World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
Original Article

Acceptability and availability of dispersible Amoxicillin tablets in Primary Healthcare: Implications in the Pharmacotherapeutic Management of childhood Pneumonia

[1]Brambifa O. Evelyn, [2]Bunu J. Samuel and [3]Usifoh F. Stella

[1]University of Lagos Pharmaceuticals, University of Lagos, Lagos State, Nigeria
[2]Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmacy, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria
[3]Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

Received: 10-09-2020 / Revised Accepted: 25-10-2020 / Published: 25-10-2020

ABSTRACT

Amoxicillin is an effective antibiotic treatment for bacterial pneumonia among children. Pneumonia still claims many young lives because some communities do not have the right formulations for children. Across-sectional quantitative survey was designed based on the World Health Organization (WHO) recommended methods. 32 Comprehensive Primary Health Centers (CPHC) were randomly selected and the first five prescriptions of Community-Acquired Pneumonia (CAP) in children under-five years were assessed for the prescriber's choice of antibiotic, giving a sample size of 160 prescriptions. The availability of Amoxicillin Dispersible Tablet (ADT) across the health facilities pharmacies was 100%. ADT as the prescriber's choice of antibiotics for CAP was 53.13%. This was closely followed by the suspension dosage form (30.63%) and the injections route.ADT was available in CPHC of Lagos State but does not translate to good access, as it was not sufficiently prescribed.

Keywords: Amoxicillin, Antibiotics, Dispersible tablet, Healthcare, Pneumonia

INTRODUCTION

Amoxicillin belongs to the penicillin antibiotics and has long been used in the treatment of bacterial pneumonia, which is believed to account for about 80% of pneumonia deaths among children [1]. Pneumonia continues to claim many young lives because many communities have limited access to child-friendly Amoxicillin formulations [2]. Improving child health is a global health priority. The global mortality rate in children under five years remains a significant and inequitable problem [1]. Apart from childhood malnutrition [3], pneumonia is another common cause of childhood

Address for Correspondence: Samuel J. Bunu, Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmacy, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria
Email: pharmsamuelbunu@gmail.com

How to Cite this Article: Brambifa O. Evelyn, Bunu J. Samuel and Usifoh F. Stella. Acceptability and availability of dispersible Amoxicillin tablets in Primary Healthcare: Implications in the Pharmacotherapeutic Management of childhood Pneumonia. World J Pharm Sci 2020; 8(11): 67-73.

mortality [1]. While most deaths resulting from Pneumonia occur in developing countries and about three-quarters in other countries, more than half of the world's annual incident cases occur in five countries including India, China, Bangladesh, Pakistan, and Nigeria [4]. Nigeria is one of the countries with more than half of the world's annual incident cases of childhood pneumonia [5, 6]. Even though its cure is well-known, inexpensive, and widely available, pneumonia is still profound in many countries [7]. WHO recommends that children should be given medicines after an appropriate evaluation and formulated for use in pediatric populations, as the pharmacokinetics and pharmacodynamics of drugs in children differ from adults and the accurate administration of medicines to children can be challenging [8, 9]. Since 2006, several studies have been done in trying to identify essential medicines for children and optimal pediatric dosage forms, leading to the publication of the WHO Model Formulary for Children [8]. Amoxicillin is a broad-spectrum antibiotic recommended as first-line treatment for childhood pneumonia in the WHO Model List of Essential Medicines and Priority Medicines List for Children [10].

In 2015, the world began working toward a new global development agenda, setting new targets in the Sustainable Development Goals (SDGs) to end childhood mortality by 2030, preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to as low as 12 deaths per 1,000 live births and under-5 mortality to 25 deaths per 1,000 live births [6]. Notwithstanding the reduction of child mortality, there is much work to be done in achieving the MDG 4 target in many countries; which is to reduce the under-5 mortality rate by two-thirds in the period between 1990 and 2015 [11]. Ensuring the availability of essential medicines for the treatment of the major causes of disease in children would help countries reduce child mortality rates [12].Pneumonia is one of the leading causes of under-five children mortality and kills an estimate of 1.1 million children every year, more than AIDS, malaria, and tuberculosis combined [13]. In Nigeria, Pneumonia alone claims the lives of approximately 177,000 under-five children annually [14]. The 2014 guidance reclassified CAP requiring treatment at a healthcare facility into three categories: very severe, severe, and non-severe pneumonia, designed to simplify the management, reduce the number of referrals, and achieve better therapeutic outcomes [15].

Treatment of pneumonia includes home care advice and antibiotic therapy [10]. Appropriate formulations are essential in the pharmacotherapy of childhood pneumonia. Many children in local communities receive inappropriate oral formulations [16]. Dispersible tablets are uncoated or film-coated, which can be dispersed in a liquid (water, breast milk) giving a homogenous dispersion before administration [17].They are more convenient for active pharmaceutical ingredients with insufficient stability in water, cost-effective to produce, easy to dispense, and require minimal manipulation which minimizes the risk of administration errors[18]. A five-day course of oral Amoxicillin is safe and clinically effective [19, 20]. Access to medications (ATM) is having the essential medicines constantly available and affordable [21]. It is a concept that comprises distinct dimensions, influenced by various relationships among availability, accessibility, quality, affordability, and acceptability [22]. As a dimension of access to medicines, availability means the type and quantity of product needed and provided respectively [23]. One of the primary goals of the Nigerian Medicine Policy is to ensure the availability of effective, quality, and affordable medicines to all Nigerians [24, 25].In the absence of appropriate dosage forms of medicines for children, and most end-users would make do with the available medicines. This sometimes results in unexpected adverse drug reactions that would require thorough monitoring and pharmacovigilance processes [26]. As a result, the administration of a medicine to a child often involves breaking an adult tablet into smaller pieces, then crushing and adding to food or liquid, leading to inaccuracies in dosing. The accurate administration of liquid medicine to a child is not assured even if the correct dose is calculated. Hence, the need to use dispersible tablets for children.

The study was aimed to assess the availability of dispersible amoxicillin and evaluate the prescriber's choice of medicine for the treatment of Pneumonia in under-5years of age children in Primary Health Centers (PHC) in the Lagos State of Nigeria.

MATERIALS ANDMETHODS

Study Design and Sampling Technique

The study was designed as a descriptive quantitative cross-sectional survey, as recommended by WHO aimed at documenting the availability of ADT, prescribers' choice of antibiotic to treat CAP, and acceptability of ADT of children under-5years of age in CPHC, Lagos State. The population consists of all Comprehensive health centers in Lagos State. Data were collected from the PHC in Lagos State. The PHC is a grass-root management approach to providing health care services to the communities. It is meant to address the main health problems in

the community by providing preventive, curative, and rehabilitative services [27]. A simple randomized sampling technique was used to calculate the sample size. The first five prescriptions for the treatment of Pneumonia at the time of the visit to the health care facilities [32] were observed for drugs of choice by prescribers. Bringing the total number of observed prescriptions to 160.

As the treatment practices of individual providers will likely be consistent and similar among providers within the same facility, in-facility sources of variation would tend to be reduced, and after a certain point, adding prescriptions to a sample within a facility provides very little new information. The principal source of variation tended to be differences in practice between health facilities. Inclusion and exclusion criteria include under-five years' children being treated for CAP, pharmacy/dispensary of selected CPHC the first five prescriptions for under-five children being treated for Pneumonia in each selected CPHC. All children over 5 years of age being treated for community-acquired pneumonia and subsequent prescriptions after the first five in each selected canter were excluded from the study.

Study instrument and Data analysis

A questionnaire, formulated based on extant literature was used to conduct the research. Questions were ordered logically. Fill-ins and checkboxes were used mostly. The questionnaire had two sections. Section A was related to socio-demographic characteristics while section B assessed the level of knowledge of medication. To access Prescriber's choice of antibiotic along with preferred dosage forms for the treatment of Pneumonia, a data collection form 1 was formulated to assess the first five prescriptions in each selected facility for the antibiotics prescribed. It had a table with a column consisting of Amoxicillin, Erythromycin, Co-trimoxazole, Ceftriaxone, Ampicillin, Ampicillin/Cloxacillin combination, and others. Six other columns to determine the strength of antibiotics, and dosage forms [tablet, dispersible tablet, suspension, capsules, or injection] were added for ease of ticking at the time of data collection. To access the availability of ADT, a data collection form 2 was formulated in the form of a table with three columns, one for the facility, second for 'Yes' if available in CPHC dispensary/pharmacy, and the third column 'No' if not available.

The self-administered questionnaires were filled by literate respondents and with assistance from the interviewer for those that were not literate. The interviewer filled forms 1 and 2 based on observations in facilities. An outcome such as percentage availability of Amoxicillin DT, prescribers' choice for treating pneumonia in under 5years children, and demographics of children under 5 being treated for Pneumonia, was measured. Data were analyzed both manually and with SPSS version 20 spreadsheet for descriptive and inferential statistics and analyzed using the chi-square method of analysis. Ethical approval was obtained from the Ethics Committee of the University of Lagos Teaching Hospital, LUTH, with ethical No: ADM/DCST/HREC/APP/2847. Patients' informed consent was also obtained. Approval to use Primary Health care facilities was obtained from the office of the Public Officer, Lagos State, and the Permanent Secretary, Primary Health Care Board, Lagos State.

RESULTS

Outcomes of the study were mainly quantitative information in four sections; demographics, knowledge of antibiotics, availability of ADT in CPHC, and prescriber's preference for treatment of CAP. Results are presented in tables 1, &2 and figure 1 & 2. The results showed more males presenting with CAP than female children. More children aged 2-23months were treated for CAP, than 24-36months, 36-47months, and 48-59months age brackets in the survey. This shows that as children got older incidence of infection is reduced.

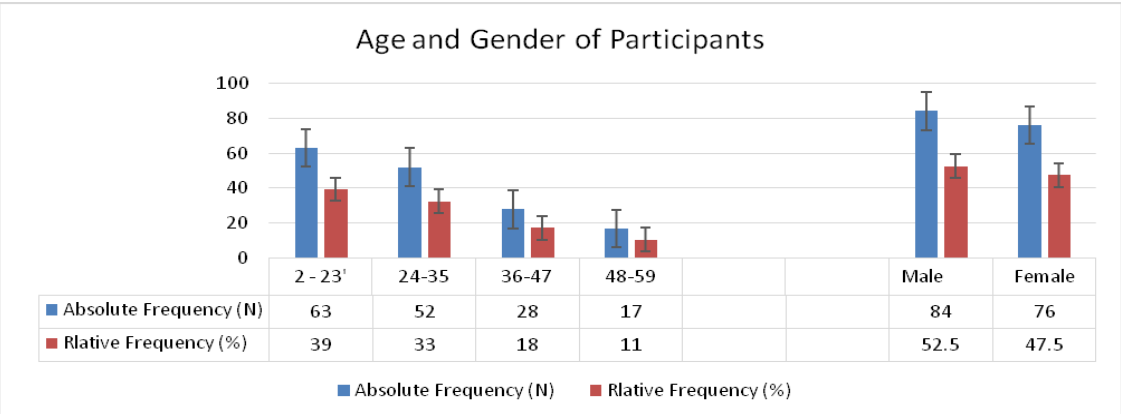

Figure 1: Age of children treated for CAP and Gender of children

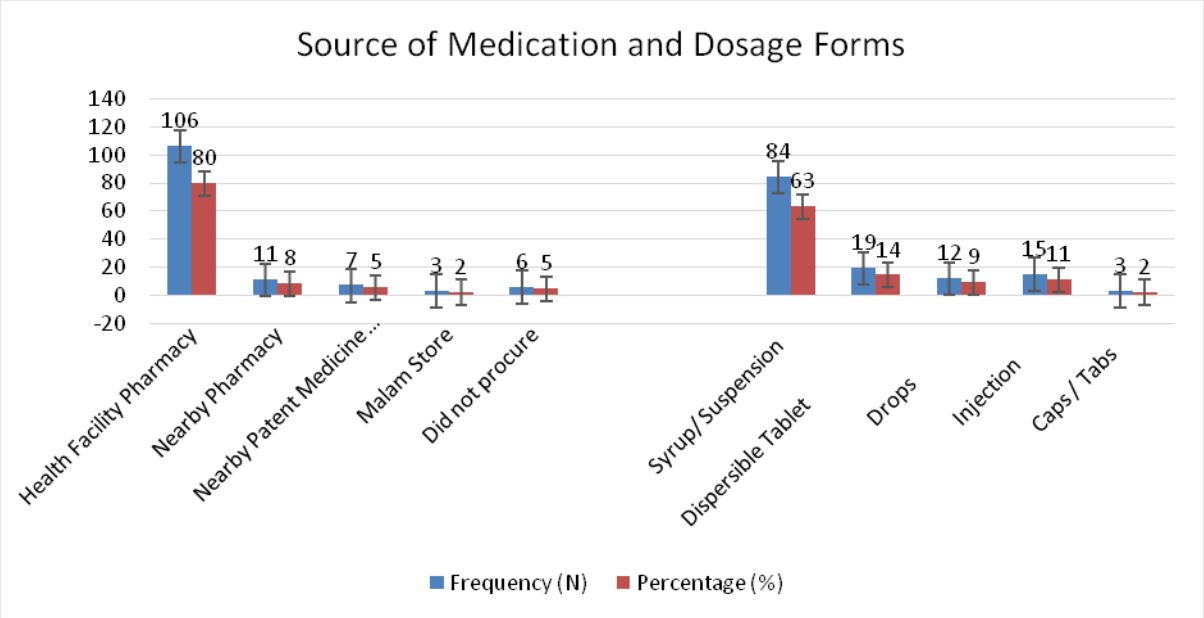

Figure 2: Sources of previously prescribed antibiotics and previous antibiotic dosage form experience by caregivers

Table 1: Data Collection Form 2: Antibiotics prescribed for Pneumonia in Under 5 children

Antibiotic	Strength	Tablet (%)	Dispersible Tablet (%)	The suspension (%)	Capsule (%)	Injection (%)
Amoxicillin	250mg	0	51	9	5	0
Amoxicillin	125mg	0	34	7	0	0
Erythromycin	250mg	4	0	8	0	0
Co-trimoxazole	480mg	0	0	9	0	0
Co-trimoxazole	240mg	1	0	0	0	0
Ceftriaxone	250mg	0	0	0	0	20
Ceftriaxone	500mg	0	0	0	0	10
Ceftriaxone	1gm	0	0	0	0	9
Ciprofloxacin	100mg	0	0	0	0	0
Ampicillin	250mg	0	0	0	0	0
Ampicillin/Cloxacillin	250mg	0	0	9	0	0
Others, Specify: Co-Amoxiclav	288mg	0	0	3	0	0
Cefuroxime	250mg	0	0	4	0	0

The total number of prescriptions surveyed was 160; however, some had more than one antibiotic for the treatment of CAP. Out of 160 prescriptions, 106 had Amoxicillin in its different strengths and dosage forms – DT, Suspension, and Capsules representing 66.25%. Out of this number, 53.13% were dispersible Amoxicillin, which is about half of all the antibiotics observed to have been prescribed for children under 5yrs being treated for CAP.

The table above shows the distribution of the antibiotic along with the dosage forms in the prescriptions observed. Some prescriptions had more than one antibiotic and more than one dosage form.

Table 2: Prescriber's choice of antibiotic for the treatment of CAP

Name / Strength of antibiotic	Frequency of occurrence in Prescriptions	Percentage %
Amoxicillin DT 250MG	51	31.87
Amoxicillin DT 125MG	34	21.25
Amoxicillin susp 250mg/5ml	9	5.63
Amoxicillin susp 125mg,5ml	7	4.38

Amoxicillin 250mg capsule	5	3.13
Erythromycin susp 250mg / 5ml	8	5.00
Erythromycin Tab 250mg	4	2.50
Co-trimoxazolesusp 480mg/5ml	9	5.63
Co-trimoxazole 240mg tab	1	0.63
Ciprofloxacin infusion 200mg/100ml	0	0
Ampicillin suspension 250mg/5ml	0	0
Ampicillin/Cloxacillin 250mg/5ml susp	9	5.63
Ceftriaxone injection 250mg	20	12.5
Ceftriaxone injection 500mg	10	6.25
Ceftriaxone injection 1gm	9	5.63

DISCUSSION

From the demographics results, a total of 52.5% of male children and 47.5% of females were involved in the survey. The highest number of children are in the age bracket of 2-23months (39%) being treated for CAP. Other age bracket includes 24-35 months (33%), 36-47 months (18%) and 48-59 months (11%), respectively (figure 1). The prevalence reducing as children grew older. This is in sync with previous work carried out where a high proportion of deaths occur (81%) in the first 2 years of life in Pneumonia patients [29]. There was an 80% availability of ADT in pharmacies of sampled Healthcare facilities. This is an excellent result; a great improvement compared with the results of work done by the Federal Ministry of Health (2006), where the population of people with access to essential medicines required for the treatment of acute and chronic sicknesses was estimated at 40% [24]. In nearby Pharmacies, there was about 8% availability of ADT, while 5%, 2%, and 5% were gotten from the patent store, roadside kiosk (Malam shop), and donations (did not procure), respectively. Syrups, suspension, and the DT were found majorly (63%) as the dosage forms for children. While drops (14%), injection (11%), and capsule/tablet (2%) were other available dosage regimens (figure 2). However, inventory in most centers was not appropriately dispensed with the aid of bin cards to show stock movement history. This lack could impede proper data collection for research work or implementation and assessment of programs/initiatives.

Prescribing patterns generally influence access to medicines especially Prescription-only medicines and stock availability. Prescriber's choice of medication along with preferred dosage forms was used to assess acceptability by prescribers. Our results showed above average (53.12%) prescriptions for CAP having ADT. Specifically, ADT 250mg had 31.87%, ADT 125mg had 21.25% among all prescriptions in the health facilities respectively, while other medications including antibiotics, were 46.88%. This shows that the dosage form has not been fully accepted (Table 2). In addressing the lack of access to good quality medicines, the WHO recommended that all countries formulate and implement a comprehensive National Drug Policy. Amoxicillin dispersible tablet is in the Essential Medicines list at some CPHC [10].

The new protocol and the availability of Amoxicillin in DT form simplify the administration and dosage of treatment. WHO recommended Amoxicillin 250 mg dispersible tablets as the most convenient formulation to treat childhood pneumonia in community settings [8].Therefore, available ADT in Pharmacies of surveyed facilities may not tally with access for children suffering from CAP as prescriptions for ADT were not so forthcoming. This agrees with the UNICEF position that some communities' settings have limited access to child-friendly formulations [2]. Also, the study is in agreement with other reports on rational and irrational use of medicines [30]. Irrational use of drugs is wasteful, expensive, and dangerous, both to the health of the patient and the population at large. The percentage of encountered prescriptions with DT was 51% Amoxicillin (250mg) & 34% Amoxicillin (125mg) and injection was 39% among others, higher than 22.8% as seen in previous work conducted by WHO [31]. However, this was not as high as the report from a similar study carried out in Northern Nigeria by *Umar et al*., where 67.7% of prescriptions were injections [32].Finally, some of the centers under study were found to prefer the injection route to the more acceptable and preferred per-oral administration for CAP, as presented in table 1. More alarming is the fact that these patients were not on admission.

CONCLUSION

Amoxicillin formulations and flexible solid oral dosage forms, such as the dispersible tablets, that can be given to older children or dispersed in water for younger children are preferred due to dosage accuracy and ease of administration. The use of dispersible tablets (DT) versus oral suspension (OS) is beneficial as it reduces the risk of dosing errors observed when administering OS. Amoxicillin 250mg Dispersible tablets can easily

replace other forms of Amoxicillin for the treatment of infections in children under 5years of age as the demand increases. Hence, its inclusion in Essential Medicine Lists by Ministries of Health. The study showed tremendous availability of ADT in the health facilities surveyed but was not sufficiently prescribed by prescribers in the health facilities. Prescribers can therefore be properly enlightened on the accuracy, safety, ease of administration, and effectiveness of the ADT and other dispersible dosage forms for its utilization in clinical practice.

REFERENCES

1. World Health Organization. Antibiotic use for community-acquired pneumonia in neonates and children: WHO evidence review ShreyMathur. Aline Fuchs, Julia Bielicki, Johannes Van Den Anker & Mike Sharland, 2018.
2. UNICEF. Supplies and Logistics. At https://www.unicef.org/supply/index_69800.html. 2018. 2018. (Accessed; 2 August, 2020).
3. Denmo O. Otele, Samuel J. Bunu, and Elisabeth Edoni. Mothers' Perception Analysis on Nutritional Health and Malnutrition among Children under 5 Years in the Niger Delta Region. Asian Journal of Research and Reports in Gastroenterology. 2020. AJRRGA.56790. 2(1): 1-9.
4. WHO. Pneumonia. http://www.who.int/mediacentre/factsheets/fs331/en/2. 016
5. Liu, I., Oza S., Hogan, D., et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *The Lancet.* 2016. 388(10063):3027-3035
6. UNICEF. Child Survival and the SDGs – UNICEF DATA. Available at: http://data.unicef.org/topic/child-survival/child-survival-sdgs/#, 2017.
7. UNICEF. Can Innovation Help Stop Children Dying From Pneumonia? http://unicefstories.org/2015/03/10/, 2015.
8. Gilson, L, Orgill, M., Shroff, Z.C. A health policy analysis reader: the politics of policy change in low- and middle-income countries. Geneva: WHO,2018; Pp152
9. Johnson WBR AA. Childhood pneumonia in developing countries. *Sfr. JResp. Med.*2013, 8[2]:4-9
10. WHO. WHO Model List of Essential Medicines for Children. http://www.who.int/medicines/publications/essentialmedicines/en/, 2015.
11. UNICEF. The State of the World's Children in 2016. A fair chance for every child. Data.unicef.org. 2016, ISBN: 978-92-806-4838-6.
12. WHO. Top 30 medicines to save mothers and children. https://www.who.int/mediacentre/news/notes/2011/mother_child_medicine_20110321/en/, 2011.
13. WHO. Library cataloging-in-publication Data. Revised WHO classification and treatment of pneumonia in children at health facilities: evidence summaries.2014.
14. World Health Organization. Revised WHO classification and treatment of childhood pneumonia at health facilities – evidence summaries. Geneva, 2015.
15. Schirm E, Hilde V, Tjalling T, et al. Lack of appropriate formulations of medicines for children in the community. *Acta pediatrician.*2004; 92. 1486-9. 10.1080/08035250310006728.
16. UNICEF. Supplies and Logistics - Dispersible Tablets**.** Available at*:* https://www.unicef.org › supply › files › Dispersible Tablets, 2014.
17. Afriyie, D., Buabeng, K.O., Danquah, C.A. Dispersible Amoxicillin tablets for children. *P Med Journal Available* at https://www.researchgate.net/publication/265293896, 2013.
18. Daousani, C., Karalis, V. Pediatric Medicines: Regulatory and Scientific Issues. *Drug research.* 2017; 67(07): 377-384
19. Mistry, P., Stirling, H., Callens, C., et al. Evaluation of patient-reported outcome measurements as a reliable tool to measure the acceptability of the taste of pediatric medicines in an inpatient pediatric population. *BMJ*. 2018; 8(7):e021961. doi: 10.1136
20. Shally Awasthi. Three day versus five-day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomized controlled trial. BMJ. 2004; Apr 3; 328(7443): 791. doi: 10.1136/bmj.38049.490255.
21. Chinwe Obuaku. Essential Medicines in Nigeria: Foregrounding Access to Affordable Essential Medicines. *African Sociological Review.*2014; *Vol18 2 2014.*
22. Venables R, Batchelor H, Hodson J. Determination of formulation factors that affect oral medicines acceptability in a domiciliary pediatric population. *Int J Pharm.*2015; 480:55–62.
23. Maryam Bigdeli, Bart Jacobs, Goran Tomson, et al. Access to medicines from a health system perspective. Health Policy Plan.2013; 28(7): 692–704. doi: 10.1093/heapol/czs108, PMCID: PMC3794462.
24. Federal Ministry of Health. Baseline Assessment of the Nigerian Pharmaceutical Sector. A publication of the Federal Ministry of Health in collaboration with the World Health Organization, DFID, and HAI. 2006.

25. Federal Ministry of Health. Essential Childhood Medicines Scale-up Plan 2012 – 2015.2012; Pp36
26. O. Miediegha & S. J. Bunu. Pharmacovigilance framework and extent of medications adverse reaction surveillance in Southern Nigeria. *World Journal of Pharmaceutical Research*. 2020; 9(6):2009-2017. DOI **:** 10.20959/wjpr20206-17727
27. David Sanders. Primary Healthcare. https://www.sciencedirect.com/topics/nursing-and-health-professions/primary-health-care, 2016.
28. World Health Organization. Indicators for monitoring National Drug Policies. A practical manual, 2nd ed. Centre de Recherche et d'Etudes pour le Développement de la Santé, CREDES, Paris, Harvard School of Public Health, Harvard University, Boston. 1999.
29. Walker CLF, Rudan I, Liu L, et al. Global Burden of childhood pneumonia and diarrhea. *Lancet*. 2013; 381 [9875]:1405-1416.
30. National Agency for Food and Drug Administration and Control. Pharmacovigilance-Post Marketing Surveillance News, 2015; 8(1). Available at: https://www.nafdac.gov.ng.
31. World Health Organization. The Rational Use of Drugs: Report of the Conference of Experts, Nairobi, 25–29 November 1985. Geneva. Available at: http://apps.who.int/medicinedocs/en/m/abstract/Js17054e/.1987.
32. Umar LW, Isah A, Musa S, et al. Prescribing Pattern and Antibiotic Use in Hospitalized Children in a Northern Nigerian Teaching Hospital. *Ann Afr Med*. 2018; 17: 26-32.