

Appraisal of Antibiotic Prescribing Profile of Patients sent for Laboratory Investigations in a Tertiary Hospital, Jos - Nigeria

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ABSTRACT:

Background: The danger associated with unguided and unmonitored prescribing of antibiotics in health institutions calls for antibiotic policies in order to avoid deviation from the standard recommended by the World Health Organization (WHO). Institutions that uphold compliance should be highly commended. This study was aimed to evaluate the prescribing pattern of antibiotics in Bingham University Teaching Hospital (BHUTH), Jos Nigeria.

Materials and Methods: Trend and adherence-check on antibiotics prescriptions in compliance with the WHO and the institutions essential drug lists (IEDL), identification of prevalent infections especially from clients sent to the laboratory for various investigations before prescriptions were reviewed from 620 Hospital cards of the General Out-Patients Department (GOPD).

Results: Gender distribution was females 343(55.3%) than males 277 (44.7%), with the majority age range of 25-34 years 227 (36.6%). From a total of 820 (single and multiple requests), stool specimen 257 (31%) was the highest, followed by urine, blood and sputum. Though, the females had higher percentage of request from the GOPD of BHUTH, but with no significant difference between the number of laboratory investigations in relation to gender at $p < 0.05$ ($p = 0.7022$). In addition, the most frequently prescribed class of antibiotics was Quinolones (51.8%). This was followed by Penicillins (21.6%), Sulfonamides (13.5%), Tetracyclins (12.2%) and Cephalosporins (0.9%) respectively from monotherapy (90.5%) and multiple therapies (9.5%). Also, there is no significant difference between the category of antibiotics prescribed and gender at $p < 0.05$ ($p = 0.6788$) in BHUTH. The most common indication for antibiotics prescribing was respiratory tract infections (26.3%). Present study indicated significant relationship between gender and common diagnoses to antibiotics prescribing at $p < 0.05$ ($p = 3.88$) in BHUTH. All (100%) prescribed antibiotics were found in both WHO and BHUTH Essential Drug Lists.

Conclusion: This study points out good compliance antibiotic prescribing practice with WHO and institutional recommended standards. It further showed that females are prescribed with antibiotics more than their male counterparts.

KEY WORD: Antibiotics, prescribing pattern; prevalent infection; Laboratory investigation; EDL adherence; BHUTH; Nigeria.

I. INTRODUCTION

Better health management could be shared via knowledge and proper information dissemination. The patterns of prescribing antibiotics in places and period has become imperative in relation to drug resistance and low adherence to current trends in health management thus, team work approach and move to break complexity in information dissemination in healthcare delivery system has become a grand challenge. Simplicity in information dissemination in global health delivery services should not be compromised¹. Antibiotics

constituted about 36% of the total drugs prescribed in this study, indicating the controlled and rational use of drugs by the hospital physicians². Antibiotic prescribing by physicians has gained due importance across the globe, mainly because of an increase in antibiotic usage, prevalence of infections, and drug resistances. This interest has turned to whether antibiotic policies can reduce the spread of resistance and even reverse current high levels³.

Predicting risks associated with the use of antibiotics that lead to resistance is the mandate of current antibiotic policy documents for any clinical settings. Antibiotic therapy for most infections irrespective of the origin should follow the guidelines in antibiotic policies⁴. The periodic auditing of antibiotic prescriptions ensures the rational use of drugs by adhering to the WHO guidelines⁵. Antibiotics are one of the pillars of modern medical care and play a major role both in the prophylaxis and treatment of infectious diseases, however, issues of their availability, selection and proper use are of critical importance to the global community⁶. Prescription of broad-spectrum antibiotics though has increased demonstrably which it may result in development of bacterial resistance; however, development of guidelines for antibiotic prescription and use of appropriate drugs for the disease can result in minimizing the unfavourable use of antibiotics in children⁷. It is extremely important that institutions and hospitals should have an antibiotic policy and ensure that choices made by individual prescribers as better physician-pharmacist relationship can promote rational antibiotics usage to a larger extent^{8,9}.

A report from a study In Nigeria by Anyanwu and Arigbe-Osula (2012), stated that 63.3% and 86.6% of prescriptions containing antibiotics, whereas the rate of antibiotic prescribing was higher for children aged 1–5 years compared to other groups combined¹⁰. Currently, Nigeria has a National Drug Policy that addresses rational prescribing, but the policy lacks scale up adoption of specific regulations on antibiotic use¹¹. Antibiotic prescribing by physicians has gained due importance across the globe, mainly because of an increase in antibiotic usage, prevalence of infections and drug resistances².

This study was aimed to evaluate the prescribing pattern of antibiotics in Bingham University Teaching Hospital (BHUTH), Jos Nigeria by way of monitoring trend and adherence-check on antibiotics prescriptions in compliance with the World Health Organization (WHO) and the Essential Medicines List of the institution.

II. MATERIAL AND METHODS

Study Design, Site and Setting

This was a retrospective cross-sectional study carried out in the General Out-Patients Department (GOPD) of the Bingham University Teaching Hospital (BHUTH), Jos, Nigeria. Bingham University Teaching hospital is a 250 Bed Facility located in Jos, North Central Nigeria. It was established as ECWA Evangel Hospital in 1959 and was the vision of SIM (then Sudan Interior Mission) missionary named Dr. Lonnie Grant to provide Health care to the Missionaries in Nigeria and also meet Health care needs of the indigenous populace¹². In 2010, ECWA, the Proprietor, converted the hospital to the Teaching Hospital of Bingham University College of Health Sciences. A Governing Board of the new Teaching Hospital inaugurated in 2011, responsible for the oversight, in accordance with the Hospital laws in Nigeria. This hospital has world class reputation in the provision of clinical services, in 1969, the first in West Africa to identify the hemorrhagic Lassa Fever Virus. Two missionary nurses died of the virus, and a third nurse, Penny Pinneo, fell ill and was flown to the USA. There the virus was isolated and named¹².

Fig 1: Google map showing study location¹³



Study population

Relevant information from a total of 620 prescription cards of clients seen in the GOPD of Bingham University Teaching Hospital Jos, Nigeria; who were sent to the various laboratory investigations outlets between July 1, 2018 - February 28, 2019.

Determination of sample size

A total of 620 prescriptions were collected for a period of 8 months (July 1, 2018 - February 28, 2019). Sample size was determined using the World Health Organization (WHO) recommendation of the minimum sample size of 600 prescriptions for drug surveys¹⁴.

Data collection and quality assurance

Prior to data collection proper, a pretest was carried out using 30 hospital cards for adequacy assessment of parameters to be determined while the collected data were checked for completeness, accuracy, and consistency at the end of each day as reported by Yimenu *et al.*,¹⁵.

Ethical consideration

Ethical approval – Reference: NHREC/21/05/2005/00610 was obtained from the Health research ethics committee of the Bingham University Teaching Hospital, Jos – Nigeria.

Statistical analysis

Data were entered into excel Ms Word and exported to SPSS version 20.0. Descriptive statistical analysis was employed while chi square was used to check relationships.

III. RESULT

Figure no 2 shows the biodata of the total population of 620 by way of age distribution and gender profile depicting females (343) and males (277).

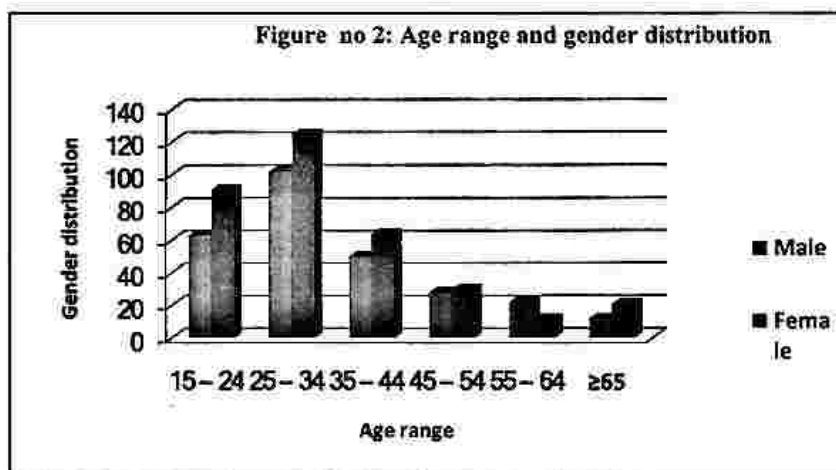


Figure no 3 shows that there was a total of 820 laboratory requests/investigations which captured single and multiple requests with stool specimen 257 (31%), urine 238 (29%), blood 136 (17%), sputum 62 (8%), vaginal swab, wound and skin scrapping 3% in each case while pus, nasal and ear swabs were also 2% in each case.

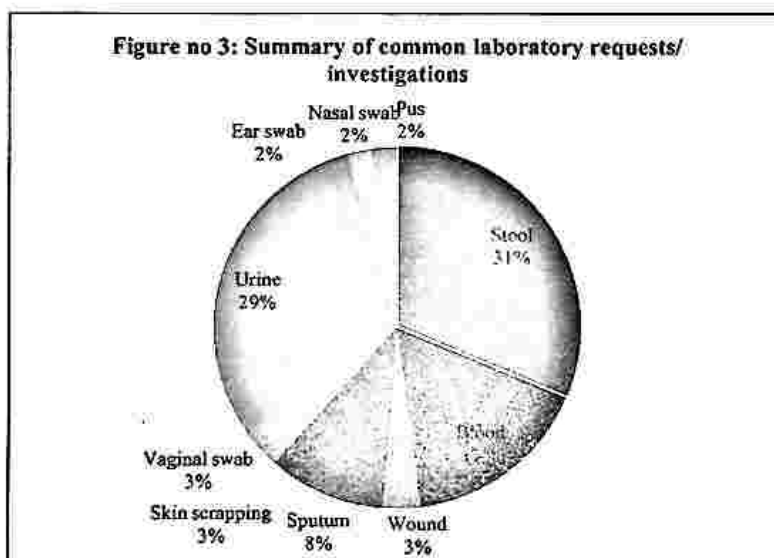


Table no 3 shows 75.6%, 12.3% and 12.1% for one, two and three requests for laboratory investigations per encounter/case respectively.

Table no 3: Frequency of laboratory investigations requested per encounter

Number of investigations per case/encounter	Frequency (%)		Total
	Female	Male	
One	343 (55.3)	277 (44.7)	620 (75.6)
Two	68 (67.3)	33 (32.7)	101 (12.3)
Three	54 (54.5)	45 (45.5)	99 (12.1)
Total	465	355	820 (100)

Figure no 4 depicts the prescribed antibiotics as Ciprofloxacin (43.9%), Amoxicillin+Clavulanate (16.1%), Metronidazole (13.5%), Doxycycline (12.2%), Levofloxacin (7.0%), Amoxicillin (5.5%), Ofloxacin (0.9%), Cephalexin (0.6%) and Cefuroxime (0.3%).

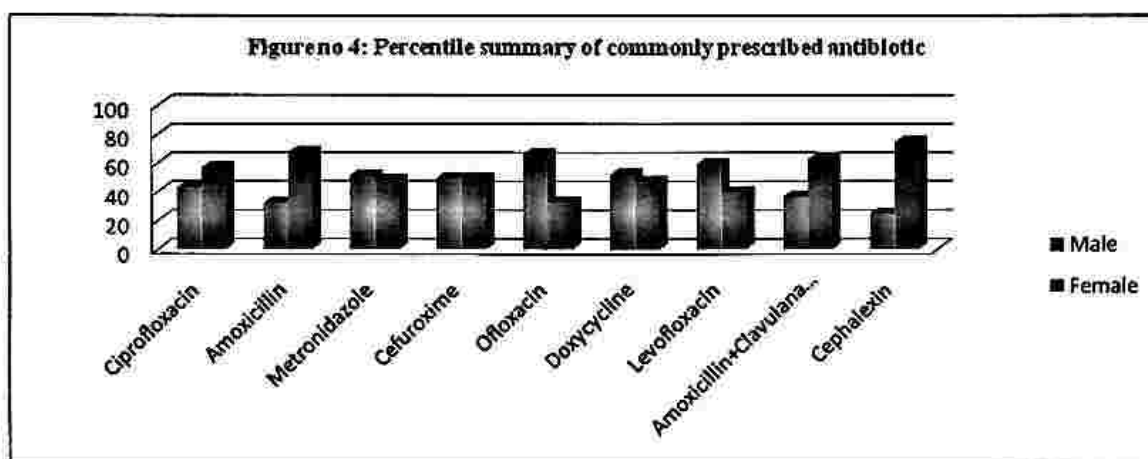


Table no 2 below illustrates the prescribed antibiotics by class as Quinolones (51.8%), Penicillins (21.6%), Sulfonamides (13.5%), Tetracyclins (12.2%) and Cephalosporins (0.9%) respectively

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Table no 2: Category/Class of antibiotics prescribed

Antibiotic category	Female (%)	Male (%)	Total (%)
Quinolones	189 (54.3)	159 (45.7)	348 (51.8)
Penicillins	93 (64.1)	52 (35.9)	145 (21.6)
Sulfonamides	44 (48.3)	47 (51.7)	91 (13.5)
Cephalosporins	04 (66.7)	02 (33.3)	06 (0.9)
Tetracyclins	39 (47.6)	43 (52.4)	82 (12.2)
Total	369	303	672

Table no 3 illustrates single, double and triple antibiotic therapy per encounter as 90.5%, 9.5% and 1.8% per encounter respectively.

Table no 3: Frequency of antibiotics prescribed per encounter

Number of prescribed drugs per case/encounter	Frequency (%)		Total
	Female	Male	
One (Monotherapy)	330 (54.3)	278 (45.7)	608 (90.5)
Two (Combination)	33 (63.5)	19 (36.5)	52 (7.7)
Three (Combination)	11 (91.7)	01 (8.3)	12 (1.8)
Total	374	298	672 (100)

Table no 4 shows STD (15.2%), GITI (24.4%), LRTI (13.0%), (UTI) 16.1%, (URTI) 13.3%, (SSTI) 8.9% and (Others) 6.1% respectively from 652 diagnoses for frequently prescribed antibiotics in BHUTH.

Table no 4: Summary of common diagnosis for frequently prescribed antibiotics

Diagnosis	Frequency (%)		Total (%)
	Female	Male	
STD	54 (55.0)	45 (45.0)	99 (15.2)
GITI	89 (56.0)	70 (44.0)	159 (24.4)
LRTI	43 (50.6)	42 (49.4)	85 (13.0)
UTI	59 (56.2)	46 (43.8)	105 (16.1)
URTI	52 (49.1)	54 (50.9)	106 (16.3)
SSTI	34 (58.6)	24 (41.4)	58 (8.9)
Others	26 (65)	14 (35)	40 (6.1)
Total	357	295	652 (100)

Key: STD = Sexually Transmitted Disease, GITI = Gastro Intestinal Tract Infection, LRTI = Lower Respiratory Tract Infection, UTI = Urinary Tract Infection, URTI = Upper Respiratory Tract Infection, SSTI = Skin and Soft Tissue Infection.

Table no 5 illustrates all (100%) the prescribed the antibiotics in this study are found in both the National/WHO and the BHUTH essential drugs lists.

Table no 5: Overview of antibiotics prescribing in relation to Essential Medicine List

Prescribed Antibiotics	WHO/ National Essential Drug List	BHUTH Essential Drug List
Ciprofloxacin	Present	Present
Amoxicillin	Present	Present
Metronidazole	Present	Present
Cefuroxime	Present	Present
Ofloxacin	Absent	Absent
Doxycycline	Present	Present
Levofloxacin	Absent	Absent
Amoxicillin+Clavulanate (Augmentin)	Present	Present
Cephalexin	Present	Present

IV. DISCUSSION

Demographic distribution

Our study showed that there were more females 343(55.3%) than males 277 (44.7%) from the prescription population reviewed. Considering the age range of the total population of 620 studied, the majority was 25-34 years 227 (36.6%), followed by 15-24 years 154 (24.8%) while the least was ≥ 65 33 (5.3%) also with the feminine gender appearing more in all the age distribution except 55-64 years and almost at par in the 35-45 years with the masculine gender – *Table no 1* and *Figure no 2*. This result is in consistence with Bertakis *et al.*, (2000) who reported that women had a significantly higher mean number of visits to their primary care clinic and diagnostic services than men¹⁶.

Common laboratory requests/investigations

From a total of 820 laboratory requests/investigations which captured single and multiple requests as observed from the 620 prescriptions, stool specimen 257 (31%) was the most requested for investigation, followed by urine, blood and sputum with 238(29%), 136 (17%) and 62 (8%) respectively. Vaginal swab, wound and skin scrapping were 3% in each case while pus, nasal and ear swabs were also 2% in each case – *Figure no 3*.

Figure no 3, further show 75.6%, 12.3% and 12.1% for one, two and three requests for laboratory investigations per encounter/case respectively, though, the females had higher percentage of request from the GOPD of BHUTH, however, there is no significant difference between the number of laboratory investigations in relation to gender at $p < 0.05$ ($p = 0.7022$).

Commonly prescribed antibiotics

In this study, the profile of antibiotics prescription was found to be Ciprofloxacin (43.9%), Amoxicillin+Clavulanate (16.1%), Metronidazole (13.5%), Doxycycline (12.2%), Levofloxacin (7.0%), Amoxicillin (5.5%), Ofloxacin (0.9%), Cephalexin (0.6%) and Cefuroxime (0.3%). From the nine commonly prescribed antibiotics in BHUTH, female had the higher percentage in four - Ciprofloxacin (56.9%), Amoxicillin (67.6%), Amoxicillin+Clavulanate (63.0%) and Cephalexin (75.0%), it was higher in another four for the male - Metronidazole (51.7%), Doxycycline (52.4%), Ofloxacin (66.7%) and Levofloxacin (59.6%) while it was 50% prescription for both gender for Cefuroxime – *Figure no 4*.

In addition, the most frequently prescribed category of antibiotics in BHUTH was Quinolones (51.8%). This was followed by Penicillins (21.6%), Sulfonamides (13.5%), Tetracyclines (12.2%) and Cephalosporines (0.9%) respectively – *Table 2*. The result from this study was also in consistence with the study conducted by Biswas *et al.*,¹⁷ who reported that Quinolones were prescribed highest in Jessore city (28.33%) and lowest in Keshabpur (6%). However, there is no significant difference between the category of antibiotics prescribed and gender at $p < 0.05$ ($p = 0.6788$) in BHUTH.

The most popular quinolones are fluoroquinolones. This however includes ciprofloxacin, lomefloxacin, norfloxacin, ofloxacin, moxifloxacin and levofloxacin. According to our study, ciprofloxacin (43.9%) was the most prescribed, with gender representation as Female (56.9%) and male (43.1%). This further buttressed higher percentage antibiotics prescription to females in BHUTH – *Figure no 4*. Powers *et al.*,¹⁸ Roberts¹⁹ and Pavliv and Booker²⁰ reported that quinolones are broad spectrum antibiotics, which means they are effective against a wide range of diseases caused by bacteria and that they were approved by the FDA to treat conditions including lower respiratory tract infections, skin infections and urinary tract infections as well as inflammation of the prostate, sinusitis, and gonorrhoea with some types of fluoroquinolones also with the following potentially dangerous side effects as arrhythmia, tendon rupture, changes in blood sugar levels, neuropathy, central nervous system problems.

It is very imperative to note that extra care should be taken when prescribing quinolones in order to avoid drug-drug interactions and adverse drug reactions especially with diabetic patients already placed on oral hypoglycemic agents and those taking corticosteroids. Many studies have implicated that the antibiotics are among the major group of drugs, which cause adverse drug reactions (ADRs)²¹.

Frequency of antibiotics prescribed per encounter

One or more antibiotics were observed to be prescribed at different encounters in this study. In other words, drug combination by way of double and triple therapies were recorded in addition to single therapy per encounter which showed a significant relationship between antibiotics prescribed and gender at $p < 0.05$ in BHUTH. *Table 3* illustrates single (Monotherapy) antibiotic therapy as 90.5% while multiple therapies were 9.5% of which 7.7% and 1.8% for double and triple antibiotics therapy per encounter respectively. This implied that antibiotics prescribing in BHUTH was mostly (90.5%) by way of monotherapy.

Documented Diagnoses

Our study depicts 652 diagnoses with STD (15.2%), GITI (24.4%), LRTI (13.0%), (UTI) 16.1%, (URTI) 13.3%, (SSTI) 8.9% and (Others) 6.1% respectively. The females continued to have the higher percentage for all the diagnosed infection except for upper respiratory tract infection (URTI) with 54 (50.9%) male and 52 (49.1%) female in BHUTH – *Table no 4*. Furthermore, our study showed that there is a significant relationship between gender and common diagnoses to antibiotics prescribing at $p < 0.05$ ($p = 3.88$) in BHUTH. The most common indications for antibiotics prescribing in BHUTH according to our study were respiratory tract infections (26.3%) that make up the URTI and LRTI – *Table no 4*. This was followed by gastrointestinal tract infection (GITI-24.4%). The present result is in tandem with the findings of Worku and Tewahido²² and Dawit *et al.*²³ who reported urinary tract (24.5%) and (36%) respectively as well as that of the ECDPC (2014) and Carl Llor and Lars Bjerrum, which stated that 80 – 90% of the antibiotics used in medicine are prescribed respiratory tract infections^{24 - 25}. Same report by Dawit *et al.*, also in accordant with our study with gastrointestinal tract infection (27.5%) as second highest indication.

Prescribing from National Essential Drugs List

This study points out good prescribing practice as it was observed that there was a 100 percent compliance antibiotic prescribing from both the National/WHO as well as the BHUTH essential drugs lists - *Table no 5*. This could be due to a strict follow-up by the hospital management and/or it could be due to the pharmaceutical procurement policy of the country, which is based on the Essential Drugs List of the country and this limits prescribers not to prescribe drugs out of the list because only drugs from the Essential Drugs List are available in the health care facility as reported by¹⁵.

V. CONCLUSION

This study reveals an effective compliance antibiotic prescribing practice when the WHO and institutional recommended standards were compared. This study further showed that females are getting more detailed laboratory investigations and prescription with antibiotics more than their male counterparts.

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REFERENCES

- [1]. Ogundeko TO *et al.*, Readability of drugs and chemicals package inserts information: A survey of the Nigerian market. *Wjpls*. 2018; (4) 5.
- [2]. Remesh A, Samna Salim AM, Gayathri UN, Retnavally KG: Antibiotics prescribing pattern in the inpatient departments of a tertiary care hospital. *Pharma Pract* 2013, 4: 71-76. 10.4103/2045-080X.112987.
- [3]. Marc J Struelens, Baudouin Byl, Jean-Louis Vincent. Antibiotic policy: a tool for controlling resistance of hospital pathogens. (1999). DOI:<https://doi.org/10.1111/j.1469-0691.1999.tb00720.x>
- [4]. Chambers HF. General Principles of antimicrobial therapy. In: Brunton LL, Lazo JS, Parker KL, editors. *Goodman and Gillman's The pharmacological basis of therapeutics*. 11th ed. New York: McGraw-Hill Press. 2006; 1095-110.
- [5]. Alanis JA. Resistance to Antibiotics: Are We in the Post-Antibiotic Era? *Arch Med Res* 2005; 36:697-705.
- [6]. Tripathi KD. *Essentials of Medical Pharmacology*. 5th New Delhi: Jaypee Brothers Medical Publishers (Pvt) Ltd. 2008; 09:627-9.
- [7]. Sayeri Dutta, Abhishek Bhattacharjee, N. Meena Devi: Prescription pattern of antibiotics in paediatric inpatients at a tertiary care hospital in North East India. 2017; 6:10.
- [8]. Shankar RP, Partha P, Shenoy NK, Easow JM, Brahmadathan KN. Prescribing patterns of antibiotics and sensitivity patterns of common microorganisms in the Internal Medicine ward of a teaching hospital in Western Nepal: A prospective study. *Ann Clin Microbiol Antimicrob*. 2003; 2:7.
- [9]. Kardas P, Pechere JC, Hughes DA, Cornaglia G. A global survey of antibiotic leftovers in the outpatient setting. *Int J Antimicrob Agents*. 2007; 30:530-6.
- [10]. Cizman M. The use and resistance to antibiotics in the community. *Int J Antimicrobial Agents*. 2003; 21:297-307.
- [11]. Federal Ministry of Health Nigeria, World Health Organisation. National Drug Policy; 2005. Available from: <http://www.health.gov.ng/doc/DrugPolicy.pdf>. [Last accessed on 2017 Jun 20].
- [12]. www.bhuth.org.ng

Appraisal of Antibiotic Prescribing Profile of Patients sent for Laboratory ..

- [13]. <http://www.google.com/map/place/Bingham+University+Teaching+Hospital@9.9302293,8.8779792,15z>-13
- [14]. WHO: How to investigate drug use in health facilities: selected drug use indicators. 1993; Geneva: WHO/DAP/93.1.
- [15]. Yimenu DK, Emam A, Elemineh E, Atalay W. Assessment of Antibiotic Prescribing Patterns at Outpatient Pharmacy Using World Health Organization Prescribing Indicators. *Journal of Primary Care & Community Health*. 2019. doi:10.1177/2150132719886942.
- [16]. Bertakis KD, Azari R, Helms LJ, Callahan, Robbins JA. Gender differences in the utilization of health care services. *J FamPract*. 2000 Feb; 49(2):147-52.
- [17]. Biswas, M., Roy, D.N., Tajmin, A. et al. Prescription antibiotics for outpatients in Bangladesh: a cross-sectional health survey conducted in three cities. *Ann ClinMicrobiolAntimicrob*.2014;13:15. <https://doi.org/10.1186/1476-0711-13-15>.
- [18]. Powers JH, Phoenix JA, Zuckerman DM. Antibiotic uses and challenges-A comprehensive review from NRCWF. *Medscape Family Medicine*. June 2010. Retrieved from: <http://www.medscape.com/viewarticle/723457>.
- [19]. Roberts, JR. Adverse reactions to fluoroquinolones. *Emergency Medicine News*. Oct 2008;30(10):16-18.
- [20]. Pavliv Danielle and Booker Nydera. Some Antibiotics are Riskier than Others: What You Should Know about Quinolones. National Center for Health Research. 1001 Connecticut Avenue NW, Suite 1100 Washington, DC 20036. 2020.
- [21]. Padmaja U, Adhikari P, Pereira P: A Prospective Analysis of Adverse Drug reactions in a South Indian hospital. *Online J Health Allied Sci*. 2009; 8: 12.
- [22]. Worku F, Tewahido D. Retrospective assessment of antibiotics prescribing at public primary healthcare facilities in Addis Ababa, Ethiopia. *InterdiscipPerspect Infect Dis*. 2018;2018:4323769. doi:10.1155/2018/4323769 [PMC free article] [PubMed] [CrossRef] [Google Scholar].
- [23]. Dawit Kumilachew Yimenu,Abdurazak Emam, Endilik Elemineh, and WagayeAtalay: Assessment of antibiotic prescribing patterns at outpatient pharmacy using world health organization prescribing indicators *J Prim Care Community Health*. 2019 Jan-Dec; 10: 2150132719886942. doi: 10.1177/2150132719886942.
- [24]. European Centre for Disease Prevention and Control (ECDPC). (2014) Key messages for primary care prescribers. Available at:<http://ecdc.europa.eu/en/eaad/antibiotics/pages/messagesforprescribers.aspx>.
- [25]. Carl Llor and Lars Bjerrum. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther Adv Drug Saf*. 2014 Dec; 5(6): 229-241.

Ogundeko T.O, et. al. "Appraisal of Antibiotic Prescribing Profile of Patients sent for Laboratory Investigations in a Tertiary Hospital, Jos - Nigeria." *IOSR Journal of Pharmacy (IOSRPHR)*. 10(11), 2020, pp. 23-30.