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A Review of the use of Rational and Quality Antibiotics in a Nigerian Tertiary Institution

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Abstract

Purpose: The study reviewed the use of rational and quality antibiotics at the Federal Medical Centre, Yenagoa, Bayelsa State. Three objectives and three research questions were drafted for the study, respectively.

Methodology: The study used a retrospective descriptive survey that lasted four months. The study relied on secondary data, which was gathered from the folders of 583 patients. From January 1, 2019 to April 30, 2019, all patients with complete information admitted to medical, surgical, and paediatric wards, as well as obstetrics and gynaecology wards, had their folders reviewed. A self-developed checklist was used to assess critical aspects of antibiotic utilisation and the use of generic names in antibiotic prescribing, a self-developed checklist was used. The data collected were collated, coded and analysed using descriptive statistics of frequency, percentage, charts, and tables.

Findings: The findings showed that out of the total folders (n=583) reviewed, the socio-demographic information showed that majority of the patients (42.2%) who received prescribed antibiotics were adult female. On the age category, out of the total folders (n=583) reviewed, majority of the folders (114) showed that those within the ages of 21-30 years represents over 19.0%. The antibiotics prescribed from the four (4) different departments showed that 26.7% of antibiotics were prescribed and utilized in medical wards. The level of compliance with some standard practices, shows that pneumonia test conducted, was highest in surgery ward, this represents 82.8%, the sensitivity test conducted, was highest in paediatric ward (46.4%). Out of the total antibiotics prescribed (n=1164), generic names were used for 59.6% cases, while 73.2% of the antibiotic prescribed were in the EDL authorised list. The results revealed that cephalosporins were the most commonly prescribed class of antibiotics, 384 (34%) followed by the nitroimidazoles 346 (29.7%) and penicillin's 138 (11.9%). Inappropriate antibiotic prescription was found to be 58.7% among the total prescribed antibiotics (n=1164). Based on the results and findings in the study, it is safe to conclude that the majority of antibiotics utilised were over prescribed, with high inappropriate use. The lack of generic use in antibiotic prescriptions and the overuse of antibiotics remain a problem in tertiary hospitals across Nigeria.

Recommendation: This study recommend that prescriptions should be prescribed with slips duly signed by a doctor and approved by a pharmacist before the administration of such drugs. Also, all public hospitals in Nigeria should develop local treatment guidelines using national and international policy guidelines for local infectious disease.

Keywords: *Antibiotics, generic names, essential medicine list, prescription, rational drug use.*

INTRODUCTION

Antibiotics are a class of antimicrobial drugs that have revolutionized contemporary medical practice. The emergence of therapeutic agents has improved health and saved millions of lives globally. Antibiotics account for the most commonly prescribed drugs in the hospital setting. Inappropriate antibiotic prescribing and the increasing levels of resistance are now issues of global concern (Charani *et al.,* 2010). According to Davy *et al.* (2005), a significant proportion of antibiotic prescriptions within hospitals have been described as inappropriate. Up to 50% of antibiotic use is inappropriate (Ashiru-Oredope *et al.*, 2012). Information about antibiotic prescribing patterns is necessary for a constructive approach to challenges that arise from the multiple antibiotics that are available (Srishyla *et al. 1994).* Excessive and inappropriate use of antibiotics in hospitals, health care facilities, and the community contributes to the development of bacterial resistance (World Health Organization, 2018).

While it is true that antibiotics have saved millions of lives and can put an end to the global growing trend of infectious diseases, this hope may not be fully realized because antibiotic effectiveness has been compromised by the emergence of bacterial resistance, the major outcome of inappropriate and irrational use of antibiotics (Abdu-Aguye, Haruna, Shehu, & Labaran, 2016; Ogunleye, et al., 2019). Inappropriate prescribing habits for antibiotics lead to ineffective and unsafe treatment of medical conditions. Moreover, irrational prescribing may worsen or prolong the illness, thereby leading to distress and harm to the patient. The World Health Organization (2018) argues that irrational prescribing does not only lead to exorbitant costs of medicine, but also its occurrence is very frequent in clinical practices in developing countries like Nigeria. Despite the growing trend of inappropriate antibiotic use across tertiary hospitals in Nigeria, there are no studies that have been done on antibiotic utilization in the Federal Medical Centre, Yenagoa, Bayelsa State, to ascertain the current state of antibiotic use in the facility. Hence, this study investigates the availability of Essential Medicine Lists, Drug Therapeutic Committee (DTC), and Standard Treatment Guidelines (STG) as well as the standard practice of antibiotic utilization in the Federal Medical Centre, Yenagoa, Bayelsa State.

Aim and Objectives of the Study

The aim of the study was to review the use of rational and quality antibiotics at the Federal Medical Centre, Yenagoa, Bayelsa State. The specific objectives were as follows to:-

i. Assess the number and types of antibiotics prescribed
ii. Assess quality of antimicrobial prescribing practice based on some established indicators
iii. Compare performance in terms of rational antibiotics prescribing among prescribers.

RESEARCH METHODOLOGY

The study adopted a mixed design method. This includes a cross-sectional hospital-based quantitative and qualitative method. The retrospective quantitative design focuses on the collection and review of antibiotics used at the Federal Medical Centre (FMC) in Yenagoa, Bayelsa State, from January to April 2019. The qualitative components involve interviews with doctors, nurses, and pharmacists at the research centre. A self-structured checklist was used for the quantitative study, while an in-depth interview with key experts involved in antibiotic dispensing at the hospital was used for the qualitative study. Eighteen critical healthcare professionals were questioned, including eight physicians, four pharmacists, four nurses, and two laboratory scientists. The

quantitative analysis was acquired from patient files in the departments of internal medicine, pediatrics, surgery, and obstetrics/gynecology. All total of 583 folders that met the inclusion were reviewed. Data collected, after coding, was analyzed using frequencies, averages, and percentages. The Statistical Package for Social Sciences (SPSS) software version 25.0 was used for all statistical calculations. The results were expressed as frequency, averages, percentages, pie charts, and bar charts.

RESULTS

The results are expressed as frequency, averages and percentages, pie charts and bar charts. A total of 1124 folders with complete patients' information were reviewed from the four (4) departments/wards of study (Internal Medicine, Pediatrics, Surgery, and Obstetrics and Gynecology). It is only 583 (51.9%) patients' folder that met the inclusion criteria on antibiotics use, hence, was used for the computation of the results in the study (see Table 1). Also, Table 1 displays the study population, of the 583 complete folders that met the inclusion criteria, pediatric department attracted the highest number of patients with 31.9%, this followed by Internal Medicine which had 28.8%. O & G had 24.4%, while surgery attracted the least frequency with 14.9%.

Socio-demographic Information of patient

Table 3 displays the socio-demographic information of all patients. The information on gender distribution shows about 179 (30.7%) of the patients were male, (246)42.2% were female, while male and female children consist of 76(13.0%) and 82 (14.1%) respectively. The results indicate that adult female, and female children made majority of the study sample. The Age distribution shows 21-30 years made majority of the study sample with 114 (19.6%), this is closely followed by age group between 31-40years with 102 (17.5%), this was followed by children less than 10years with a 16.1%, those between the age brackets of 11-20years represented with 15.1%, the least frequency age category were between ages of 71years and about as shown in table 4.

Table 1: Socio-demographic information of patients (n=583)

Variable	Frequency	Percentage
Gender		
Male	179	30.7
Female	246	42.2
Male Children (less 18years)	76	13.0
Female Children (less 18years)	82	14.1
Age Group (Years)		
0-10	94	16.1
11-20	88	15.1
21-30	114	19.6
31-40	102	17.5
41-50	72	12.3
51-60	73	12.5
61-70	22	3.8
71 above	18	3.1
Total	**583**	**100**

Indications for Prescribed Antibiotics

Figure 1 shows indications for which antibiotics were prescribed. Majority of antibiotics were prescribed for respiratory tract infections (RTI) 31.40%, followed by gastrointestinal disorders 24.2% and genitourinary infections 15.5%. However, 0.5% of prescribed antibiotic has no indication stated.

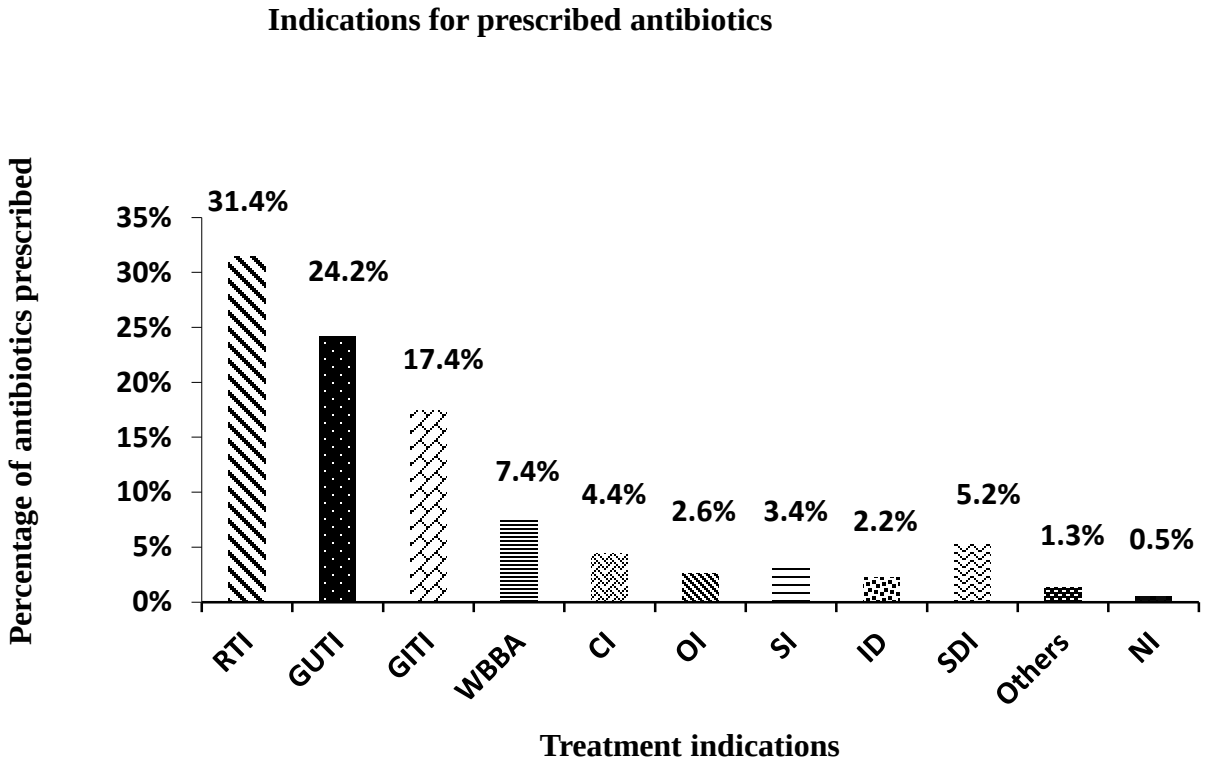

Figure 1: Indications for which antibiotics were prescribed (n=1164)

Key: RTI: Respiratory Tract Infections; GUTI: Genitourinary Infections; GITI: Gastrointestinal infections; WBBA: Wounds/Burns/Body Injuries/Assaults; CI: Cerebral Infections; OI: Organ Infections; SI: Systemic Infections; ID: Immunological Disorders, SDI: Skin/Dermal Infection; OT: Others; NI: No Indication

Class Distribution of Prescribed Antibiotics

The total of 1164 antibiotic prescriptions was encountered in all the wards were from 8 major class and others antibiotic classes (see figure 2 below). The cephalosporins were the most commonly prescribed class of antibiotics, 384 (34%) followed by the nitroimidazoles 346 (29.7%) and penicillin's 138 (11.9%). Only 15 (1.25%) of antibiotics from the carbapenem class was prescribed during the study period.

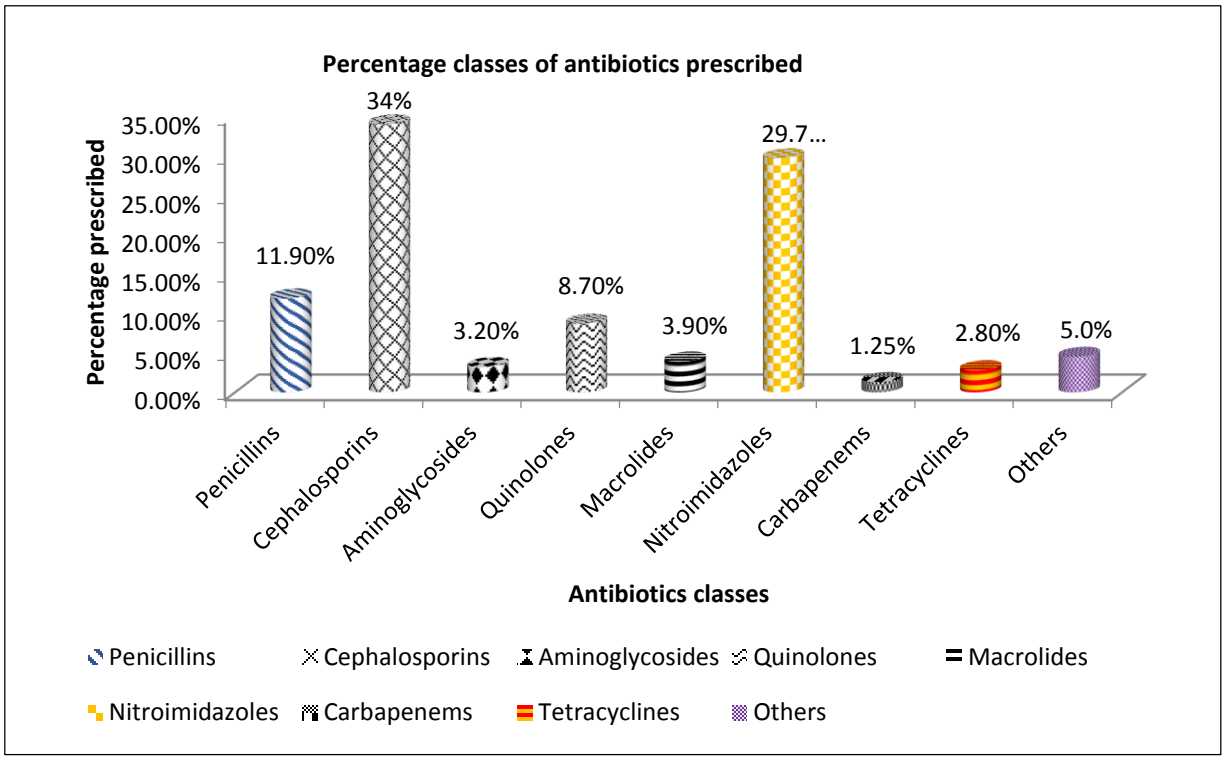

Figure 2: Percentage classes of antibiotics prescribed (n=9)

(Classes are based on Anatomical Therapeutic Chemical Classification System Others included chloramphenicol, clindamycin, nitrofurantoin and trimethoprim/ sulphamethoxazole).

Quality of Prescription

Inappropriate antibiotics prescription

Inappropriate antibiotics prescriptions were found in 342 patients (58.7%). This value represents antibiotics prescription without any clear or wrong indication, wrong regimen and use of trade names, and empirical prescribing. Deviation from one or more of these was regarded as inappropriate antibiotics prescribing as indicated in figure 3.

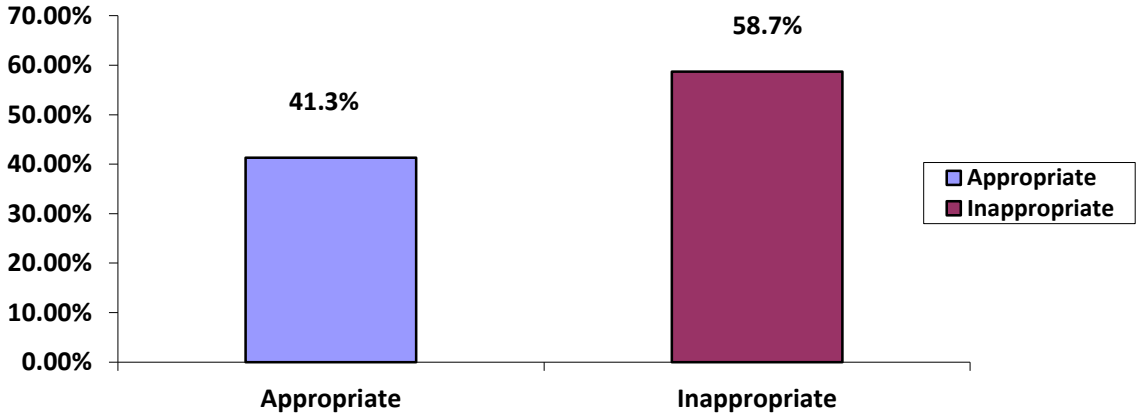

Figure 3: Percentage inappropriate antibiotics prescribing (n=583)

DISCUSSION

The use of rational and high-quality antibiotics at the Federal Medical Centre in Yenagoa, Bayelsa State, has provided insight into how drugs are administered to patients, as well as the frequency with which they are used, either appropriately or inappropriately. It also helps in providing a better understanding of the nature of the healthcare delivery system in the study area (Tamuno & Fadare 2012). In this study, a total of 583 folders were reviewed. The gender socio-demographic information revealed that the majority of the patient folders reviewed, 114 (19.6%), were between the ages of 21 and 30. However, some studies have established that antibiotic use is more common in children when compared to adults. Children often receive antibiotics when compared to adults. The results of this study are in agreement with similar studies conducted by Adisa et al. (2018). The findings revealed that the majority (42.2%) and (14.1%) of the participants were female adults and children. These findings suggest that more females received antibiotic prescriptions in the study area.

This finding is supported by a meta-analytical review which reported that females were 27% more likely to receive an antibiotic prescription when compared to males in their lifetimes (Schroder et al., 2016). In another related study, Israel et al. (2015) reported that female patients received more antibiotic prescriptions when compared to male patients. However, some other studies have contradicted these findings (Abdu-Aguye et al., 2016; Ogunleye et al., 2019). In Nigeria, Abdu-Aguye et al. (2016) and Ogunleye et al. (2018) both reported that the majority of male patients received antibiotic prescriptions compared to female patients. Thus, these results revealed a mixed pattern of antibiotic prescriptions, with some studies supporting the female patients' receiving more antibiotics, while others contradicting these reports.

Thus, the finding in this study implies that antibiotic prescriptions patients receive may not be influenced by gender, as several factors could determine the outcome. These factors may include the study design, target population, type of study, study area, and purpose of the study. The results from this study suggest that the prescribed antibiotics for patients do not follow gender. The type and pattern of antibiotic utilization revealed that a total of 583 patients received a total of 1164 prescriptions for 34 different types of antibiotics. Of the antibiotics, Metronidazole was the most prescribed (338 times), representing 29% of all the total prescriptions. This finding is supported by other related studies that have been previously conducted (Oduyebo et al., 2017; Atif et al. 2017; Abubakar, 2020). Moreover, among the antibiotic classes that were prescribed, the results revealed that cephalosporin was the most prescribed, representing 34%. This finding is consistent with several other previous studies that have reported similar findings (Umeokonkwo et al., 2019; Umar, Isah, Musa & Umar, 2020; Skender, Singh, Stalsby-Lundborg, & Sharma, 2021).

Findings on the appropriate and inappropriate antibiotic use showed that high levels (58.7%) of inappropriate antibiotic prescription were found in this study. This is consistent with previous studies that have reported similar findings (Nwolisa, Erinaugha, & Ofoleta, 2006; Pradeepkumar, Alameri, Narayana, Reddy, & Ramaiah, 2017). In contradiction, a related study conducted in Nigeria reported lower levels of inappropriate antibiotic prescribing (45.6%) (Uchenna & Adebiyi 2011). The problem of inappropriate antibiotic prescribing has been linked with several consequences, including worsening of the disease condition, increased risk of complications, length of hospital stay, increased morbidity and mortality rate, as well as a huge healthcare burden (Tamuno & Fadare, 2012; Llor & Bjerrum, 2014; Chijoke-Nwauche et al., 2018). The findings in

this study suggest that inappropriate utilization of antibiotics should only be avoided and discouraged, as appropriate prescription is necessary and at correct doses, intervals, and duration will help patients recover. As a result, when used correctly, antibiotics provide a relatively cost-effective and non-invasive solution to disease conditions, reduce the risk of complications, shorten the length of stay in hospitals, lower morbidity and mortality rates, and reduce the enormous healthcare burden.

While the findings showed a higher frequency of inappropriate prescriptions, the pattern of prescriptions suggests that antibiotics were over prescribed, without empirical or microbiological evidence, thus giving rise to a high incidence of inappropriate prescribing. In the study area, essential antibiotics were out of stock for prolonged periods, and the hospital had no standard budgeting or drug procurement system. Also, while there are systems, structures, as well as policies guiding the use of antibiotics in the study, there is, however, no implementation or adherence to these guidelines on antibiotic prescription. Taking into consideration the experiences from other countries, this is pertinent for the Federal Medical Centre, Yenagoa, where this study was conducted to adopt a sustainable Antimicrobial Stewardship Programme (ASP) with the aim of addressing the challenges with antibiotic utilization in the hospitals, with the aim of improving rational antibiotic use as well as creating public awareness of the negative outcomes of inappropriate use of antibiotics in the study area and by extension Nigeria.

CONCLUSION AND RECOMMENDATIONS

This study examined the use of rational and quality antibiotics at the Federal Medical Centre, Yenagoa, Bayelsa State. Based on the results and findings in the study, it is safe to conclude that the majority of antibiotics utilised were over prescribed, with high inappropriate use. The lack of generic use in antibiotic prescriptions and the overuse of antibiotics remain a problem in tertiary hospitals across Nigeria. Also, there is a need for re-orienting and training of clinicians on rational drug use to avoid severe consequences such as worsening of the disease condition, increased risk of complications, prolonged hospital stay, increased morbidity and mortality rate, as well as huge healthcare costs. Based on the findings, it is recommended that prescriptions should be prescribed with slips duly signed by a doctor and approved by a pharmacist before the administration of such drugs. And that all public hospitals in Nigeria should develop local treatment guidelines using national and international policy guidelines for local infectious diseases. These guidelines should be reviewed and updated periodically to reflect emerging prevalence as well as resistance patterns.

REFERENCES

Abdu-Aguye, S. N., Haruna, A., Shehu, A., and Labaran, K. S. (2016). An assessment of antimicrobial prescribing at a tertiary hospital in north-western Nigeria. *African Journal of Pharmacology and Therapeutics*, *5*(4).

Abubakar, U. (2020). Antibiotic use among hospitalized patients in northern Nigeria: a multicenter point-prevalence survey. *BMC infectious diseases*, *20*(1), 1-9.

Abula, T., and Kedir, M. (2004). The pattern of antibiotic usage in surgical in-patients of a teaching hospital, northwest Ethiopia. *The Ethiopian Journal of Health Development*, *18*(1)

Adisa, R., Orherhe, O. M., and Fakeye, T. O. (2018). Evaluation of antibiotic prescriptions and use in under-five children in Ibadan, SouthWestern Nigeria. *African health sciences*, *18*(4), 1189-1201

Alfa, J., and Adigwe, O. P. (2014). Rational use of medicines in Nigeria: A critical review. *J Biol Agric Healthc*, *4*, 89-99.

Apisarnthanarak, A., Danchaivijitr, S., Khawcharoenporn, T., Limsrivilai, J., Warachan, B., Bailey, T. C., and Thammasart university Antibiotic Management Team. (2006). Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clinical infectious diseases*, *42*(6), 768-775.

Ashiru-Oredope, D., Sharland, M., Charani, E., McNulty, C. and Cooke, J. (2012). Improving the quality of antibiotic prescribing in the NHS by developing a new Antimicrobial Stewardship Programme: Start Smart—Then Focus. *Journal of antimicrobial chemotherapy*, *67*(suppl_1), i51-i63.

Atif, M., Azeem, M., Saqib, A., and Scahill, S. (2017). Investigation of antimicrobial use at a tertiary care hospital in Southern Punjab, Pakistan using WHO methodology. *Antimicrobial Resistance & Infection Control*, *6*(1), 1-12.

Brink, A. J., Mendelson, M., Van den Bergh, D., and Richards, G. A. (2016). Passing the baton to pharmacists and nurses: new models of antibiotic stewardship for South Africa?: guest editorial. *South African Medical Journal*, *106*(10), 947-948.

Buccellato, E., Melis, M., Biagi, C., Donati, M., Motola, D., and Vaccheri, A. (2015). Use of antibiotics in pediatrics: 8-years survey in Italian hospitals. *PLoS One*, *10*(9), 1-10.

Chijoke-Nwauche, I. N., Chukwumezie, C. A., and Udezi, T. W. (2018). Prescribing indicators: a review in the general outpatient clinic of a Nigerian Tertiary Hospital. *Journal of Health Science Research*, 10-15.

Cantas, L., Shah, S. Q. A., Cavaco, L. M., Manaia, C., Walsh, F., Popowska, M., and Sørum, H. (2013). A brief multi-disciplinary review on antimicrobial resistance in medicine and its linkage to the global environmental microbiota. *Frontiers in Microbiology*, *4*, 96..

Ceyhan, M. E. H. M. E. T., Yildirim, I., Ecevit, C., Aydogan, A., Ornek, A., Salman, N., and Coskun, Y. (2010). Inappropriate antimicrobial use in Turkish pediatric hospitals: a multicenter point prevalence survey. *International Journal of Infectious*

Charani, E., Cooke, J., and Holmes, A. (2010). Antibiotic stewardship programmes—what's missing?. *Journal of antimicrobial chemotherapy*, *65*(11), 2275-2277.

Chijoke-Nwauche, I. N., Chukwumezie, C. A., & Udezi, T. W. (2018). Prescribing indicators: a review in the general outpatient clinic of a Nigerian Tertiary Hospital. *Journal of Health Science Research*, 10-15.

Cooke, F. J., and Holmes, A. H. (2007). The missing care bundle: antibiotic prescribing in hospitals. *International journal of antimicrobial agents*, *30*(1), 25-29.

Erah, P. O., and Ehiagwina, M. O. (2010). Assessment of rational prescribing and relative cost of antibiotics for in-patients treated in selected tertiary health care facilities in Southern Nigeria. *International Journal of Pharma and Bio Sciences*, *1*(1), 1-15.

Goff, D. A., and Rybak, M. J. (2015). Global antimicrobial stewardship: challenges and successes from frontline stewards. *Infectious Diseases and Therapy*, *4*(1), 1-3.

Israel, E. U., Sylvester, E. G., and Akwaowoh, A. E. (2015). The use of antibiotics in a Nigerian tertiary healthcare facility. *Am J Biomed Sci Engineering*, *1*(3), 25-31.

Katzung, B. G. (2017). *Basic and clinical pharmacology*. McGraw-Hill Education.

Kebede, H. K., Gesesew, H. A., Woldehaimanot, T. E., and Goro, K. K. (2017). Antimicrobial use in paediatric patients in a teaching hospital in Ethiopia. *PLoS One*, *12*(3), 1-8.

Llor, C., Bjerrum, L., Munck, A., Cots, J. M., Hernández, S., and Moragas, A. (2014). Access to point-of-care tests reduces the prescription of antibiotics among antibiotic-requesting subjects with respiratory tract infections. *Respiratory Care*, *59*(12), 1918-1923.

Mugada, V., Paruchuri, A., and Munagala, M. (2016). Drug utilization evaluation of anticancer drugs in a tertiary care teaching hospital: A descriptive observational study. *Journal of Applied Pharmaceutical Science*, *6*(10), 098-101.

Nwolisa, C. E., Erinaugha, E. U., and Ofoleta, S. I. (2006). Prescribing practices of doctors attending to under fives in a children's outpatient clinic in Owerri, Nigeria. *Journal of tropical pediatrics*, *52*(3), 197-200.

Oduyebo, O. O., Olayinka, A. T., Iregbu, K. C., Versporten, A., Goossens, H., Nwajiobi-Princewill, P. I., ... and Ogunsola, F. T. (2017). A point prevalence survey of antimicrobial prescribing in four Nigerian tertiary hospitals. *Annals of Tropical Pathology*, *8*(1), 42.

Ogunleye, O. O., Fadare, J. O., Yinka-Ogunleye, A. F., Anand Paramadhas, B. D., and Godman, B. (2019). Determinants of antibiotic prescribing among doctors in a Nigerian urban tertiary hospital. *Hospital practice*, *47*(1), 53-58.

Onubogu, U. C., and Anochie, I. C. (2014). Empiric Antibiotic prescription among febrile under-five children in the University of Port Harcourt Teaching Hospital, Rivers state, Nigeria. *Nigerian Journal of Paediatrics*, *41*(3), 234-238.

Pradeepkumar, B., Alameri, T., Narayana, G., Reddy, Y. P., and Ramaiah, J. D. (2017). Assessment of antibiotic prescribing pattern in pediatric patients: A cross-sectional hospital-based survey. *CHRISMED Journal of Health and Research*, *4*(4), 235.

Raveh, D., Levy, Y., Schlesinger, Y., Greenberg, A., Rudensky, B., and Yinnon, A. M. (2001). Longitudinal surveillance of antibiotic use in the hospital. *Qjm*, *94*(3), 141-152.

Schroder, W., Sommer, H., Gladstone, B. P., Foschi, F., Hellman, J., Evengard, B., and Tacconelli, E. (2016). Gender differences in antibiotic prescribing in the community: a systematic review and meta-analysis. *Journal of Antimicrobial Chemotherapy*, *71*(7), 1800-1806.

Skender, K., Singh, V., Stalsby-Lundborg, C., and Sharma, M. (2021). Trends and patterns of antibiotic prescribing at orthopedic inpatient departments of two private-sector hospitals in Central India: A 10-year observational study. *PloS one*, *16*(1), e0245902.

Tamuno, I., and Fadare, J. O. (2012). Drug prescription pattern in a Nigerian tertiary hospital. *Tropical Journal of Pharmaceutical Research*, *11*(1), 146-152.

Umar, L. W., Isah, A., and Shuaibu Musa, B. U. (2018). Prescribing pattern and antibiotic use for hospitalized children in a Northern Nigerian Teaching Hospital. *Annals of African medicine*, *17*(1), 26-32.

Umar, L. W., Isah, A., Musa, S., and Umar, B. (2020). Outpatient prescribing and antibiotic use for children in a tertiary hospital. *Sahel Medical Journal*, *23*(2), 109.

Umeokonkwo, C. D., Madubueze, U. C., Onah, C. K., Okedo-Alex, I. N., Adeke, A. S., Versporten, A., and Onoh, R. (2019). Point prevalence survey of antimicrobial prescription in a tertiary hospital in South East Nigeria: a call for improved antibiotic stewardship. *Journal of global antimicrobial resistance*, *17*, 291-295.

Woldu, M. A., Suleman, S., Workneh, N., and Berhane, H. (2013). Retrospective study of the pattern of antibiotic use in Hawassa University referral hospital pediatric ward, Southern Ethiopia. *Journal of Applied Pharmaceutical Science*, *3*(2), 93-98.

Xiao, Y., Zhang, J., Zheng, B., Zhao, L., Li, S., and Li, L. (2013). Changes in Chinese policies to promote the rational use of antibiotics. *PLoS medicine*, *10*(11), e1001556.