0)	
No	6 (60.0)	10 (100.0)

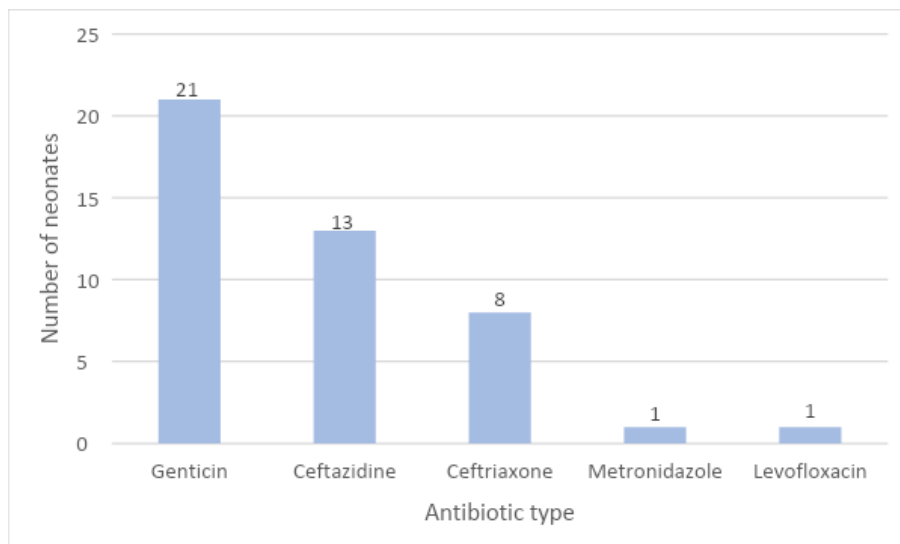
The five most commonly prescribed drugs in the children medical wards and the emergency ward were Ceftriaxone, gentamycin, cefuroxime, metronidazole and crystalline penicillin, (Figure 1), while the five most common antibiotics prescribed in the special care baby unit were Gentamycin, Ceftazidime, Ceftriaxone, Metronidazole and Ofloxacin, (Figure 2). The majority of the patients with **antibiotics** prescribed had only one drug (97.1%) while the remaining had two (2.7%) and three (0.2%) drugs respectively.

**Figure 1: Bar chart showing the number of patients receiving different antibiotic drugs in the Children Medical Ward 1, 2 and the emergency room**





**Figure 2: Bar chart showing the number of neonates receiving different antibiotic drugs in the Special Care Baby Unit (SCBU)**



## Discussion

This point prevalence study yields important findings regarding the most commonly prescribed antibiotics for in-patients and the utilization of **microbiological** culture and sensitivity testing in the choice of antibiotics for patient care. It also identifies areas of focus that need to be addressed when developing interventions to increase the rational use of antibiotics within the hospital setting.

The study revealed that a majority of in-patients in the hospital at the time of the study were receiving antibiotics buttressing the fact that antibiotics are one of the most prescribed medications in our world today. This is similar to the reports of another study in South-east Nigeria (78.6%)<sup>14</sup> and Uganda (79%).<sup>15</sup> The prevalence of antibiotic use in this present study is however higher than the findings of Sviestina and Mozgis<sup>16</sup> who observed that only between 26% to 38% of inpatients in their point prevalence study in Childrens' Clinical university hospital, Riga, Latvia (Northern Europe) were receiving antibiotics. The likely reason for the difference in the prevalence of antibiotic use may be because, in the Riga study, the hospital has an established ward-based clinical pharmacist service. The clinical pharmacist makes regular visits to the ward and joins the ward rounds. There is also a special antibiotic prescription form and an antibiotic stewardship team, all intending to decrease unnecessary and incorrect use of antibiotics. This practice in Northern Europe is the ideal. Hospitals should have an infection control team comprised of a physician and an infection control practitioner, and a microbiology laboratory that can isolate and identify pathogens from clinical cultures and carry out in vitro susceptibility using acceptable standard methods.

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Furthermore, in this present study, all patients on admission for less than 24 hours were excluded. Patients in this group are less likely to have already commenced antibiotics and if included, may have caused a lower prevalence. Lower prevalence of antibiotic use was also seen in other countries like Ghana (51.4%),<sup>18</sup> Benin (64.6%)<sup>19</sup> and the United States (49.9%).<sup>20</sup>

The major route of administration of the antibiotics in this present study was intravenous. This is also similar to the findings of the Riga study where 76 to 86% of all prescriptions were via the intravenous route.<sup>16</sup> In practice, the intravenous route is usually used in the treatment of severe systemic infections in hospitalized patients. Moreso, some patients may

have already taken oral antibiotics to no avail, before presenting at the healthcare facility. However, lower rates of intravenous antibiotic use are preferred because there is reduced risk of thrombophlebitis, cannula related infections, lower cost of care and possibly earlier discharge.<sup>21</sup>

The most commonly used antibiotics in this present study were Ceftriaxone (cephalosporin group) and Gentamycin (aminoglycoside group). This is similar to the reports in South-east, Nigeria<sup>14</sup> and Uganda.<sup>15</sup> In contrast, Fadare et al<sup>22</sup> in South-west Nigeria reported the penicillin group (amoxicillin and amoxicillin/clavulanic acid) to be the most commonly prescribed antibiotics followed by the cephalosporin class (Cefuroxime) and the macrolide Erythromycin. The reason for this difference may be that the study in South-west Nigeria was carried out in an outpatient clinic as against in patients in this present study. Most infections treated on **an** out-patient basis are mild diseases that can be managed by oral antibiotics from the penicillin group. Sviestina and Mozgis,<sup>16</sup> in their study in Riga also reported penicillins and other Beta-lactam antibiotics as the most commonly used antibiotics. They observed an increasing trend in the use of cephalosporins which was linked to the development of resistance.<sup>16</sup>

Furthermore, only 29.4% of the children on antibiotics had a microbiology culture result. This is common in our setting as there are several obstacles to the prompt availability of culture results. Patient-related factors include being unable to afford the tests. Patients pay for healthcare out of pocket unlike in the western countries where health care insurance relieves this burden. Moreover, some health care facilities do not possess equipped laboratories and/or personnel to carry out these investigations in a timely fashion.<sup>1</sup> Hence, many patients admitted for varying infections are treated and discharged based on empirical data of previous susceptibility patterns. A lack of diagnostic equipment has been termed the 'Achilles heel' of antibiotic resistance containment.<sup>23, 24</sup> This unguided practice can be

detrimental to the patient outcome as morbidity and mortality from common infections would not be prevented. In addition to the use of microbiology culture results to aid appropriate prescription of antibiotics within the hospital setting, antimicrobial stewardship represents an umbrella of interventions aimed at ensuring rational use of antibiotics.<sup>8</sup> Findings from a Cochrane systematic review have proven that antimicrobial stewardship interventions in routine clinical **practice** can safely reduce unnecessary antibiotic use in hospitals.<sup>2</sup>

The components of antibiotic stewardship include leadership commitment, accountability, drug expertise, action, tracking, reporting and education.<sup>8</sup> The leadership in hospitals and departmental heads need to dedicate the necessary human and financial resources to the course. The responsibility of antimicrobial stewardship should be assigned to specific individuals working in teams who can be held accountable for ensuring the success of the **program**. Deliberate actions that promote appropriate prescribing, like the use of a hospital antibiotic policy, should be **practiced**. Antimicrobial tracking should be done by monitoring antibiotic prescribing and resistance patterns. Periodic meetings for regular reporting of information on antibiotic use and resistance patterns to doctors, nurses and relevant staff should be organized. Clinicians should also be constantly educated on antibiotic resistance and optimal prescribing. Research has shown that clinician education combined with other strategies can drastically reduce the rate of antibiotic prescriptions.<sup>25</sup> Medical students, as well, should not be left out in these training, as their younger minds are more likely to readily imbibe best practices. As much as possible, antibiotic prescriptions should be made by the highest cadre of **doctors** available, as younger doctors may lack experience and not make the best decisions with regards to choice and dose of antibiotic to administer.<sup>26</sup>

Other antibiotic utilization strategies include antibiotic restriction and antibiotic cycling.<sup>27</sup> Antibiotic restriction involves the selective removal or control of specific agents or classes of antibiotics. The less commonly used an antibiotic is in a given region the less likely it is to

develop resistance. Likewise, antibiotic cycling refers to the deliberate removal of antimicrobial of choice to treat a particular infectious syndrome in a specific geographic unit, to re-introduce it at a pre-determined time in the future.<sup>27</sup> These methods utilize a similar principle in reducing or slowing down the process of development of resistance for specific antimicrobials. The use of combination therapy (use of more than one antimicrobial) in the treatment of active infection also guards against the problem of resistance.

Several **programs** have been put in place all over the world to wage war against the problem of antibiotic resistance. They include **programs** like 'Alliance for the prudent use of antibiotics' (1981), 'WHO global strategy for containment of Antimicrobial resistance' (2001) and 'Global antibiotic resistance partnership' (2008).<sup>28</sup> The 18<sup>th</sup> of November has also been set aside in Europe since 2008 as an awareness day for **the** rational use of antibiotics.<sup>28</sup> These **programs** have made giant strides in curbing the problem of antibiotic resistance, however, some challenges in Nigeria have limited their impact. These problems include paucity of data, weak surveillance, poor policy enforcement, little or no formal collaboration amongst regional surveillance programs and limited microbiology laboratory capacity.<sup>13,29</sup>

### **Study strengths/ limitations**

This study was able to take a snapshot of the antibiotic prescription/utilization pattern as well as the use of microbiology culture results to guide treatment. It brought to light the commonly used antibiotics and the poor use of culture **results** to inform patient care. A demerit of this work, however, is that the sample size **of forty** is small. Also, the findings of this study could not be **rightfully extrapolated** to the whole of Port Harcourt since this was done in a single hospital. This study was done in inpatients and thus does not reflect the outpatient prescribing patterns of the hospital. Furthermore, being a PPS, the study is unable to explain the high use of cephalosporins. **It also does not put into consideration that infectious diseases occur in seasons and there may be differences in the choice of antibiotic use in different seasons.**

## **Conclusion**

Antibiotic resistance is a global problem but the solutions have a strong local component. Action against antibiotic resistance requires increased awareness by health professionals and even the general public, as well as behaviour change for all, which is often the most difficult end to achieve. Doctors and other professionals should prescribe antibiotics only when necessary, based on existing guidelines.

## **Disclaimer regarding Consent and Ethical Approval:**

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors

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## **Competing interest disclaimer**

The author declares that there are no competing interests. The products named in this research are commonly and predominantly used products in our area of research and country. There is no conflict of interest between the author and producers of the products because there is no intention to use these products as an avenue for any litigation but the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal effort of the author.

## **Author's contribution**

CO conceived the idea, designed the study, collected, analyzed and interpreted the data, and drafted the manuscript. The author read and approved the final manuscript.

## References

1. Bebell LM, Muiru AN. Antibiotic use and emerging resistance—how can resource-limited countries turn the tide? *Glob Heart*. 2014; 9(3): 347–358.
2. Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2017 (2). Art. No.: CD003543. DOI: 10.1002/14651858.CD003543.pub4.
3. Irawati L, Alrasheedy AA, Hassali MA, Saleem F. Low-income community knowledge, attitudes and perceptions regarding antibiotics and antibiotic resistance in Jelutong District, Penang, Malaysia: a qualitative study. *BMC Public Health* .2019; 19:1292.
4. Milić, N.; Milanovic, M.; Letić, N.G.; Sekulić, M.T.; Radonić, J.; Mihajlović, I.; Miloradov, V. Occurrence of antibiotics as emerging contaminant substances in the aquatic environment. *Int. J. Environ. Health Res.* 2013; 23:296–310.
5. Martínez, J.L. Natural antibiotic resistance and contamination by antibiotic resistance determinants: The two ages in the evolution of resistance to antimicrobials. *Front. Microbiol.* 2012:3.
6. Col NF, O'Connor RW. Estimating worldwide current antibiotic usage: report of Task Force 1. *Rev Infect Dis.* 1987; 9:232–243.
7. World Health Organization. Antimicrobial resistance: global report on surveillance. Geneva: World Health Organization; 2014.
8. Sartelli M, Weber DG, Ruppé E, Bassetti M, Wright BJ, Ansaloni L. Antimicrobials: a global alliance for optimizing their rational use in intra-abdominal infections (AGORA). *World Journal of Emergency Surgery*,2016;11(33):1-32.
9. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis.* 2010; 10:597–602
10. World health organization (WHO) 2001. Global strategy for containment of antimicrobial resistance.
11. Oduyebo O O, Olayinka A T, Iregbu KC, Versporten A, Goossens H, Nwajiobi-Princewill P I, et al. A point prevalence survey of antimicrobial prescribing in four Nigerian Tertiary Hospitals. *Ann Trop Pathol* 2017; 8:42-46.
12. Omoyibo EE, Oladele AO, Ibrahim MH, Adekunle OT. Antibiotic Susceptibility of Wound Swab Isolates in a Tertiary Hospital in Southwest Nigeria. *Ann Afr Med.* 2018; 17(3): 110–116.
13. Enato EFO, Uwaga CF. Profile of antimicrobial drug use patterns in a Nigerian metropolitan city. *Int J Health Res.* 2011;4(1): 37-44.
14. Umeokonkwo CD, Madubueze UC, Onah CK, Okedo-Alex IN, Adeke AS, Versporten A, et al. Point prevalence survey of antimicrobial prescription in a tertiary hospital in South-East Nigeria: a call for improved antibiotic stewardship. *J Glob Antimicrob Resist.* 2019; 17:291–295.

15. Kiguba R, Karamagi C, Bird SM. Extensive antibiotic prescription rate among hospitalized patients in Uganda: but with frequent missed-dose days. *J Antimicrob Chemother* 2016; 71: 1697–1706.
16. Sviestina I, Mozgis D. Observational Study of Antibiotic Usage at the Children's Clinical University Hospital in Riga, Latvia. *Medicina* 2018; 54(74): 1-13.
17. Rosenthal VD, Maki DG, Graves N. The International Nosocomial Infection Control Consortium (INICC): goals and objectives, description of surveillance methods, and operational activities. *Am J Infect Control*. 2008; 36:1–12.
18. Labi A-K, Obeng-Nkrumah N, Nartey ET, Bjerrum S, Adu-Aryee NA, Ofori-Adjei YA, et al. Antibiotic use in a tertiary healthcare facility in Ghana: a point prevalence survey. *Antimicrob Resist Infect Control*. 2018;7(1):15.
19. Aho TA, Bankolé HS, Adéoti FM, Gbohoun AA, Assavèdo S, Amoussou-Guénou M, et al. Prevalence of nosocomial infections and anti-infective therapy in Benin: results of the first nationwide survey in 2012. *Antimicrob Resist Infect Control*. 2014;3(1):17.
20. Magill S, Edwards JR, Beldavs ZG, Dumyati G, Janelle SJ, Kainer MA, et al. Emerging infections program healthcare-associated infections and antimicrobial use prevalence survey team. Prevalence of antimicrobial use in US acute care hospitals, May-September 2011. *JAMA*. 2014;312(14):1438–1446.
21. Cyriac JM, James E. Switch over from intravenous to oral therapy: a concise overview. *J Pharmacol Pharmacother*. 2014; 5:83.
22. Fadare J, Olatunya O, Oluwayemi O, Ogundare O. Drug prescribing pattern for under-fives in a paediatric clinic in South-Western Nigeria. *Ethiop J Health Sci*. 2015; 25(1): 73-78.
23. Okeke IN, Peeling RW, Goossens H, Auckenthaler R, Olmsted SS, de Lavison JF, et al. Diagnostics as essential tools for containing antibacterial resistance. *Drug Resist Updat*. 2011; 14:95–106.
24. Berkelman, R.; Cassell, G.; Specter, S.; Hamburg, M.; Klugman, K. The "Achilles heel" of global efforts to combat infectious diseases. *Clin Infect Dis*. 2006; 1:1503-1504.
25. Lee C, Lee JH, Kang L, Jeong BC, Lee SH. Educational Effectiveness, Target, and Content for Prudent Antibiotic Use. *BioMed Research International*, 2015, Article ID 214021,1-13.
26. Ajemigbitse AA, Omole MK, Ezike NC, Erhun WO. Assessment of the knowledge and attitudes of intern doctors to medication prescribing errors in a Nigeria tertiary hospital. *Journal of basic and clinical pharmacy*.2014; 5(1): 7-14.
27. Dubberke ER, Fraser VJ. Cycling and other strategies to slow and reverse antibiotic resistance. [https://www.medscape.com/viewarticle/494369\\_print](https://www.medscape.com/viewarticle/494369_print)
28. Gelband H, Delahoy M. Policies to Address Antibiotic Resistance in Low- and Middle-Income Countries National and International Action on Antimicrobial Resistance. The centre for disease dynamics, Economics and Policy, Discussion Paper, 2014.
29. Ofori-Asenso R, Brhlikova P, Pollock AM. Prescribing indicators at primary health care centres within the WHO African region: a systematic analysis (1995–2015). *BMC Public Health* 2016; 16(724): 1-14.



