KNOWLEDGE, ATTITUDES AND PRACTICES OF ANTIBIOTICS PRESCRIPTION AMONG RESIDENT DOCTORS IN AHMADU BELLO UNIVERSITY TEACHING HOSPITAL (ABUTH) ZARIA, NIGERIA

BY

POPOOLA-ZAKARIYYA BASHIR

DEPARTMENT OF PHARMACOLOGY AND THERAPEUTICS
FACULTY OF PHARMACEUTICAL SCIENCE
AHMADU BELLO UNIVERSITY
ZARIA, NIGERIA

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A THESIS SUBMITTED TO THE SCHOOL OF POSTGRADUATE STUDIES AHMADU BELLO UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTER OF SCIENCE IN PHARMACOLOGY

DEPARTMENT OF PHARMACOLOGY AND THERAPEUTICS,
FACULTY OF PHARMACEUTICAL SCIENCE,
AHMADU BELLO UNIVERSITY,
ZARIA, NIGERIA

APRIL, 2012

DECLARATION

I hereby declare the originality of this work carried out by me Dr Popoola-Zakariyya Bashir in the Department of Pharmacology and Therapeutics, faculty of pharmaceutical science, Ahmadu Bello University, Zaria. Under the supervision of Prof. Ibrahim Abdu-Aguye and Prof. (Mrs.) Helen Ochuko Kwanashie, in partial fulfillment of the requirement for the award of M.sc degree in pharmacology and therapeutics. The work of other investigators referred to in this study is duly acknowledged. No part of this study has been previously submitted for a degree or diploma.

_____ _____

Popoola-Zakariyya, Bashir Date

CERTIFICATION

This thesis entitled "**KNOWLEDGE, ATTITUDES AND PRACTICES OF ANTIBIOTICS PRESCRIPTION AMONG RESIDENT DOCTORS IN AHMADU BELLO UNIVERSITY TEACHING HOSPITAL (ABUTH) ZARIA, NIGERIA"** by Popoola-Zakariyya, Bashir meets the regulations governing the award of the degree of Master of Science of Ahmadu Bello University, Zaria, and is approved for its contribution to scientific knowledge and literary presentation.

_____ _____

Prof. Ibrahim Abdu-Aguye — Date
MBBS (Ibadan), M.Sc Pharm (ABU), FMCP,
Professor of Pharmacology,
(Chairman, Supervisory Committee)
Department of Pharmacology and Therapeutic
Ahmadu Bello University, Zaria

_____ _____

Prof. (Mrs.) Helen O. Kwanashie — Date
B.Sc., M.Sc Biochem (Ibadan), PhD Pharm (ABU),
Professor of Pharmacology,
(Member, Supervisory Committee)
Department of Pharmacology and Therapeutic
Ahmadu Bello University, Zaria

_____ _____

Dr N.M. Danjuma — Date
PhD (ABU)
Head, Department of Pharmacology and Therapeutic
Ahmadu Bello University, Zaria

_____ _____

Prof. J. Adebayo, BA., MA., PhD (ABU) — Date
Dean, Postgraduate School,
Ahmadu Bello University, Zaria

DEDICATION

This thesis is dedicated to my late father Alhaji Popoola Oyewole Zakariyya, for the principles that guided his life, and fostering my education till he passed on. To my mother Hajiya Rukayya Zakariyya, for her unconditional support, understanding and prayers in the face of adversity and hardship.

To my wife Mrs Ganiyat Ibrahim Zakariyya and children Habibah and Fauziyya Bashir Zakariyya and to everybody that gave me support in the course of the work, to you all I say thank you.

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ABSTRACT

Background: Assessment of the knowledge, attitudes and practice of resident doctors and medical officers in ABUTH Zaria, on antibiotics prescription in order to develop interventions to improve antimicrobial resistance.

Methods: A total of 309 respondents was surveyed using a 30 stem questionnaire which was distributed to residents doctors and medical officers in ABUTH Zaria,

Results: A total of 251 (81.3%) responded to the survey from 17 different departments which was grouped into six specialties, only 106 (42.2%) of the respondents indicated they had worked in infectious disease unit (IDU), 212 (84.5%) acknowledged they were aware of rational drug use (RDU), while 233 (92.8%) indicated they were aware of national drug formulary (NDF), of those who knew about NDF, only 101 (40.2%) routinely use NDF to aid their prescription.

Majority 200 (79.7%) of the respondents do not know the hospital antimicrobial susceptibility pattern. Even though 204 (98.8%) of the respondents indicated they had prescribed antibiotics in the past six months, 123 (49.2%) admitted prescribing greater than five antibiotics in the past seven days pre survey. Many 161 (64.7%) of the respondents believed it is the responsibility of the doctors to explain to patients how to take the antibiotics prescribed, this show a significant relationship between designations of respondents, (χ^2, p=0.038). Majority 232 (92.8%) of the respondents acknowledged antibiotics resistance as a national problem, 213 (85.2%) indicated it as a problem in their clinical practice, while 197 (79.1%) believe it is a problem in the hospital. The knowledge that antibiotics resistance is a problem in the hospital is influenced by the level of residency training, which shows a significant relationship (χ^2, p=0.003). Only 32

(13.6%) and 26 (10.4%) of respondents have the knowledge of WHO prevalence of inappropriate antibiotics use and Methicillin resistance *Staphylococcus aureus* (MRSA), a significant relationship was found with respect to level of training (designation) of respondents, (χ^2, p=0.035). Four factors were considered as potential cause of antibiotics resistance, too low dose of antibiotics prescription, too many broad spectrum of antibiotics prescription, too long duration of antibiotics. A significant relationship (χ^2, p=0.022) was found between respondents designation and their perception of long duration of antibiotics usage as an important cause of antibiotics resistance. Respondents indicate educational session on prescription and availability of local or national guideline as most helpful in improving antibiotics prescription. Speaking to pharmaceutical representative and restriction of prescription of all antibiotics were considered as unhelpful in improving antibiotics prescription.

Conclusions: This study revealed the respondents have some knowledge on some of the important causes of resistance to antibiotics, that the hospital do not have an antibiogram for antibiotics sensitivity, and that a formal education on antibiotics prescription is required. These data provides helpful information for the design of strategies to optimize adherence to good antibiotics prescription.

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LIST OF ABBREVIATIONS

A.B.U	-	Ahmadu Bello University
ABUTH	-	Ahmadu Bello University Teaching Hospital
AMA	-	American medical association
ASM	-	American society for microbiology
APHA	-	American public health association
ACCoT	-	A=ampicillin, C=chloramphenicol, Co=co-trimoxazole, T=tetracycline
CDC	-	Center for disease control
EDL	-	Essential drug list
ENT	-	Ear, nose and throat
FDA	-	Food and drug administration
F.M.O.H	-	Federal Ministry of health
GDP -	-	Gross domestic product
ICU	-	Intensive care unit
INRUD	-	International network for the rational use of drugs
IDU	-	Infectious disease unit
MDR-TB	-	Multidrug-resistant tuberculosis
MRSA	-	Methicillin resistance *staphylococcus aureus*
NHIS	-	National health insurance scheme
NDF	-	National drug formulary
NHIS	-	National health insurance scheme
NNIS	-	National nosocomial infection surveillance
NIH	-	National institutes of health

NAFDAC	-	National agency for food and drug administration and control
ORS	-	Oral rehydration therapy
PBP	-	Penicillin–binding proteins
PHC	-	Primary health care
RUD	-	Rational use of drug
UV	-	Ultraviolet
URTI	-	Upper respiratory tract infection
WHO	-	World Health Organization
WHA	-	World health assembly

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

According to World Health Organization (WHO), a drug is any substance that, when absorbed into the body of a living organism, alters normal bodily function (WHO, 1969). In pharmacology, a drug is a chemical substance used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being.

Drugs are expensive, making up a large portion of health care cost; hence optimal or rational use is necessary. According to Otoom *et al*. (2002), in Jordan, expenses on drugs account for 2% of gross domestic product (GDP) while the actual amount spent by Nigerians is unknown, most of the drug expenses are borne by patients out of their pockets. It is imperative to optimize benefit from expenditure on drugs purchased by selecting an Essential Drug List and promoting rational use of drugs (RDU) (Sanbo *et al*., 2004). Essential drugs are drugs that fulfill the real needs of the majority of the population in diagnostic, prophylactic, therapeutic and rehabilitative services using criteria of risk benefit ratio, cost effectiveness quality, practical administration, patients' compliance and acceptance (WHO, 1993).

WHO defined rational use of drug as: the correct, proper and appropriate use of medicines. This translate that patients receives the appropriate medicine in the proper dose, for an adequate period of time, and at the lowest cost to them and their community (WHO, 2010).

The definition implies that rational use of drugs, especially rational prescribing should meet the following criteria:

I. Appropriate indication: the decision to prescribe drug(s) is entirely based on medical rationale that drug therapy is an effective and safe treatment.

II. Appropriate drug: the selection of drugs is based on efficacy, safety, suitability and cost considerations.

III. Appropriate patient: no contraindications exist and the likelihood of adverse reactions is minimal, and the drug is acceptable to the patient. \

IV. Appropriate information: patients should be provided with relevant, accurate, important and clear information regarding his or her condition and the medications that are prescribed.

V. Appropriate monitoring: the anticipated and unexpected effects of medications should be appropriately monitored.

Irrational use of medicines is a major problem worldwide. The overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards. Examples of irrational use of medicines include: use of too many medicines per patient (poly-pharmacy); inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections; over-use of injections when oral formulations would be more appropriate; failure to prescribe in accordance with clinical guidelines; inappropriate self-medication, often of prescription-only medicines; non-adherence to dosing regimens (Holloway, 2005).

Another WHO paper for the World Health Assembly (WHA) says that irrational medicines use includes use of more medicines than are clinically necessary, inappropriate use of anti-microbial agents for non-bacterial infections (Holloway, 2005).

Drug use is a complex subject involving the prescriber, the patient, and pharmaceutical institution. It is influenced by complex interaction of factors such as drug availability, prescribers' experience, and promotional activities of the pharmaceutical industries, cultural factors and communication system (WHO, 1985).

According to Holloway (2005), irrational drug use causes rise of anti-microbial resistance which shows increasing trend worldwide, leading to adverse health consequences. WHO reports that countries have done little to promote rational use of medicines and this has now become a very serious global public health problem, with serious health and economic implications. Worldwide, more than 50% of all medicines are prescribed, dispensed or sold inappropriately, and 50% of patients fail to take them correctly (Holloway, 2005). Only two thirds of the world's population have regular access to medicines, and of the people who do receive medicines, more than half of those people are prescribed medicines incorrectly and of the people that are prescribed medicines, more than half of those people fail to take them correctly, (Holloway, 2005).

Arithmetically, that would mean that less than a quarter of medicines prescribed are used appropriately. Data on trends in medicines use showed that the average number of drugs used increased from 2.2 to 2.7 per patient between 1990 and 2003. Only 40-50% of patients were treated in compliance with standard treatment guidelines (Holloway 2005). The standard treatment guideline is an important tool for the attainment of comprehensive

and effective health care delivery services thereby achieving the goals of the national drug policy, which inter alia are: the availability of safe, efficacious and affordable medicines to satisfy the healthcare needs of the majority of the population and ensure the rational use of drugs.

Holloway (2005), gave some data on the adverse consequences of irrational drug use:

a) Between 2.3 to 4.7 million new cases of hepatitis B and C and 160,000 new cases of HIV per year, resulting from 15 billion injections per year, half of which are non-sterile.
b) Between 4% to 10% of hospital in-patients suffer an adverse drug reaction in developed countries. This is the fourth to sixth leading cause of death in the US and costs $130 billion in the US and £466 million in the UK yearly.
c) There is increasing anti-microbial resistance, with resistance of up to 70-90% to original first-line antibiotics for dysentery (*shigella*), pneumonia (*pneumococcal*), gonorrhoea (*neisseria gonorrhoeae*), and hospital infections (*Staph. aureus*).

Holloway (2005) said very little is being spent to promote rational use of medicines. The global sales of prescription drugs in 2000 were $282.5 billion and drug promotion costs in the US were $15.7 billion the same year. In 2002-03, global WHO expenditure was $2.3 billion, of which the WHO expenditure on promoting rational drug use was only 0.2%. According to Holloway *et al*., (2005), there was inadequate implementation of rational medicines use in countries, with only 26% of countries having a national strategy and only 50% of countries having public education in the past years. Irrational drug use is a very serious global public health problem and much more policy implementation is needed at national level. Rational use could be greatly improved if a fraction of the

resources spent on medicines were spent on improving its use. Major cause of irrational medicines use in developing countries was the unethical promotion of drugs by drug companies, which practiced double standards in marketing and labeling (in developed and developing countries) and gave incentives to doctors to induce them to use more medicines.

Large portion of antibiotics produced were sold as inputs in animal feed to fatten the animals, and as there was little control of this in developing countries, this had contributed to resistance of the bacteria and viruses in the animals which were then passed on to resistance in microbes that affect humans (Hogerzeil *et al*., 1993). Anti-microbial resistance is one of the world's most serious public health problems (WHO, 2005). Many of the microbes that cause infectious disease no longer respond to common anti-microbial drugs such as antibiotics, antiviral and antiprotozoal drugs. The problem is so serious that unless concerted action is taken worldwide, we run the risk of returning to the pre-antibiotic era when many more children than now died of infectious diseases and major surgery was impossible due to the risk of infection. WHO country data (2002-03) showed the following anti-microbial resistance global prevalence rates: malaria (chloroquine resistance in 81 out of 92 countries); tuberculosis (0-17% primary multi-drug resistance); HIV/AIDS (0-25% primary resistance to at least one antiretroviral drug); gonorrhoea (5-98% penicillin resistance); pneumonia and bacterial meningitis (0-70% penicillin resistance in streptococcus pneumonia); diarrhoea: shigellosis (10-90% ampicillin resistance, 5-95% cotrimoxazole resistance); hospital infections (0-70% resistance of staphylococcus aureus to all penicillins and cephalosporins) WHO (2005).

The extensive misuse of anti-microbial agents leads to bacterial pathogens becoming resistant, thereby rendering treatment ineffective. The rapid and alarming spread of anti-microbial resistance around the world has not been matched by a concerted and powerful public health response. Moreover, few new antibiotics are being developed to replace those rendered ineffective through resistance. The WHO paper lists measures that governments can take WHO (2005), one of the interventions suggested relate to drug sales promotion. Pharmaceutical promotion has been shown to often have negative effects on prescribing and consumer choice, but regulation of promotional activities has been proven to be one of the few effective interventions. Countries are therefore advised to consider regulating and monitoring the quality of drug advertising and the pharmaceutical industries promotional practices, and enforcing sanctions for violations.

WHO advocates 11 key interventions to promote more rational use:

I. Establishment of a multidisciplinary national body to coordinate policies on medicine use.
II. Use of clinical guidelines.
III. Development and use of national essential medicines list.
IV. Establishment of drug and therapeutics committees in districts and hospitals.
V. Inclusion of problem-based pharmacotherapy training in undergraduate curricula.
VI. Continuing in-service medical education as a licensure requirement.
VII. Supervision, audit and feedback.
VIII. Use of independent information on medicines.
IX. Public education about medicines.
X. Avoidance of perverse financial incentives.
XI. Use of appropriate and enforced regulation.

According to Center for Disease Control (CDC) (2009), it is estimated that roughly 50% of antibiotics are unnecessarily prescribed in both inpatient and office settings. This is especially true for upper respiratory tract infections (URIs) like cough and cold illness, most of which are caused by viruses. Prescribing antibiotics for viral URIs is the most common misuse of these drugs (CDC 2009). These infections will resolve on their own without antibiotics. In children, antibiotics are the most common cause of emergency department visits for adverse drug events. Children may have up to nine colds each year. Four out of 10 children who present to an outpatient provider with the common cold receive an antibiotic (CDC 2009), even though antibiotics are never indicated for a common cold, clinicians cite lack of time, perceived patient expectations, and diagnostic uncertainty as reasons that antibiotics may be prescribed when not needed. For example, prescribing an antibiotic can be quicker than taking the time to counsel a patient on appropriate use and about why antibiotics are not needed for viral illnesses. In addition, physicians are trained to be wary of missing serious treatable diseases and may prescribe an antibiotic when uncertain of the diagnosis because they are concerned about liability. In inpatient settings, clinicians often point to pneumonia and urinary tract infections as being important areas needing improvement with respect to antibiotic use. Antibiotics are sometimes given when they are not needed to patients with syndromes that might look like pneumonia or in patients with indwelling urinary catheters who have bacteria in the urine but no evidence of infections. Another important area for improvement in inpatient settings is unnecessary duplication of therapy. For example, clinicians will sometimes prescribe two intravenous agents to treat a suspected anaerobic infection, when this is almost never necessary.

To ensure valid, consistent and reliable identification of drug use problems, WHO has developed a set of standardized indicators, these indicators have been tested successfully in 12 developing countries including Nigeria by Hogerzeil *et al.* (1993). The indicators for the study of facility are divided into core and complimentary indicator. The core indicators evaluate prescriber, patient and facilities. Results of the evaluation of drug use pattern using this indicator have been found useful in description of current treatment practices, comparison of the performance of individual facilities or prescribers, periodic monitoring and supervision of specific drug use behaviors and identification of potential drug problems and effect patient care (Hogerzeil *et al.*, 1993). WHO believes that generic prescriptions should be encouraged as such prescriptions are often cheaper than branded substitute of equal potency. The national essential drug list (EDL), national drug formulary (NDF) and national health insurance scheme (NHIS) also advocate the use of generic names in prescription within the government facilities.

Antibiotics are often prescribed unnecessarily in Nigeria as in other developing country (Adikwu, 1998). WHO1999 stipulates that only 20% of outpatient prescription should contain antibiotics. In Nigeria, 65% of prescriptions in a particular hospital study were antibiotics (Adikwu, 1998). The inappropriate use of injections is another common form of irrational use of drugs. Between 36% and48% of patients encounters injection in Uganda, Sudan and Nigeria, drugs need to be adequately labeled with clear instruction on how and when they should be taken (Hogerzeil *et al.*, 1993). Reports on these parameters of rational use of drugs are very scanty in our environment. According to Schwartz *et al.* (1989), non scientific prescribing practices are due to structural, social and symbolic forces. In qualitative study of Nigerian prescriber, Chukwu *et al.* (2002) found that none

could correctly enumerate all four steps involved in the prescription process, This process can be separated into five phases: prescription drop-off, patient profile review, order entry, final check, and pick-up (Lynne, 2009).

To improve drug use, Arustiyono, (1999) recommended four broad approaches, as educational, managerial, regulatory, and general, a combination of which may be synergistic. Among the educational approaches are provision of continuous medical education for prescribers, encouragements of better physician-patient, and pharmacist-patients' interaction, development of standard treatment guidelines for common medical problems and provision of training in rational drug use through workshop and group discussions. Managerial approaches proposed are developments and implementing essential drug list or national formularies. Interventions that would actually work to change prescriber behavior and decrease the public's demand for antibiotics is clinician and patient education through assessment of their knowledge, attitude and practice, which is the most effective approach to reduce inappropriate antibiotic use.

1.2 STATEMENT OF RESEARCH PROBLEM

The medically inappropriate, ineffective and economically inefficient use of drugs is a common global problem but worse in developing countries such as Nigeria (Hogerzeil *et al*., 1993). Common patterns of irrational prescribing include: a) the use of drugs when no drug therapy is indicated; b) the use of the wrong drug for a specific condition requiring drug therapy, e.g. tetracycline in childhood diarrhoea where oral rehydration therapy (ORS) would have been sufficient; c) the use of drugs with doubtful efficiency, e.g. the use of antimotility agents in acute diarrhoea; d) the use of unnecessarily

expensive drugs. While the problem of irrational drug use appears to be worldwide; its scope has, not been adequately researched in Nigeria's public or private health facilities, hence this study.

1.2 JUSTIFICATION OF THE STUDY

Arustiyono (1999), argued that prescription provides insight into a prescriber's attitude to the disease being treated and the nature of the health care delivery system in the community. Ahmadu Bello University Teaching Hospital (ABUTH) Zaria is one of the premier hospitals in Nigeria charged with the provision of preventive, promotive, curative and rehabilitative medical services. The study of the pattern of drug use with respect to antibiotics prescription among resident doctors at the hospital would indicate the attitude of prescribers at the health facility and give a picture of the status of health care in the hospital relating to RDU.

Changes in antimicrobial prescribing patterns will necessitate changes in physician behavior, it is important to better understand what physicians know about antimicrobial agents, how they acquired and maintained that knowledge, and what factors influence their prescription of antimicrobial. A better understanding of these underlying factors will permit the development of more effective interventions. Previous surveys have been done to assess both physician knowledge about antimicrobials and attitudes concerning antimicrobial use and resistance (Neu, 1975). To my knowledge, no previous physician surveys on antibiotic use have included a direct knowledge, attitude and practice assessment of antibiotic use or included resident doctor in various clinical departments in Nigeria. The problem of irrational drug use has not been adequately researched in Nigeria's private and public health facilities such as Ahmadu Bello University Teaching

Hospital, Zaria (ABUTH). Hence, this research seek to survey resident doctors in ABUTH in various departments to measure their knowledge, attitudes, and practices about antibiotic use and resistance and to learn more about how they acquire and maintain their knowledge, in order to formulate recommendations.

1.4 AIM AND OBJECTIVES

The general aim of this study is to evaluate the extent of rational drug use with respect to knowledge attitude and practice of antibiotics prescription among resident doctors at Ahmadu Bello University Teaching Hospital, Zaria Nigeria, and to make recommendations for its improvement.

The specific objectives of this study are:

a) To assess the knowledge, attitude and practice of prescribers to the principles and practice of antibiotics prescription and resistance.
b) To recommend modalities for improving antibiotic drug use at ABUTH based on findings from above.

CHAPTER TWO

LITERATURE REVIEW

2.1 DEFINITION OF ANTIBIOTICS

The term antibiotic was coined by Selman Waksman in 1942 to describe any chemical substance produced by various species of microorganism (bacteria, fungi, actinomycetes) that is antagonistic to the growth or life of other microorganisms in high dilution and may eventually destroy them. The term antibiotics is often used synonymously with the term antibacterial(s), an antibacterial is a compound or substance that kills or slows down the growth of bacteria, this definition excluded substances that kill bacteria but are not produced by microorganisms such as gastric juices and hydrogen peroxide. (Goodman and Gilman's, 7th edition)

Antibiotics differ markedly in physical, chemical, pharmacological properties, antibacterial spectra, and mechanism of action. Most have been chemically identified, and some have been synthesized, a few are available only as crude or partially purified extracts (Goodman and Gilman's, 7th edition)

2.2 CLASSIFICATION OF ANTIBIOTICS

Many antibiotic compounds are classified on the basis of chemical or biosynthetic origin into natural, semi-synthetic, and synthetic. Another classification system is based on biological activity on microorganism as: bactericidal agents and bacteriostatic agents, the classification is arbitrary because most bacteriostatic drug can become bactericidal at high concentration.

Bactericidal agents are more effective and act most effectively on rapidly dividing organism, kill the target bacterium or fungus by inhibiting their cell wall (penicillins and cephalosporins), or cell membrane (polymixins), or interfere with essential bacterial enzymes (Quinolone and sulfonamides) thus target bacterial functions or growth processes, they are used to treat host with low immune systems and diseases such as endocarditic, meningitis, osteomyelitis, and other invasive bacterial infections (Calderon and Sabundayo, 2007).

Bacteriostatic agents on the other hand inhibit bacterial growth by targeting protein synthesis, and rely on the normal host defenses mechanism to destroy the microorganisms whose multiplication has been stopped by the bacteriostatic agent. They include; aminoglycosides, macrolides, and tetracyclines, sulphonamides, clindamycin, and chloramphenicol, and can be used to treat infections such as cystitis (Finberg *et al*., 2004).

Further categorization is based on their target specificity. Narrow-spectrum antibacterial antibiotics target specific types of bacteria, such as Gram-negative or Gram-positive bacteria, whereas broad-spectrum antibiotics affect a wide range of bacteria.

After a long time interruption in discovering new classes of antibacterial compounds, three new classes of antibiotics have been brought into clinical use. These new antibacterials are cyclic lipopeptides (including daptomycin), glycylcyclines (e.g., tigecycline), and oxazolidinones (including linezolid) (Cunha, 2009).

2.2.1 Classification of antibacterials based on chemical structure

1. Cell Wall Inhibitors

Antibacterials act at different site in the target organism, the cell wall is inhibited by drugs which include the Glycopeptides (vancomycin), Cycloserin, and the β–lactams (penicillins, cephalosporines).

Peptidoglycan is the critical attack site in cell wall inhibition; it is a cross-linked polysaccharides and peptides complex, which gives the bacterial cell wall strength. Interference with the call wall function allows the cell to absorb water, swell and burst. The antibiotic agents usually diffuse easily through Gram positive cell walls, but in Gram negative they need to go through narrow walls and it's harder. Peptidoglycan is not found in eukaryotes.

Bacteria make four types of penicillin–binding proteins (PBP), PBP help in linking the peptidoglycan strand into the existing molecule and are numbered according to molecular weight. PBPs differ in affinities for β–lactams, they also differ in amounts and functions in cell walls, and their enzymes are different in Gram-positives, Gram-negatives and anaerobic bacteria. The binding of β–lactam to PBP determine how the bacteria will look, for example binding to PBP 3 causes bacteria to grow into long filaments and die, while binding to PBP 1 results in bulging and bursting of the cell wall. With PBPs inhibited, the autolysins are unopposed which can also contribute to the antibacterial effect.

2. Cell Membrane Inhibitors

The cytoplasmic membrane is the site of most of the microbial cells biochemical activities, The cell membrane inhibitors cause disorganization of the membrane and are divided into cationic, anionic, and neutral agents, they include the following agents, antibacterials (polymyxin), Antifungals (amphotericin), Imidazoles (fluconazole , itraconazole , and vorconazole).

3. Nucleic Acid Synthesis Inhibitors

a) Inhibitors of DNA replication: Quinolones and Nitroimidazole

Fluoroquinolones act directly with the microbial DNA, block the action of DNA gyrase and DNA topoisomerase IV that control and modify the topological states of DNA in cells. They do this by relieving supercoils, which are formed during the unwinding of DNA for replication or transcription. Drugs such as rifampicin also act directly with the microbial RNA. There are a few types of topoisomerases:

Type 1: Makes transient single stranded breaks in DNA and removes supercoils one at a time. In eukaryotes, both topoisomerase 1 and 2 can remove both positive and negative supercoils. In bacteria topoisomerase 1 can only remove negative supercoils.

Type 2: Makes transient double stranded breaks and removes supercoils two at a time, and is more efficient but requires energy from ATP hydrolysis. Bacterial topoisomerase II is also called DNA gyrase and has two functions (a) to remove positive supercoils during DNA replication, and (b) to introduce negative supercoils, so the DNA molecule can be packed into the cell. It is made of two A and two B subunits. Bacterial topoisomerase IV can only relax supercoils, it can't make supercoils. Topoisomerase IV has 2 subunits, ParC and ParE.

b) Inhibitors of RNA polymerase: Antibiotics such as rifamycins binds to a β-subunit of RNA polymerases and prevents initiation of DNA transcription. Mammalian mitochondrial RNA synthesis is not impaired significantly.

c) Inhibitors of nucleotide metabolism: Nucleic acid analogue such as acyclovir bind to viral enzyme (thymidine kinase and DNA polymerase) that are essential for DNA synthesis and thus halt viral replication and

4. Protein Synthesis Inhibitors

a) Inhibitors of 30S subunit: Aminoglycosides antibiotics bind to specific ribosomal proteins and to a major deep grove in the rRNA of a cell in such a way that incorrect amino acid sequences are entered into peptide chain leading to the formation of abnormal protein which are fatal to the microbe. Streptomycin has a different mechanism from the aminoglycosides, it binds to the S12 protein and causes the ribosome to misread the genetic code.

b) Inhibitors of 50S subunit

Macrolides, Chloramphenicol, Ketolides, Lincinoids are inhibitors of 50s subunits, they bind to the peptidyl side of the 50S subunit, impair peptidyltransferase, interferes with the translocation of the peptide chain from A to P site, and promotes dissociation of peptidyl-tRNA from the ribosomes.

5. Metabolic Inhibitor

Also known as anti metabolite, they include trimethoprim and the sulfonamides, Sulfonamides and trimethoprim block the biosynthesis of tetrahydrofolate, which is a carrier of 1C fragments and is necessary for DNA, RNA, and cell wall synthesis.

2.3 PHARMACODYNAMICS OF ANTIMICROBIAL

The successful outcome of antimicrobial therapeutic compounds depends on several factors. These include host defense mechanisms, the location of infection, and the Pharmacokinetic and Pharmacodynamics properties of the antibacterial (Pankey, 2004). Bactericidal activities of antibacterials depend on the bacterial growth phase, and it often requires ongoing metabolic activity and division of bacterial cells (Mascio, 2007). The activity of antibacterials depends frequently on its concentration (Wiegand, 2008), to predict clinical outcome of antibacterial, the pharmacodynamic (antimicrobial activity) is usually combined with pharmacokinetic profile of an antibacterial, thus several pharmacological parameters are used as markers of drug efficacy (Spanu *et al*., 2004).

2.4 GENERAL SIDE EFFECTS OF ANTIBIOTICS

Common side-effects of antibiotics include diarrhoea, nausea and vomiting, antibiotics can also affect the vaginal flora, and may lead to overgrowth of Candida species in the vulvo-vaginal area, due to disruption of the composition of the normal flora, leading to overgrowth of pathogenic bacteria. Additional side-effects of antibiotics can result from interaction of Quinolones with systemic corticosteroid when co administered, leading to elevated risk of tendon damage. Some people are allergic to antibiotics, particularly penicillins, allergic reactions cause swelling of the face, itching and a skin rash, in severe cases, breathing difficulties.

2.5 DRUG-DRUG INTERACTIONS

Anticoagulant

Antimicrobials may potentiate oral anticoagulant by reducing bacterial synthesis of vitamin K in the large gut, leading to alteration of gut flora, there may also be an effect on enterohepathic recycling where bacteria release active drug from the conjugate.

Contraceptive pills

Antibacterials may affect the efficiency of birth control pills e.g rifampicin, this may be due to hepatic enzyme activation leading to increased breakdown of the pill's active ingredients, and destruction of the intestinal flora, which might result in reduced absorption of estrogens in the colon. (Weaver and glassier, 1999)."

Alcohol

According to Lwanga (2008), interactions between alcohol and certain antibacterials may occur, and cause side-effects with decrease effectiveness of antibacterial therapy.

"Antibacterials such as metronidazole, tinidazole, cefoperazone, cefmenoxime, and furazolidone, cause a disulfiram-like chemical reaction when co administered with alcohol, by inhibiting its breakdown by acetaldehyde dehydrogenase, and this may result in vomiting, nausea, and shortness of breath. Other effects of alcohol on antibacterial activity include altered activity of the liver enzymes that break down the antibacterial compound. In addition, serum levels of doxycycline and erythromycin succinate, may be reduced by alcohol consumption, thus resulting in reduced efficacy and diminished pharmacotherapeutic effect (Stockley, 2002)"

Enzyme inhibition

Antibiotics such as erythromycin are an enzyme inhibitor and interfere with the metabolic inactivation of drugs such as wafarin, carbamazapine and theophyline, increasing their effect.

2.6 ANTIBIOTIC RESISTANCE

The availability of effective antimicrobials in future requires that the drug development keep pace with drug resistance, bacteria are capable of developing resistance to antibiotics by evolving an array of clever alteration that allow them to survive in the presence of antibiotics, inappropriate use of antimicrobial like any other medicines causes resistance, and leads not only to poor patient outcome, unnecessary adverse reactions and wasted resources, but also to emerging resistance of bacteria to antimicrobials. The phenomenon of resistance is seen not only in bacteria and mycobacteria (multidrug resistant tuberculosis (TB), for example), but also in protozoa infections (resistance to chloroquine as an antimalarial) and viral infections (HIV and antiretrovirals). The emergence of resistance to antibacterial drugs is a common phenomenon and often results from the gradual processes that take place during antibacterial drug therapy, in which the antibacterial primarily select bacterial strains with enhanced capacity to survive high doses of antibacterials, leading to preferential growth of resistant bacteria to occupy the biological space created by the drug, while growth of susceptible bacteria is inhibited (Pearson, 2007).

Bacteria have a number of ways which they become antibiotic-resistant. This include (1) The Intrinsic antibacterial resistance in which an antibiotic target may be absent from the bacterial genome. (2) Acquired resistance which results from a mutation in the bacterial

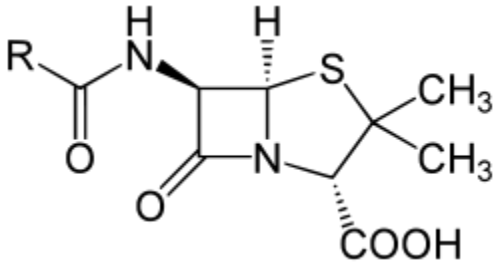
chromosome or the acquisition of (plasmid) extra-chromosomal DNA (Nikaido, 2009), acquired antibacterial resistance often occurs through vertical transmission of mutations and horizontal genetic exchange of DNA, the antibacterial resistance genes are exchanged between different bacterial strains or species via plasmids that carry the resistance genes that confer resistance to multiple antibacterials. Cross-resistance to several antibacterials may also occur when a resistance mechanism encoded by a single gene conveys resistance to more than one antibacterial compound (Baker-Austin *et al*., 2006). (3) While mutation is frequently the cause, resistance to antimicrobial agents may also be acquired through transfer of genetic material from one bacterium to another by a bacteriophage (a virus which infects bacteria), transduction, transformation, or conjugation (Goodman and Gilman's, 7th edition).

Antibacterial-resistant strains and species, known to as "superbugs", now contribute to the emergence of diseases which were formally controlled, for example, multidrug-resistant tuberculosis (MDR-TB). NDM-1 is a newly identified enzyme conveying bacterial resistance to a broad range of beta-lactam antibacterials (Marquez, 2005).

2.7 CHARACTERISTIC OF SPECIFIC ANTIBIOTICS

Antibiotics are characterized based on their structural class, and antibiotics within a structural class will generally have similar patterns of effectiveness, toxicity, and allergic potential. Most commonly used types of antibiotics are: Penicillins, Fluoroquinolones, Cephalosporins, Macrolides, Tetracyclines and Chloramphenicol, each class is composed of multiple drugs which are unique in some ways.

2.7.1 Penicillins



Penicillin (sometimes abbreviated **PCN** or **pen**) is a group of antibiotics derived from *Penicillium* fungi. They include penicillin G, procaine penicillin, benzathine penicillin, and penicillin V. The penicillins are the oldest class of antibiotics. Penicillins have a common chemical structure which they share with the cephalosporins, and are historically significant, because they are the first drugs that were effective against many previously serious diseases such as syphilis and Staphylococcus infections. Penicillins are still widely used today, though many types of bacteria are now resistant. All penicillins are beta-lactam antibiotics, and are used in the treatment of bacterial infections caused Gram-positive organisms. Penicillins are generally bactericidal, inhibiting formation of the cell wall.

There are four types of penicillins:

1. The narrow spectrum penicilins, which include:

a) Natural penicillins: They are based on the original penicillin-G structure, and are effective against gram-positive strains of streptococci, staphylococci, and some gram-negative bacteria such as meningococcus. Examples include benzyl penicillin, phenoxymethylpenicillin and phenethicillin.

b) Penicillinase-resistant penicillins: They are active even in the presence of the bacterial enzyme that inactivates most natural penicillins. This includes antibiotics such as cloxacillin, flucloxacillin and methicillin

2.) Broad spectrum penicillins: They are effective against a wider range of bacteria, e.g aminopenicillins such as ampicillin and amoxicillin.

3.) Mecillinams: These are effective against Gram-negative bacteria, excluding pseudomona aeruginosa e.g mecillinam, pivmecillinam

4.) Antipseudomonal : e.g carboxypenicillins and ureidopenicillins

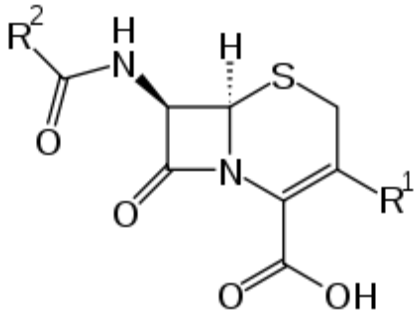
Mechanism of action

Penicillin and other β-Lactam antibiotics work by inhibiting the formation of peptidoglycan cross-links in the bacterial cell wall, β-Lactam antibiotics act by inhibiting penicillin-binding proteins, which normally catalyze cross-linking of bacterial cell walls. Penicillins are thus bactericidal and are only effective against multiplying organism. The β-lactam moiety (functional group) of penicillin binds to the enzyme DD-transpeptidase that links the peptidoglycan molecules in bacteria, allowing the enzymes that hydrolyze the peptidoglycan cross-links to continue to function, and weakens the cell wall of the bacterium, leading to cytolysis or death due to difference in osmotic gradient between the bacteria interior and its environment. In addition, the build-up of peptidoglycan precursors triggers the activation of bacterial cell wall hydrolases and autolysins, which further digest the bacteria's existing peptidoglycan.

Penicillins side effects

Penicillins are one of the least toxic drugs known, common side effects of penicillin are diarrhea, nausea, and vomiting. In rare cases penicillins can cause immediate and delayed allergic reactions - specifically, skin rashes, drug fever, angio-neurotic oedema and anaphylactic shock. Rarely penicillin can also cause haemolytic anaemia.

2.7.2 Cephalosporins



The **cephalosporins** are a class of β-lactam antibiotics originally derived from a fungus *Acremonium*, which was previously known as Cephalosporium. They have a mechanism of action identical to that of the penicillins. But their basic chemical structure differs in other respects, resulting in some difference in the spectrum of antibacterial activity. Like the penicillins, cephalosporins interfere with synthesis of the bacterial cell wall and so are bactericidal. Cephalosporins are grouped into generations base on their antimicrobial properties. Each generation has a broader spectrum of activity than the one before.

The first generation cephalosporins include: cephalothin, cephazolin, cephapirin, cephradine, cephalexin, cefadroxil. They possess generally excellent coverage against most gram-positive pathogens and variable coverage against most gram negative pathogens.

The second generation cephalosporins include: cefoxitin, cephamandole, cefuroxime. They possess excellent coverage to the gram-positive spectrum as the first generation cephalosporins, and also have expanded gram-negative spectrum.

The third generation cephalosporins include: cefsulodin, cefdaloxime, ceftazidime, ceftizoxime, cefotaxime, ceftriaxone e.t.c. They are mainly active against gram-negative organisms, and have the advantage of convenient dosing schedules, but are expensive. However, some members of this group have decreased activity against gram-positive organisms. .

The fourth generation cephalosporins: are broad-spectrum agents with activity against gram-positive organisms, and have a greater resistance to beta-lactamases (bacterial enzymes that may destroy antibiotic before it can do its work) than the third generation cephalosporins. Many fourth generation cephalosporins can cross blood brain barrier and are effective in meningitis. They include: cefclidine, cefepime, cefluprenam, cefozopran, cefpirome, cefquinome.

Mechanism of action

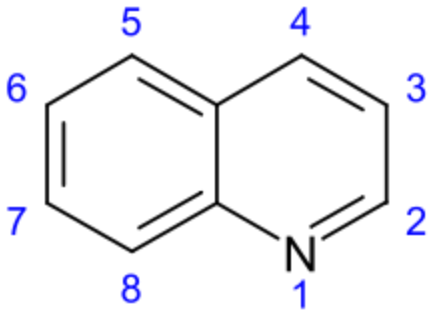
Cephalosporins are bactericidal and have the same mode of action as other beta-lactam antibiotics (such as penicillins) but are less susceptible to penicillinases. Cephalosporins disrupt the synthesis of the peptidoglycan layer of bacterial cell walls which is responsible for the cell wall structural integrity. They mimic the final transpeptidation step in the synthesis of the peptidoglycan which is facilitated by transpeptidases known

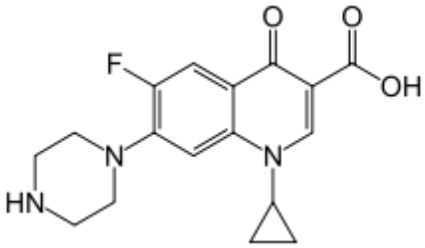
as penicillin-binding proteins (PBPs), and competitively inhibit PBP cross linking of peptidoglycan.

Cephalosporin side effects

Common side effects associated with cephalosporin are similar to that of penicillin, they include: diarrhoea, nausea, mild stomach cramps or upset. Approximately 10% of patients with allergic hypersensitivity to penicillins will also have cross-reactivity with cephalosporins. If cephalosporins are continued more than two weeks, thrombocytopenia, neutropenia, interstitial nephritis or abnormal liver function test may occur. Some cephalosporins, especially latamoxef, interfere with blood coagulation factors and cause haemorhage.

2.7.3 Fluoroquinolones





Fluoroquinolones are synthetic antibiotics that belong to the family of antibiotics called Quinolones. Fluoroquinolones are the newest class of antibiotics, their generic name often contains the root floxacin. The fluoroquinolones are broad-spectrum bacteriocidal drugs and can be administered both intravenously and orally. Commonly used fluoroquinolones include ciprofloxacin, levofloxacin, lomefloxacin, norfloxacin, sparfloxacin, clinafloxacin, gatifloxacin, ofloxacin, trovafloxacin.

Mechanism of action

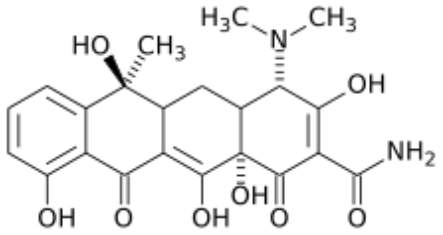
Quinolones and fluoroquinolones are chemotherapeutic bactericidal drugs, which interfere with DNA replication, their mode of action is complex but includes inhibiting DNA gyrase, the enzyme that maintains the helical twist in DNA. These antibiotics interact with components of eukaryotic ribosomal particles and, cause Selective toxicity to eukaryotes, (Elsea, 1992). This class has been shown to damage mitochondrial DNA (Suto, 1992).

Quinolones are often used to treat intracellular pathogens such as *Legionella pneumophila* and *Mycoplasma pneumoniae* because they can enter cells easily via porins.

Fluoroquinolones side effects

Common side effects include gastrointestinal upset such as nausea, vomiting, diarrhea, abdominal pain. Less common side effect includes CNS effect such as, headache, confusion, dizziness, and convulsion. phototoxicity (more common with lomefloxacin and sparfloxacin). Some Quinolones are potent enzyme inhibitors and impair the metabolic inactivation of other drugs, increasing their effect. Quinolones cause arthropathy in immature animals and should be avoided in children and growing adolescents.

2.7.4 Tetracyclines



Tetracycline antibiotics are broad-spectrum bacteriostatic agents that inhibit bacterial protein synthesis, commonly prescribed tetracycline antibiotics are: tetracycline, doxycycline, minocycline, oxytetracycline, they are effective against a wide variety of microorganisms, including rickettsia and amoebic parasites. Tetracyclines are used in the treatment of infections of the respiratory tract, sinuses, middle ear, urinary tract, skin, intestines, Gonorrhoea, moderately severe acne and as a scar tissue remover.

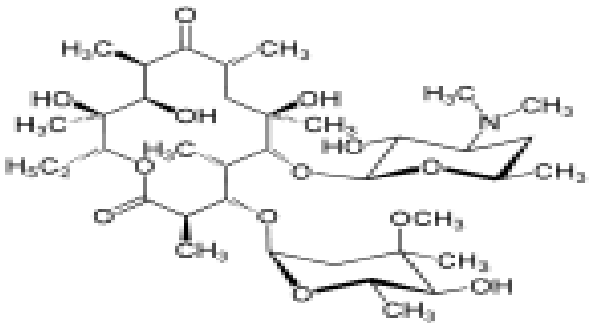
Mechanism of action

Tetracyclines bind to the 30S subunit of microbial ribosomes, and inhibit protein synthesis by blocking the attachment of charged aminoacyl-tRNA; this action is inhibitory and reversible upon withdrawal of the drug. Mammalian cells are not vulnerable to the effect of tetracyclines as these contain no 30S ribosomal subunit and therefore do not actively concentrate the drug.

Tetracycline side effects

Common side effects associated with tetracyclines include cramps, heartburn, diarrhea, sore mouth or tongue, and photosensitivity; expired drugs can cause a dangerous syndrome resulting in damage to the kidneys. Rarely, tetracyclines may cause allergic reactions, severe headache and vision problems which may be signs of dangerous secondary intracranial hypertension. Tetracycline antibiotics should not be used in children under the age of 8, and specifically during periods of tooth development. Rarely tetracycline cause benign intracranial hypertension.

2.7.5 Macrolides



The macrolide antibiotics are derived from Streptomyces bacteria, and belong to the polyketide class of natural products. The macrolides are bacteriostatic, but can also be bactericidal in high concentrations, they binds with bacterial ribosome, and inhibit protein synthesis. Commonly prescribed macrolide antibiotics are: erythromycin, clarithromycin, azithromycin, roxithromycin, troleandomycin, and are used to treat respiratory tract infections (such as pharyngitis, sinusitis, and bronchitis), genital, gastrointestinal tract, and skin infections.

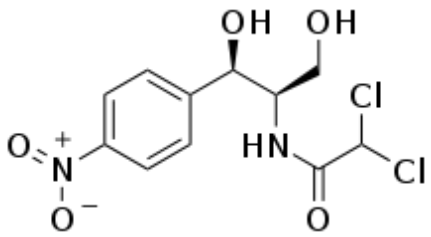
Mechanism of action

The mechanism of action of macrolides is inhibition of bacterial protein biosynthesis by binding reversibly to the P site on the 50S subunit of the bacterial ribosome, they prevent peptidyltransferase from adding the peptidyl attached to tRNA to the next amino acid (similarly to chloramphenicol) and as well inhibits ribosomal translocation, thus enhance premature dissociation of the peptidyl-tRNA from the ribosome (Gary Kaiser, 2009).

Macrolides side effects

Side effects associated with macrolides include nausea, vomiting, and diarrhea; infrequently, temporary auditory impairment may occur. Rarely Azithromycin may cause allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions. Oral erythromycin may be highly irritating to the stomach and cause cholestatic hepatitis and fever which may be confused with viral hepatitis, or acute pancreatitis. Erythromycin is an enzyme inhibitor and interferes with the metabolic inactivation of drugs such as wafarin, carbamazapine and theophyline, increasing their effect.

2.7.6 Chloramphenicol



Chloramphenicol is a bacteriostatic antimicrobial, it binds to the 50S subunit of the ribosome, thereby inhibiting bacterial protein synthesis. Chloramphenicol is effective against a wide variety of Gram-positive and Gram-negative bacteria, including most anaerobic organism.

Mechanism of action

Chloramphenicol binds to A2451 and A2452 residues in the 23S rRNA of the 50S ribosomal subunit, preventing peptide bond formation, it also inhibits peptidyl transferase activity of the bacterial ribosome, both chloramphenicol and the macrolide class of antibiotic interact with ribosomes, Chloramphenicol directly interferes with substrate binding, while macrolides sterically block the progression of the growing peptide.

Chloramphenicol Side effect

Treatments with chloramphenicol antibiotics may cause bone marrow toxicity, which may occur in two distinct forms: a direct toxic effect of the drug cause bone marrow suppression, and is usually reversible, and idiosyncratic reaction though rare cause aplastic anemia, which is, unpredictable, and unrelated to dose and generally fatal. Other side effect includes gastrointestinal upset, optic and peripheral neuritis.

2.8 PROBLEMS IN THE USE OF ANTIMICROBIALS

Paul Marino, (2007) argued that the first rule of antibiotics is try not to use them, and the second rule is try not to use too many of them.

Inappropriate use of antimicrobials an important type of drug misuse, misuse is often due to uncertainty about the diagnosis, drug susceptibility of the organisms, Self prescription and the use of antimicrobial as growth promoters in agriculture. Inappropriate antibacterial treatment, sub-optimal antibacterials treatment and overuse of antibiotics have contributed to the emergence of antibacterial-resistant bacteria. Many antibacterials are frequently prescribed to treat symptoms or diseases that do not respond to

antibacterial therapy or are likely to resolve without treatment (Larson, 2007). Common areas of misuse particularly associated with antibiotics include:

i. Excessive use of prophylactic antibiotics in travelers
ii. Failure of medical professionals to prescribe the correct dosage of antibacterials on the basis of the patient's weight and history of prior use.
iii. Failure to take the entire prescribed course of the antibacterial, incorrect dosage and administration, or failure to rest for sufficient recovery.
iv. Treatment of minor respiratory and gastrointestinal infections, viral infections and self-limiting bacterial diseases that do not benefit from use of antimicrobials
v. Incorrect choice of antimicrobial for common problems, for example the use of a broad-spectrum antimicrobial when a narrow-spectrum agent would be sufficient
vi. Insufficient dose and duration of dispensed or purchased antibiotics, because patients cannot afford the cost of the antimicrobial
vii. Inappropriate choice of antimicrobial for surgical prophylaxis
viii. The tendency to use newly introduced and expensive antimicrobials, when there is no evidence supporting better drug susceptibility of the newer drug over an older one.

The inappropriate use of antimicrobials is an important factor that causes resistance; the susceptible (sensitive) bacteria are killed leaving the resistant ones behind (selection pressure). Widespread usage of antibacterial drugs in hospitals has also been associated with increases in bacterial strains and species that no longer respond to treatment with the most common antibacterials (Hawkey, 2008), leading to more prevalent of antimicrobial resistance in hospital settings than in the community, because of the selection pressure on

organisms caused by the high intensity of antimicrobial use. Basic infection control procedures are often not practiced, so the transfer of resistant organisms between patients, and between patients and staff, is common. Increasing resistance in the hospital setting contributes to increasing resistance in the community, which is of serious public health importance, thus multifactorial interventions aimed at both physicians and patients can reduce inappropriate prescription of antibiotics (Metlay *et al*., 2007).

The emergence of antibacterial resistance has prompted restrictions on antibacterial use in the United Kingdom (UK) in the 1970 (Swann report, 1969), and the European Union (EU) has banned the use of antibacterials as growth-promotional agents since 2003. Moreso, several organizations (e.g., The American Society for Microbiology (ASM), American Public Health Association (APHA) and the American Medical Association (AMA)) have called for restrictions on antibiotic use in food animal production and an end to all non-therapeutic uses.

2.9 IMPROVING ANTIMICROBIAL USE AND CONTAINING RESISTANCE

The need for the judicious use of antimicrobials cannot be overemphasized. All the strategies that are used to promote more rational use of medicines generally are also relevant for antimicrobials. Such strategies are aimed at prescribers, dispensers, those who administer medicines, those responsible for the selection and purchase of medicines, and consumers.

Important strategies to improve antimicrobial use, in order to contain the development of resistant pathogenic organisms, include:

- An effective antimicrobial subcommittee to set norms and monitor antimicrobial use in order to reduce misuse and contain the development of resistant organisms.

- Use of antimicrobial treatment guidelines updated according to antimicrobial resistance surveillance data, together with sustained education and supervision on rational use of antimicrobials.
- Classification of antimicrobial prescribing in hospitals into non-restricted, restricted and very restricted to avoid indiscriminate use of antimicrobials of last resort.
- Audit of antimicrobial use, by department or by drug, together with feedback and other appropriate measures in order to correct inappropriate use.
- Improved diagnostic facilities to aid clinicians not to prescribe antimicrobials unnecessarily,
- Antimicrobial resistance surveillance in order to inform clinicians about the susceptibility patterns of bacteria causing infections in individual patients so ensuring correct antimicrobial choice.
- Use the collated information to choose which antimicrobials should be on the formulary list; this requires the disaggregation of resistance patterns in community-acquired and nosocomial infections.
- Where laboratory facilities are not available, it may be necessary to rely on surveillance information from the nearest available laboratory in a similar hospital setting. Such information may be used to identify first-choice antimicrobials which can be used empirically, i.e. without information on the susceptibility patterns of individual patients.

2.10 FORMS OF IRRATIONAL DRUG USE

Irrational drug use occurs at various level of health care provision, for instance at the national level, the availability of substandard or counterfeit drugs is an example of irrational drug use. WHO data base on counterfeit drugs reported that 77% of counterfeit were from developing countries. According to NAFDAC, the problem of counterfeiting is exacerbated by regulatory double standards adopted by exporting countries and the lack of inbuilt security measures during product development by drug manufacturers to forestall counterfeiting.

At the health systems level presence of drugs that are not required at setting, drug shortages, and presence of large quantities of expired drugs are manifestations of inappropriate use of drugs.

At the prescriber's level, inappropriate use could be observed from how prescriptions are written. Vikram *et al*. (2005), found prescriptions written on scraps of paper with scanty details of the prescriber for the client, and argued that this may produce difficulties in filling out the prescription. Odusanya (2004), also noted that poor prescribing habits include prescribing too many drugs for a patient, called polypharmacy, Uzochukwu et *al*. (2004) postulated that prescriber's embark on poly pharmacy in their attempt to treat a number of possible diseases simultaneously.

At the dispenser level, irrational use includes incorrect interpretation of the prescription; retrieval of wrong ingredients, inadequate labeling, unsanitary procedures and problems with drug packaging. Kutyabami (2007) gives other examples at this level as drug shortages, poor drug records, poor storage facilities and lack of appropriate dispensing equipment and materials. Consumers of drugs can exhibit significant examples of inappropriate use of drugs such as sharing of drugs and self- medication.

2.11 CAUSES OF IRRATIONAL DRUG USE

The causes of irrational drug use are multifaceted, at the international level, irrational drug use are caused by multinational pharmaceutical companies who engage in drug promotion and marketing. These are done by provision of information to both health workers and patients through direct advertising. Lexchin (1992) found that in the French speaking countries, over half of the information provided by drug companies did not match the official drug monographs.

At the level of the country, weak laws and regulations encourage dubious individuals and selfish interest to get involved in drug handling and supplies leading to irrational drug use. According to NAFDAC, "the federal government of Nigeria implemented a drugs importation licensing regime between 1983 and 1988 mainly on the basis of political patronage, this allowed many people with no knowledge about drugs and pharmaceuticals to become importers while genuine pharmacists, manufacturers and importers were forced to patronize these charlatans. As a result, the drug importation and distribution system in Nigeria became chaotic with the market flooded with fake/counterfeit and substandard products. In Nigeria as in other developing countries, laws and regulations require personnel, equipment and a political environment, which is conducive to act effectively. These are significantly lacking (NAFDAC, 2007).

Many developing countries are unable to satisfy their drug requirements relying rather on importation**.** In the analysis by NAFDAC, "there are presently 86 local pharmaceutical manufacturing companies producing less than 30% of Nigeria's drug need. The

remaining 70% is imported at high cost limiting access of the population to needed medicines.

At the health system level, irrational drug use could be caused by:

- Unreliable suppliers of drugs, whose quality and cost of supplies may be suspect.
- Poor planning of the drug needs of the unit.
- Poor information management system.
- Lack of monitoring and supervision.

According to some authors, the physicians practice environment and interactions with pharmaceutical sales representatives are important determinants (Lee, 1964). Others believe that education, quality of practice and whole- person orientation , physicians age, rural practice, number of Patients and type of or lack of board certification or specialization are factors (Baker, 1972). Prescribers may cause irrational drug use due to inadequate examination of the patient, incomplete communication between the patient and the doctor, lack of documented medical history and inadequate laboratory resources, all these result in inaccurate diagnosis.

Dispensers are usually the last health professionals in the drug use process to interact with the patients. Syhakang *et al*., (2001) in a report from the Laos people's democratic republic found that private pharmacies had more knowledgeable dispensers than public pharmacies. Also, patient perception of the quality of health knowledge by dispensers would affect the seriousness attached to information given by them to patients. Dispensers in patent medicine stores are often people who lack requisite medical training thereby resulting in irrational use of drugs.

Patients are the ultimate users of drugs at the health care system, correct prescribing alone does not guarantee proper usage of drugs. Non adherence to prescription by patients is very common, their decisions are often influenced by factors such as cultural beliefs, communication skills and attitudes of health workers, accessibility to and nature of health service delivery point (Kutyabami, 2007).

2.12 INDICATORS OF RATIONAL DRUG USE

As part of efforts to improve drug use practices and prescribing behavior in developing countries, the International Network for the Rational Use of Drugs (INRUD) in collaboration with the WHO Action Program on Essential Drugs, realized the need for an objective and standard method of assessment, leading to the formation of drug indicators. These drug use indicators are basic, highly standardized and field tested in 12 developing countries by Hogerzeil *et al*. (1993). Some of these indicators recommended by the WHO are:

- Core Drug Use indicators
- Prescribing indicators
    - Average number of drugs per encounter.
    - Percentage of drugs prescribed by generic name.
    - Percentage of encounters with an antibiotic prescribed.
    - Percentage of encounters with an injection prescribed.
    - Percentage of drugs prescribed from essential drugs list or formulary.
- Patient care indicators

- Average consultation time.
- Average dispensing time.
- Percentage of drugs actually dispensed.
- Percentage of drugs adequately labeled.
- Patients' knowledge of correct doses.

- Facility indicators

- Availability of essential drugs list or formulary to practitioners.
- Availability of key drugs.

- Complementary Drug Use Indicators

- Percentage of patients treated without drugs.
- Average drug cost per encounter.
- Percentage of drug cost spent on antibiotics.
- Percentage of drug cost spent on injections.
- Percentage of prescriptions in accordance with treatment guideline.
- Percentage of patients satisfied with the care they receive.
- Percentage of health facilities with access to impartial drug information.

The Management Science for Health group believes these indicators are useful for:

- Determination of where drug use problems exist.
- Provision of a monitoring mechanism.
- Motivation of health care providers to improve and follow established health care standard.

In this study, a survey of prescribers knowledge, attitude and practice on RDU with respect to antibiotics prescription using questionnaire would be performed to further

elucidate on the study of the core indicators. According to Erah *et al*., (2003), antibiotics are often prescribed unnecessarily in Nigeria and other developing countries while the WHO, gave 20% as maximum rate of antibiotic prescription for patients; most reports from all categories of health facilities report rates above 50%. Antibiotic use in Nigerian primary and secondary care facilities were reportedly between 50% and 55% despite the fact that secondary care facilities usually have doctors as prescribers while the PHC did not. Surprisingly, public hospitals used antibiotics more (75%) than private hospitals (55%) in a study from Warri, Nigeria (Erah *et al*., 2003), this revealed appreciable gaps in the knowledge of prescribers regarding antibiotics prescription.

2.13 EFFECTS OF IRRATIONAL DRUG USE

Irrational drug use has important effects. This includes reduction in the quality of drug therapy leading to increased morbidity and mortality, Poor quality of drug therapy would reduce the overall standard of health care delivered to the community. According to Laporte (1985), a prescription provides an insight into a prescriber's attitude to the disease being treated and the nature of health care delivery system in the community. Odusansa (2004) also observed that antibiotics were prescribed for many conditions they were not indicated for, and indicated this as a form of poor quality care. The World Health Assembly in 2005 'concluded that irrational use of medicines damages health and waste resources. Sambo *et al*. (2004), also argued that in India and Nigeria, the vast majority of drug costs are borne out of pocket, hence the burden of irrational drug use falls directly on the patient, leading to reduced availability of funds for other vital needs and increased costs of health care. Irrational drug use also reduces access to quality drugs

by those who need them (WHO, 1997). Increased risks of unwanted effects such as adverse drug reactions and emergence of drug resistance, e.g. malaria or multiple drug resistant TB are other effects of irrational drug use. (Holloway, 2005)

CHAPTER THREE

METHODOLOGY OF THE STUDY DESIGN

3.1 BACKGROUND INFORMATION ABOUT THE STUDY AREA

The study is a hospital-based cross-sectional descriptive study, carried out amongst resident doctors in ABUTH Shika-Zaria. The population of the study area consists of 1,022 health care workers, out of which 350 are resident doctors, 435 nurses and 101 laboratory staff. Ahmadu Bello University Teaching Hospital, the study area sits on the north western outskirts of Zaria, about 3 km from Ahmadu Bello University (A.B.U) main campus and 2 km from Shika town. It started as an Institute of Health with A.B.U. in 1967 and was taken over by the Federal Ministry of Health in 1985. In its course of development, it operated in temporary sites at Anguwan Rimi, Kaduna; Tudun-Wada, Zaria and Malumfashi. A need to centralize its services resulted in the move to the present permanent site in Shika following the ministerial directive in 1999. The permanent site of ABUTH Shika-Zaria was officially commissioned by the then Nigerian President, Chief Olusegun Obasanjo on the 11th of November 2005. This was followed by an obligatory relocation of all staff from the three temporary sites to the permanent site.

The hospital is the largest in the North-West geopolitical zone, with regards to both structure and personnel. It comprises of several departments which includes Internal Medicine, Surgery, Out-patient, radiology, Physiotherapy, Paediatric, Obstetrics and Gynaecology, Ophthalmology, Ear, Nose and Throat (E.N.T), Haematology, Chemical pathology, Pathology, Microbiology etc. The hospital renders services such as:

i. **Clinical services**: Paediatrics, medicine, surgery, obstetrics and gynaecology, ophthalmology, orthopedic, oncology (for which it is a noted centre of excellence) etc.
ii. **Laboratory services**: Chemical pathology, haematology, pathology, microbiology.
iii. **Training services**: Training of medical undergraduates and postgraduate, nursing, radiology and medical laboratory students etc.
iv. **Insurance**: The hospital is a National Health Insurance Scheme (N.H.I.S) accredited provider.

3.2 KNOWLEDGE, ATTITTUDE AND PRACTICE

"Knowledge, attitude and practice is a triad of factors which are interactive and interdependent. Emphasis is usually laid on each component of the triad, on the value of ethical conduct in raising the application of the component in real life to a peak."

"Knowledge is the capacity to acquire, retain and use information; it is a mixture of comprehension, experience, discernment and skill."

"Attitude refers to inclinations to react in a certain way to certain situations; to see and interpret events according to certain predispositions; or to organize opinions into coherent and interrelated structures."

"Practices is the application of rules and knowledge that leads to action. Good practice is an art that is linked to the progress of knowledge and technology and is executed in an ethical manner" (Ibrahim, 1995).

3.3 STUDY DESIGN

The study was a cross-sectional descriptive study of pattern of rational drug use with respect to knowledge, attitude and practice of antibiotics prescription among resident doctors using an adapted modified structured self administered questionnaire. The questionnaire adapted was used for a survey in France and Scotland to study antibiotic usage among doctors, (Pulcini *et al*., 2011).

3.3.1 Study Population

The study populations were all resident doctors and medical officers in all clinical departments Ahmadu Bello University teaching hospital Zaria, Nigeria. The resident doctors comprise the junior registrar and the senior registrar.

Inclusion criteria

All resident doctors and medical officers in Ahmadu Bello University Teaching Hospital Zaria

Exclusion criteria

- Non-resident doctors (consultants)
- Resident doctors on posting outside ABUTH Zaria

- Resident doctors on leave at the data collection period.

3.3.2 Sampling Method and Sample Size

A multi stage sampling technique with proportional allocation of resident doctor from various departments for the study was employed, after which simple random sampling technique by balloting without replacement was employed to select respondent per department.

The sample size 'n' to be drawn among the resident doctors was calculated using the formula $n=Z^2pq/d^2$

Where:

n = minimum required sample size.

z = value of standard normal deviate (corresponding to [100-ci/2] %) at 95% = 1.96.

p = proportion of antibiotics prescription success or prevalence from previous study.

Therefore p = 0.28 (Arjun *et al.*, 2004).

q = proportion of failure (=1-p)

d = margin of error at 95% confidence interval = 0.05

Therefore,

$$n = \frac{1.96^2 \text{x } 0.28\text{x}0.72}{0.05^2}$$

n = 309

Adjusting for non respondents = 10% of 309 (minimum required sample size)

$$\frac{10 \text{ x } 309}{100} = 30.9$$

Total sample size = 340.

3.3.3 Data Collection Procedure

Questionnaire administered for data collection contained, questions that were both open ended and close ended. It consisted 61 items self administered questionnaire to collect information from respondents about their current specialties, knowledge of the causes, importance and problems of antibiotic resistance, the knowledge of the National and local prevalence of antibiotic resistance and misuse, the attitudes of antibiotics prescription and interventions to improve antibiotic prescription, the frequency with which they prescribe antibiotics, and past training in antibiotic prescription. Most questions about perceptions and attitudes, was assessed with five-point Likert-style response options, from very unhelpful / unimportant / unconfident, to very helpful / important/ confident. To assess knowledge of the prevalence of antibiotic resistance, respondents were asked to estimate the prevalence of resistance in their hospital for two specific bacterium–antibiotic combinations relevant to clinical practice: Escherichia coli resistance to trimethoprim in community-acquired infections, and Staphylococcus aureus resistance to methicillin in hospital-acquired infections in the hospital. Knowledge of the local prevalence of antibiotic misuse was assessed. Nine essential steps of an antibiotic prescribing process, seven possible causes of antibiotic resistance and possible interventions were included in the questionnaire. The questionnaire was pre-tested among ten resident doctors to check comprehension, clarity and reliability of the questions, after which the tool was revised accordingly and finalized for use. All participants were assured of the confidentiality of their responses.

3.3.4 Survey Distributions

Approval of the research project by the Institutional Review Board of ABUTH was sought, and clearance for consideration to carry out the study was obtained from Hospital

Ethical Committee vide letter before embarking on the research. The survey questionnaire was distributed to selected doctors in the department of Medicine, Surgery, Accident and Emergency, Obstetrics and Gynecology (Obs/Gyn) Peadiatics, Microbiology, Clinical Haematology, Ophthalmology Orthopedics and Oncology. The survey tool also contained a consent form to participate in the study. Filled questionnaire were collected over four weeks on receipt of the questionnaire.

3.3.5 Statistical Methods

"Percentages were calculated for the categorical data. Univariate analysis using the chi-square test for categorical data, or Fisher's exact test when needed was applied". Results were presented for each clinical unit of the hospital and all data were analyzed using SPSS software, version 17. All p-value <0.05 was considered to be significant.

3.3.6 Limitations

The limitation encountered include getting all the resident doctors to partake in the survey since some were on postings outside the hospital while some were on leave during the study period of this research.

CHAPTER FOUR
RESULTS

4.1 SOCIO-DEMOGRAPHIC PROFILE OF RESPONDENT

Table 4.1 Shows that a total of two hundred and fifty one (251) resident doctors responded to the questionnaire. Their ages ranged from 25-50 years, most being between 30-40years (mean age of 35±4.7 years). The majority 79.7% (200) of respondents were males, the registrars formed 51.8% (130) of respondents and many 55% (138) were within 1-3 years of residency training from seventeen different specialties grouped into six of which physicians and surgeon were the majority.

Table 4.1: Socio-demographic profile of respondents in ABUTH Zaria, 2011

Age (years)	Frequency (n=251)	Percent (%)
25-29	24	9.6
30-34	93	37.1
35-40	99	39.4
41-44	13	5.2
45-50	10	4.0
Sex		
Male	200	79.7
Female	51	20.3
Designation		
Medical officers	27	10.8
Registrars	130	51.8
Senior registrar	94	37.5
Residency training (years)		
None	27	10.8
1-3	138	55.0
4-6	76	30.3
7-9	7	2.8
>10	2	1.2
Specialty		
Medical officers	27	10.8
Physicians	64	25.5
Surgeons	73	29.1
Peadiatricians	28	11.2
Obstetricians and gynaecologists	32	12.7
Laboratory physicians	27	10.8

4.2 EXPERIENCE OF RESPONDENTS IN INFECTIOUS DISEASE UNIT (IDU) IN ABUTH ZARIA

A total of 42.2% of the respondents indicated they have worked in infectious disease unit (IDU) and no significant relationship was found between occupational level (designation) of respondent and previous experience in IDU as shown in table 4.2.1 and table 4.2.2.

Table 4.2.1: Distribution of experience of respondents in infectious disease unit (IDU) in ABUTH Zaria, 2011

Experience in IDU	Frequency	Percent (%)
Yes	106	42.2
No	145	47.8
Total	251	100

Table 4.2.2: Relationship between designation of respondents in ABUTH Zaria and previous experience in infectious disease unit (IDU), 2011

Designation	Previous experience in infectious disease unit		Total
	Yes	No	
Medical officers	11	16	27
Registrars	55	75	130
Senior registrars	40	54	94
Total	106	145	251

χ^2= .012; df =2; p= .994 ; n=249

4.3: KNOWLEDGE OF RATIONAL DRUG USE (RDU) AMONG RESPONDENTS IN ABUTH ZARIA

Most of the respondents 84.5% (212) acknowledged they were aware of RDU, 50.8% (127) learnt about RDU through lectures, 40.2% through residency training, while the rest of the respondents got their information through seminar and workshop. Among those who knew about RDU, majority 51.9% (110) were registrars, 67.3% (169) poorly defined RDU and only 3.2% (8) had an excellent definition of RDU. No significant relationship was found between level of residency training (designation) of respondents and knowledge of RDU. This information is shown in table 4.3.1, 4.3.2, 4.3.3 and 4.3.4.

Table 4.3.1: Knowledge of rational drug use (RDU) among respondents in ABUTH Zaria, 2011

Knowledge of RDU	Frequency	Percent (%)
Yes	212	84.5
No	39	15.5
Total	251	100

Table 4.3.2: Sources of information about rational drug use among respondents in ABUTH Zaria, 2011

Sources	**Frequency** (n=251)	**Percent (%)**

Lectures	127	50.8
Residency training	100	40.2
Seminar	59	23.7
Work shop	32	12.9

Table 4.3.3: Relationship between designations of respondents in ABUTH Zaria and awareness of RDU, 2011

Designation	**Awareness of RDU**		**Total**
	Yes	**No**	
Medical officers	24	3	27
Registrars	110	20	130
Senior registrars	78	16	94
Total	212	39	251
χ^2= 2.447; df= 2; p= 0.294; n=246			

Table 4.3.4: Assessment of respondents definition of rational drug use (RDU) in ABUTH Zaria, 2011

Remark	**Frequency**	**Percent (%)**
Poor	169	67.3
Good	36	14.3
Very good	38	15.1
Excellent	8	3.2
Total	251	100

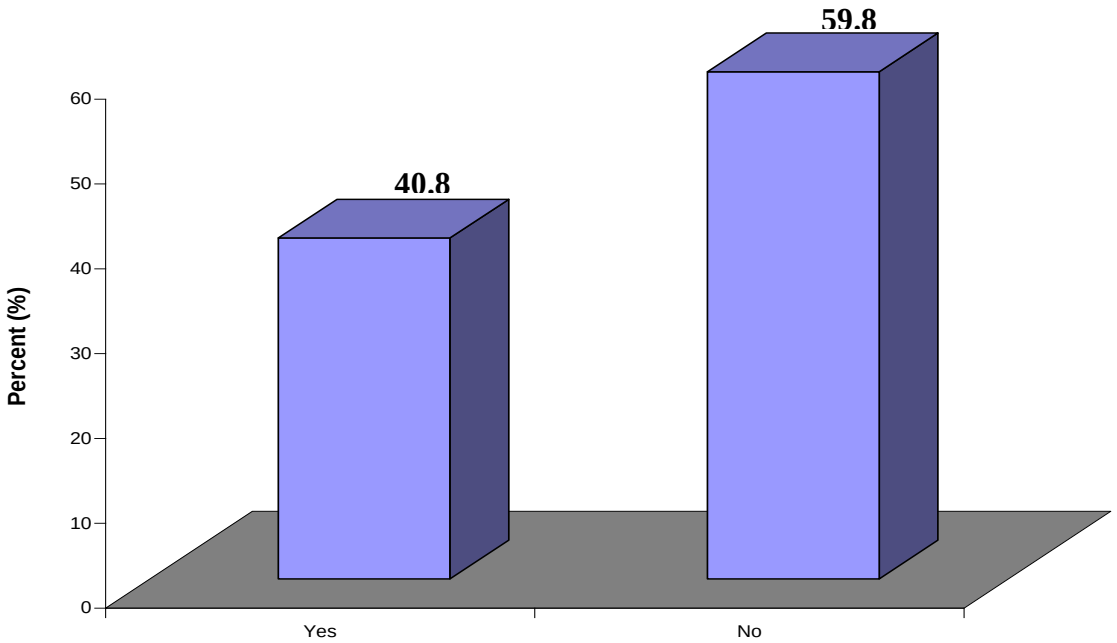
4.4: AWARENESS OF NATIONAL DRUG FORMULARY AND ROUTINE USAGE

The majority of respondents 92.8% (233) indicated they were aware of NDF but only 40.2% (101) routinely use NDF to aid their prescription, as indicated in tables 4.4.1 and depicted in figure 4.4.1.

Table 4.4.1: Awareness of national drug formulary (NDF) and its usage to aid prescription among respondents in ABUTH Zaria, 2011

Awareness/Usage	Response		Total (%)
	Yes (%)	No (%)	
Awareness of NDF	233 (92.8)	18 (7.2)	251 (100)
Routine usage of NDF	101 (40.2)	150 (59.8)	251 (100)

Figure 4.4.1: Routine usage of NDF to aid prescription among respondents in ABUTH Zaria, 2011



4.5: ANTIBIOTICS PRESCRIPTION AND RESISTANCE

4.5.1 Knowledge of the prevalence of local antimicrobial susceptibility and resistance

Majority 79.7% (200) of the respondents do not know the hospital antimicrobial susceptibility pattern, 90% (226) do not know (not sure) of prevalence *Escherichi coli* (*E. coli*) resistance to trimethoprim, while 89.6% (225) also do not know (not sure) of *Staphilococus aureus* (*S. aureus*) resistance to methicillin in the hospital as shown in table 4.5.1.

Table 4.5.1: Knowledge of the prevalence of local antimicrobial susceptibility and resistance among respondents in ABUTH Zaria, 2011

Knowledge of prevalence of-	Correct estimates	Response	
		Yes (%)	No/ Not sure (%)
Local antimicrobial susceptibility pattern	-	51 (20.3)	200 (79.7)
E-coli resistance to trimethoprim	21-50%	25 (10)	226 (90)
MRSA*	2-20%	26 (10.4)	225 (89.6)

MRSA*- Methicillin resistance *Staphilococcus aureus*

4.5.2 Knowledge and practice of antibiotics prescription

Most respondents 98.8% (248) indicated they had prescribed antibiotics in the past six months, and 49.9% (123) admitted prescribing greater than five antibiotics in the past seven days, no significant difference was found between residents designation and number of prescriptions per week. 87.1% (217) of the respondents also acknowledged they do explain to patients how to take the prescribed antibiotics. Perception on who should explain to patients how to take the prescribed antibiotics between doctors and pharmacists do not differ much, 64.7% (161) believed it is the responsibility of the doctors while 63.9% (159) believed it is the responsibility of pharmacists. A significant relationship was found between the respondents who acknowledged explaining to patients as the responsibility of the doctors, response by the medical officers was responsible for the significant difference observed ($\chi^2 = 6.515$; df=2; p=0.038; n=249).

Majority of the respondents 92.8% (232) acknowledge antibiotics resistance as a national problem, 85.2% (213) indicated it as a problem in clinical practice, while 79.1% (197) perceived it as a problem in the hospital. The knowledge that antibiotics resistance is a problem in the hospital is influenced by level of residency training which shows a significant relationship. The difference in the knowledge of senior registrars and medical officers is responsible for the significant difference observed, with only 55.6% (15) of the

medical officers indicating antibiotics resistance as a problem in the hospital (χ^2=15.899; df=4; p=0.003; n=249).

Only few doctors 13.6% (32) have the knowledge of World Health Organization (WHO) proportion of inappropriate antibiotics prescription. A significant relationship was found with respects to level of training of respondents, the knowledge of the medical officers on the proportion of inappropriate antibiotics prescription is responsible for the significant difference observed (χ^2=16.573; df = 8; p= .035; n=235). As shown in table 4.5.2

Table 4.5.2: Knowledge and Practice of antibiotics prescription among respondents in ABUTH Zaria, 2011

Parameters	**Medical officers** **n =27 (%)**	**Registrars** **n =130 (%)**	**Senior registrars** **n =94 (%)**	**p-value**	**Combine answers** **n =251 (%)**
Antibiotics prescription within past six months	27 (100)	128 (98.5)	93 (98.9)	0.791	248 (98.8)
Antibiotics prescribed in the last seven (7) days					
<2	2 (7.4)	37 (28.5)	25/93 (26.9)	0.090	64/250 (25.5)
3-5	3 (11.1)	32 (24.6)	28/93 (30.1)	0.090	63/250 (25.1)
>5	22 (81.5)	61 (46.9)	40/93 (43.0)	0.090	123/250 (49.0)
Explain to patient how to take antibiotics	21/25 (84.0)	111 (85.4)	85 (90.4)	0.476	217/249 (87.1)
Appropriate personnel to explain to patients	11/26 (42.3)	86 (66.2)	64/93 (68.8)	0.038	161/249 (64.7)
Doctors	19/26 (73.1)	75 (57.7)	65/93 (69.9)	0.102	159/249 (63.9)
Pharmacist					
Knowledge of hospital antimicrobial susceptibility pattern	11/26 (42.3)	25 (19.2)	15/87 (17.2)	0.031	51/251 (20.3)
knowledge of antibiotic resistance					
National problem	23 (85.2)	119/129 (92.2)	90/94 (95.7)	0.311	232/250 (92.8)
Problem in hospital	15 (55.6)	101/128 (78.9)	81/94 (86.2)	0.003	197/249 (79.1)
Problem in clinical practice	22 (81.5)	108/129 (83.7)	83/94 (88.3)	0.590	213/250 (85.2)
Awareness of WHO antibiotics					

appropriateness/use 21-50%	1/25 (4.0)	17/122 (13.9)	14/88 (15.9)	0.035	32/235 (13.6)

4.5.3 Disease conditions considered appropriate for antibiotic prescription

A few proportions of respondents 12.7% (32) consider antibiotics prescription for malaria treatment appropriate, while 22.3% (56) consider antibiotics prescription for treatment of upper respiratory tract infection (URTI) appropriate. No significant relationship was found between designation of respondents and the disease conditions. As shown in table 4.5.3 and 4.5.4.

Table 4.5.3: Disease conditions considered appropriate for antibiotics prescription by respondents in ABUTH Zaria

	Response (%)		**Total**
Disease	**Yes (%)**	**No (%)**	
Malaria	32 (12.7)	219 (87.3)	251
Enteric fever	225 (89.6)	26 (10.4)	251
URTI (common cold)	56 (22.3)	195 (77.7)	251
LRTI	229 (91.2)	21 (8.4)	251

Table 4.5.4: Relationship between designations of respondents in ABUTH Zaria and Disease conditions considered appropriate for antibiotics prescription

Designation	**Disease conditions consider appropriate for antibiotics prescription**

	Malaria		URTI (Common cold)	
	Yes	**No**	**Yes**	**No**
Medical officers	3	24	10	17
Registrars	17	113	23	107
Senior registrars	12	82	23	71
Total	32	219	56	195
χ^2=.078; df=2;p= .962 n=251			χ^2= 5.230; df= 2; p=.073; n= 251	

4.5.4 Knowledge of potential cause of antibiotics resistance

In table 4.5.5 and 4.5.6 four factors were acknowledged as important cause of antibiotic resistance: prescribing too low dose of antibiotics, too many antibiotics prescription, too many broad spectrum antibiotics and too long duration of antibiotics. The factors most frequently considered unimportant were: poor hand hygiene, paying too much attention to pharmaceutical advertisements and excessive use of antibiotics in live stocks. A significant relationship was found between respondents designation on their perception about too long duration of antibiotics usage as an important cause of antibiotics resistance (p-value =0.022), and excessive use of antibiotics in livestock (p-value =0.028). Paying too much attention to pharmaceutical advertisements was indicated as an unimportant cause of antibiotics resistance, a significant relationship was found (p-value =0.032). The response of the senior registrar is responsible for the significant difference observed.

Table 4.5.5: Knowledge of potential causes of antibiotics resistance among respondents in ABUTH Zaria

Causes of antibiotics resistance	Response n =251		Total (%)
	Important (%)	Unimportant (%)	
Too many antibiotics prescriptions	212 (85.5)	21 (8.4)	233 (92.8)
Too many broad spectrum antibiotics used	200 (79.9)	20 (8.0)	220 (87.6)
Too long duration of antibiotics treatment	162 (64.9)	48 (19.1)	210 (83.7)
Too low dose of antibiotics	225 (89.2)	11 (4.4)	235 (93.6)
Excessive use of antibiotics in livestock	93 (37.1)	57 (22.7)	150 (59.8)
Poor hand hygiene	88 (34.7)	88 (35.1)	176 (70.0)
Not removing focus of infection	187 (74.5)	23 (9.2)	210 (83.7)
Paying too much attention to pharmaceutical advertisements	111 (44.2)	63 (25.1)	174 (69.3)

Table 4.5.6: Relationship between designation of respondents and knowledge of potential causes of antibiotics in ABUTH Zaria

Potential causes of resistance	Medical officers (%)	Registrars (%)	Senior Registrars (%)	p-value
Too many antibiotics prescriptions	22 (10.4)	104 (49.1)	86 (40.6)	0.052
Too many broad spectrum antibiotics used	20 (10.0)	100 (50.0)	80 (40.0)	0.065

Too long duration of antibiotics treatment	13 (8.0)	81(50.0)	68 (42.0)	0.022
Too low dose of antibiotics	23 (10.3)	117 (52.2)	84 (37.5)	0.700
Excessive use of antibiotics in livestock	9 (15.8)	33 (57.9)	15 (26.3)	0.028
Poor hand hygiene	9 (10.0)	51 (58.0)	28 (31.8)	0.235
Paying too much attention to pharmaceutical advertisements	10 (15.6)	37 (57.8)	17 (26.6)	0.032

4.6 ATTITUDE OF ANTIBIOTICS PRESCRIPTION AMONG RESPONDENTS IN ABUTH ZARIA

4.6.1 Factors influencing attitude of antibiotics prescription

Majority of the respondents indicated that their attitude on antibiotic prescribing processes are more likely guided by past experience / training, advice from senior colleague, use local guideline or lab results. They are less likely to seek advice from pharmacists, infectious disease specialists, or microbiologist. Comparing response among respondents, registrars and senior registrars are more likely guided by these factors than the medical officers, a significant relationship was found in response to seeking advice from microbiologist and pharmacist between the designation of the respondent, as shown in table 4.6.1 and 4.6.2.

Table 4.6.1 Factors which influences attitude of antibiotics prescription among respondents in ABUTH Zaria

Factors influencing attitudes of antibiotics prescription	Response	
	Yes (%)	No (%)
Previous experience / training / knowledge	227 (97.2)	7 (2.8)
Seeking advice from a senior colleague	191 (76.1)	60 (23.9)
Seeking advice from an infectious disease specialists (IDS)	82 (32.7)	169 (67.3)
Seeking advice from microbiologists	116 (46.2)	135 (53.8)
Seeking advice from pharmacists	60 (23.9)	191 (76.1)
Use local guidelines	167 (66.5)	84 (33.5)
Lab result	187 (74.5)	64 (24.5)

Table 4.6.2 Relationship between designation of respondents and perception of factors that influences attitude of antibiotic prescription in ABUTH Zaria

Factors influencing attitude of antibiotics prescription	Medical officers (%)	Registrars (%)	Senior registrars (%)	p-value	Combine answers (%) n=251

Previous experience /training /knowledge	27 (11.1)	125 (51.2)	92 (37.7)	0.481	244 (97.2)
Seeking advice from a senior colleague	20 (10.5)	94 (49.2)	77 (40.3)	0.242	191(76.1)
Seeking advice from an infectious disease specialists (IDS)	10 (12.2)	36 (43.9)	36 (43.9)	0.217	82 (32.7)
Seeking advice from microbiologists	12 (10.3)	44 (37.9)	60 (51.7)	0.000	116 (46.2)
Seeking advice from pharmacist	8 (13.3)	22 (36.7)	30 (50.0)	0.026	60 (23.9)
Use local guidelines	19 (11.4)	80 (47.9)	68 (40.7)	0.217	167 (66.5)
Lab results	24 (12.8)	97 (51.9)	66 (35.3)	0.146	187 (74.5)

4.6.2 Attitude of respondents during antibiotics prescribing process in ABUTH Zaria

Respondents indicated high level of confidence in nine different scenario during antibiotics prescribing process, with 22.6% (52) being unconfident and 12.2% (28) uncertain in withholding antibiotics if patients has fever, as shown in table 4.6.3.

Table 4.6.3 Distribution of Confident level of respondents in nine different scenarios during antibiotics prescribing process in ABUTH Zaria

Statement	**Response (%)**		
	Confident	**Unconfident**	**Uncertain**
Formulating accurate diagnosis of sepsis or infection.	233 (94.4)	10 (4.0)	4 (1.6)
Withholding antibiotics if patient has fever	150 (65.2)	52 (22.6)	28 (12.2)
Selecting the correct antibiotics	232 (95.5)	10 (4.1)	1 (0.4)
Choosing the correct dose and interval of administration	233 (95.1)	10 (4.1)	2 (0.8)
Using combination therapy if appropriate	232 (95.1)	8 (3.3)	4 (1.6)
Choosing between intravenous and oral administration	236 (96.0)	9 (3.7)	1 (0.4)
Interpreting microbiological results	231 (93.9)	10 (4.1)	5 (2.0)
Planning to stop antibiotic treatments after investigation.	221 (91.0)	11 (4.5)	11 (4.5)
Planning duration of antibiotics treatment	227 (92.7)	15 (6.1)	3 (1.2)

4.6.3 Knowledge of potential intervention to improve antibiotics prescription

Respondents indicated educational session on prescription and availability of local or national guideline as most helpful in improving prescription of antibiotics while, speaking to a pharmaceutical representative and restriction of prescription of all antibiotics as unhelpful in improving antibiotics prescription, as show in table 4.6.4.

Table 4.6.4 interventions considered helpful in improving rational antibiotics prescription among respondents in ABUTH Zaria

Potential intervention to improve antibiotics prescription	Helpful (%)	Unhelpful (%)
Educational session on prescription	242 (96.4)	1(0.4)
Availability of local/national guideline	234 (96.8)	1 (0.4)
Availability of local/national resistance data	227 (90.4)	7 (2.8)
Computer- aided prescription	104 (41.4)	43 (17.1)
Presence of an antimicrobial management team	215 (85.7)	2 (0.8)
Readily accessible microbiological advice	230 (91.7)	1 (0.4)
Readily accessible advice from infectious disease physician	233 (92.8)	1 (0.4)
Readily accessible advice from pharmacists	195 (77.7)	7 (2.8)
Readily accessible advice from infection control team	228 (90.8)	1 (0.4)
Advice from senior colleague	226 (90.0)	1 (0.4)
Speaking to a pharmaceutical representatives	94 (37.5)	47 (18.7)
Restriction of prescription of certain antibiotics	176 (70.1)	22 (8.8)

Restriction of prescription of all antibiotics	70 (27.9)	134 (53.4)
Regular audit and feedback on antibiotic prescription on the ward	226 (90.0)	5 (2.0)

4.6.4 Relationship on knowledge of potential intervention to improve antibiotics prescription among respondents in ABUTH, Zaria

A significant relationship was found between the designation of respondents on the indication of educational session on antibiotics prescription as most helpful intervention in improving antibiotic prescription ($p = 0.015$), response by the medical officers was responsible for the significant difference observed as shown in table 4.6.5.

Table 4.6.5 Interventions considered to improve rational antibiotics prescription among respondents in ABUTH Zaria

Potential intervention to improve antibiotics prescription	Medical officers	Registrars	Senior registrars	p-value	Combine answers (%)
Educational session on prescription	25 (10.3)	125 (51.7)	92 (38.0)	0.015	242 (96.4)
Availability of local/national guideline	25 (10.3)	127 (52.3)	91 (37.4)	0.436	234 (96.8)
Availability of local/national resistance data.	23 (10.1)	116 (51.1)	88 (38.8)	0.067	227 (90.4)
Computer- aided prescription	14 (13.5)	55 (55.8)	32 (30.8	0.44	104 (41.4)
Presence of an antimicrobial management team	22 (10.2)	111 (51.6)	82 (38.1)	0.395	215 (85.7)
Readily accessible microbiological advice	23 (10.1)	119 (51.7)	88 (38.3)	0.628	230 (91.7)
Readily accessible advice from infectious disease physician	25 (10.7)	120 (51.5)	88 (37.8)	0.626	233 (92.8)
Readily accessible advice from pharmacist	21 (10.8)	102 (52.3)	72 (36.9)	0.654	195 (77.7)
Readily accessible advice from infection control team	25 (11.0)	121(53.1)	82 (36.0)	0.413	228 (90.8)
Advice from senior colleague	25 (11.1)	117 (51.8)	84 (37.2)	0.432	226 (90.0)
Speaking to a pharmaceutical representatives	11 (11.4)	52 (55.3)	31 (33.0)	0.207	94 (37.5)
Restriction of prescription of certain antibiotics	20 (11.4)	90 (51.1)	66 (37.5)	0.860	176 (70.1)
Restriction of prescription of all antibiotics	7 (10.0)	34 (48.6)	29 (41.4)	0.599	70 (27.9)
Regular audit and feedback on antibiotic prescription on the ward	21 (9.3)	118 (52.2)	87 (38.5)	0.693	226 (90.0)

CHAPTER FIVE

DISCUSSION

This study found out that of the 251 resident doctors who responded, their ages ranged between 25-50years with a mean age of 35years, only 42.2% had previously worked in infectious disease unit (IDU). Though 84.5% of the respondents acknowledge they were aware of rational drug use (RDU), of those who responded 50.8% indicated their major source of information about RDU was through lectures, only 3.2% had an excellent definition of RDU. A higher percentage (92.8%) of the respondents indicated they are aware of the national drug formulary (NDF), a few (40.2%) respondent uses the NDF to aid their prescription, This finding is consistent with the findings of Chedi *et al.* (2010), in which only one out of the six healthcare institutions studied has a hospital formulary, the remaining five had neither a Hospital formulary nor the national essential drug list (NEDL). Adebayo and Hussain (2009) also noted this in his study in which 96.6% of his respondents in a Nigerian military hospital were aware of the existence of the national essential drug list (NEDL). Although 92.8% of the respondents acknowledged antibiotics resistance as a national problem, 79.1% and 85.2% indicated it as problem in the hospital and their clinical practice respectively, These findings are consistent with findings in France and Scotland by Pulcini *et al.* (2010), in which 95% of respondents agreed that antibiotics resistance was a national problem while 63% believed it was a problem in

their practice, but higher than the value reported Arjun *et al.* (2004), in which 87% of his respondents agreed that resistance was a national problem but only 55% believed it was a problem in their hospital. Higher level training with years of practice appears to be associated with a better awareness of antibiotics resistance in this study as a significant difference was observed in the response of the respondents ($p<0.05$), the difference in the knowledge of senior registrars and medical officers is probably responsible for the significant difference observed, with only 55.6% (15) of the medical officers indicating antibiotics resistance as a hospital problem ($\chi^2=15.899$; df=4; p=.003; n=249). This is similar to the study of Wester *et al.* (2002), which found that previous personal experience with antibiotics resistance was the best predictor of a better recognition of the problem of antibiotics resistance in practice.

Attitudes regarding the different components of the antibiotic prescribing process varied according to the nine different scenarios made available in the questionnaire. Respondents were confident in all the scenarios including making a diagnosis, but less confident in not prescribing antibiotics if patients had fever which shows a significant relationship among the level of training of respondent ($\chi^2= 6.626$; df=2; p=0.036; n=202). This findings is comparable with the finding of Pulcini *et al.* (2010), however the high level of confidence found in this study in making a presumptive diagnosis for antibiotics prescription is not supported by evidence, as misdiagnosis has been shown to be the leading cause of unnecessary antibiotic prescriptions (Pulcini *et al.*, 2007).

Educative interventions to improve antibiotic prescription and use of local/national guideline was indicated as being most helpful potential intervention to improve antibiotics prescription rather than restricting antibiotic use, more so, restriction of

prescription of some antibiotics was perceived as potentially helpful by the majority of respondents, while restriction of prescription of all antibiotics and speaking to a pharmaceutical representative was indicated as unhelpful. However availability of advice from an infectious diseases specialist and a microbiologist as well as audit and feedback strategies were also highly valued by respondents. These findings are consistent with an Australian study surveying medical staff attitudes to an antibiotic approval and stewardship programme (Banan *et al*., 2009), and also noted by Pulcini *et al.* (2010).

Majority (79.7%) of the respondents do not know the hospital antimicrobial susceptibility pattern, 89.6% do not know national prevalence of *staphylococcus aureus* resistance to methicillin and 90% do not know *E-coli* resistance to trimethoprim, the national prevalence as found by Adebayo *et al.* (2011), ranges between 1.5-20% in his study on methicillin resistance *staphylococcus aureus* (MRSA) in Nigeria. Only few respondents (13.6%) have knowledge of the prevalence of inappropriate antibiotics prescriptions, though lower, this finding is also noted by Pulcini *et al.* (2010), in which only 31% of his respondents in France gave the correct answer for prevalence of antibiotic misuse. Any antibiotic prescription between 21%-50% is considered inappropriate by WHO (Pulcini *et al.*, 2007). The hospital probably does not have a regulatory policy on antibiotics prescription, as evident in this study in which a few percentage 12.7% and 22.3% of the respondent agreed to give antibiotics in disease such as malaria and upper respiratory tract infection (common cold) respectively. A few (22.7%) and (35.1%) of the respondents acknowledged excessive use of antibiotics in live stock and poor hand hygiene as unimportant source of resistance, all these factors are potential source of

resistance as indicated by the WHO fact sheet 2011 in containing antimicrobial resistance.

Finally 97.2% and 76.1% of the respondents indicated previous experience and advice from senior colleague as a factor which influences their attitude of antibiotics prescription, the three measures rated as most helpful intervention for improving antibiotics prescription were educational session on prescription (96.4%), availability of local/national guide line (96.8%), and advice from infectious disease physician (92.8%), this finding is consistence with the findings noted by Pulcini *et al.* (2010) in which over 95% of his respondents agreed that educational session and availability of national guidelines were most helpful intervention for improving antibiotics prescription.

CHAPTER SIX

SUMMARY, LIMITATIONS, CONCLUSION AND RECOMMENDATIONS

6.1 SURMMARY

World health organization (WHO) defined rational use of drug as: use of medicines which requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community (WHO, 1985).

The general objective of this study was to evaluate the extent of rational drug use with respect to knowledge attitude and practice of antibiotics prescription among resident doctors and medical officers in Ahmadu Bello University Teaching Hospital, Zaria Nigeria, and to make recommendations for its improvement.

A multi stage sampling technique with proportional allocation of resident doctors from various departments for the study was employed, after which simple random sampling technique by balloting was used to select respondent per department. Approval of the research project by the Institutional Review Board of ABUTH was obtained vide letter, after which the survey questionnaire was distributed to eligible of resident doctors and collected back over four weeks, a total of 309 sample size was estimated, of which 251

residents responded from seventeen (17) different departments, the data obtained were collected, collated and analyzed for identification of areas requiring recommendations.

Major findings of the research were, a higher percentage of respondents 84.5% acknowledged they were aware of RDU, while 92.8% indicated they were aware of NDF, but only 40.2% routinely use NDF to aid their prescription.

Majority of the respondents do not know the hospital antimicrobial susceptibility pattern. 64.7% of the respondents believed it is the responsibility of the doctors to explain to patients how to take the antibiotic prescribed, this show a significant relationship between designation of respondents ($p<0.038$).

Majority of the respondents acknowledge antibiotics resistance as a national problem, a problem in clinical practice, and a problem in the hospital. A significant relationship ($p<0.003$) was found in the respondents response that antimicrobial resistance was a problem in the hospital. Only few respondent were found to have the knowledge of WHO prevalence of inappropriate antibiotics use, this shows a significant relationship with respect to level of training of respondents, ($p<0.035$).

Four factors were considered as potential causes of antibiotics resistance, too low dose of antibiotics prescription, too many broad spectrum of antibiotics prescription, and too long duration of antibiotics, a significant relationship was found on their perception of long duration of antibiotics usage ($p<0.022$) as an important cause of antibiotics resistance.

Respondents indicate educational session on prescription and availability of local or national guideline as most helpful intervention in improving antibiotics prescription,

while speaking to pharmaceutical representative and restriction of prescription of all antibiotics as unhelpful in improving antibiotics prescription.

6.2 LIMITATIONS

This study however has some limitation among which is the possibility that respondents may give socially desirable answers instead of revealing their true options, this is minimized by ensuring complete respondent confidentiality. Secondly non availability of local research documents for comparability of finding, which call for comparison with international journal whose tool, was adapted for research. Some findings in the research may have also supported the internal validity of the research for instance a high percentage (81.7%) of the respondents said they had no training on antibiotic prescription in the past year, while 78.5% said they were not restricted in the prescription of any antibiotics and 53.4% indicated restriction of prescription of all antibiotics as unhelpful. 37.5% respondents rated the value of accessible advice from a pharmaceutical representative as being only helpful in improving antibiotic prescription, despite the perceived evidence of what would be regarded as a more desirable answer. The 95% confident interval for the combine answer is quite narrow for a research like this, thereby strengthening the confidence of the findings of this research, the varied response from various specialties on various variables of the research tools suggest that the answer given by the respondent is a true reflection of practice.

6.3 CONCLUSION

Repeated calls for better regulation of medicines must not obstruct appropriate access, antibiotic use will continue to grow in low and middle-income countries to meet underserved needs. Such increasing use must therefore be tied to rational use. Improved drug access without significant improvements in appropriate use will have dire consequences, with continued emergence of "superbugs" and untreatable infections. More so improvements in the appropriate use of antibiotics generally reduce health costs as the majority of antibiotic use in most communities is unnecessary.

This formative study has confirmed the presence of known irrational antibiotics prescribing practices and has highlighted areas which should be accorded priority in intervention programme.

- Adherence to the use of NDF in aiding prescription.
- Educative interaction to improve antibiotics prescription and knowledge of prevalence or inappropriate antibiotic.
- Establishment of hospital antibiogram for antimicrobial susceptibility.
- Establishing a regulatory policy on antibiotics prescription.
- Surveillance mechanism to monitor rational antibiotics prescription.

While standard treatment guidelines and rational drug use are important steps, this research corroborates the proposition that these measures in themselves are not sufficient to reduce inappropriate prescription (Hogerzeil, 1994 and Okwaare *et al.,* 1994).

Containing antimicrobial resistance is the theme of world health day 2011. The world health organization is developing a comprehensive policy package for health ministries addressing

nearly all stakeholders. This should be an opportunity to launch sustainable action to contain resistance, to raise awareness, similarly to track and contain spread of resistance with improved information and better clinical decision support through the development and use of bedside diagnostics.

6.4 RECOMMENDATIONS

It is therefore recommended that in order to combat antibiotics resistance in our hospital settings, there should be an implementation of limited regulation, development of sustainable hospital antibiogram and local guideline should be adopted by the hospital through policy formulation by the hospital managements and stakeholders.

Adequate knowledge in antibiotics prescription should be considered as a challenge and be included as part of continue medical education training for medical doctors by medical and dental council of Nigeria.

Formation of drugs and therapeutics committees in hospital to monitor rational drug use (INRUD).

Quality improvement intervention using an audit and feedback methods are likely to be successful as a surveillance mechanism to monitor rational antibiotics prescription and curb antimicrobial resistance if implemented by the hospital or a national regulatory body such as NAFDAC, as they will combine all factors valued by the respondents in order to improve prescribing practices of antibiotics.

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APPENDICES

APPENDIX 1

Questionnaire

DEPARTMENT OF PHARMACOLOGY AND THERAPEUTHICS, AHMADU BELLO UNIVERSITY, ZARIA

RATIONAL DRUG USE: KNOWLEDGE, ATTITUDE AND PRACTICE OF ANTIBIOTICS PRESCRIPTION AMONG RESIDENT DOCTORS IN AHMADU BELLO UNIVERSITY TEACHING HOSPITAL [A.B.U.T.H.] ZARIA, NIGERIA.

Dear colleague

Kindly spare sometime to complete this questionnaire as appropriate.

NOTE: ALL information given in the questionnaire shall be treated with strict confidentiality and used

Thank you. **Researcher:** Dr Popoola Z.B.

General Information

1. Age……

2. Sex. Male ☐$_1$ **Female** ☐$_2$

3. Designation. Medical Officer ☐$_1$ Junior Registrar ☐$_2$ Senior Registrar ☐$_3$

4. How many years have you been in medical practice? .....

5. How many years have you been in residency training? .....

6. What is your specialty?

Internal Medicine ☐$_1$	Surgery ☐$_2$
Paediatrics ☐$_3$	Anaesthesia ☐$_4$
Obstetrics / Gynaecology ☐$_5$	Psychiatry ☐$_6$
Microbiology ☐$_7$	ophthalmology ☐$_8$
Orthopaedics ☐$_9$	haematology ☐$_{10}$
Radiology ☐$_{11}$	community medicine ☐$_{12}$
Chem. Pathology ☐$_{13}$	Oncology ☐$_{14}$
Pathology ☐$_{15}$	Medical officer ☐$_{16}$
	Family medicine☐$_{17}$

7. Have you previously worked on an Infectious diseases ward?
(Either as a, medical officer, junior or senior resident)? Yes ☐$_1$ No☐$_2$

Knowledge/Decision making

8. Do you know about rational drug use? Yes☐$_1$ No☐$_2$

9. If yes what is your source of information?

1. Lecture ☐$_1$
2. Residency training ☐$_2$
3. Seminar ☐$_3$
4. Work shop ☐$_4$
5. Others specify …… ☐$_5$

10. My definition of rational drug use Is……
……
……
……
……

11. Do you know about Essential Drug List [EDL]? Yes☐$_1$ No☐$_2$

12. Do you know about National Drug Formulary [NDF]? Yes☐$_1$ No☐$_2$

12. Do you use NDL or NDF routinely in prescription? Yes☐$_1$ No☐$_2$

13. Have you prescribed an antibiotic within the past 6 months? Yes☐$_1$ Go to question 14
No☐$_2$ Go to question 20

14. How many prescriptions for antibiotics have you written In the last 7 days?
≤ 2 ☐$_1$
3 to 5 ☐$_2$
≥5 ☐$_3$

15. Do you explain to your patients how to take the antibiotics medication you prescribed?
Yes☐$_1$ No☐$_2$

16. Who do you think should explain to patients how to take medication?
Doctor ☐$_1$
Pharmacist☐$_2$
Not sure ☐$_3$

17. Do you know the hospital antimicrobial susceptibility pattern?
Yes ☐$_1$
No ☐$_2$

18. How confident do you feel in the following scenarios when prescribing an antibiotic by yourself?

	Very unconfident	Unconfident	Confident	Very Confident	Uncertain
• **Making an accurate diagnosis of infection /sepsis?**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Not prescribing an antibiotic if the patient has fever or when you are not sure about your diagnosis**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Choosing the correct antibiotic**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Choosing the correct dose and interval of administration**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Using a combination therapy if appropriate**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Choosing between intravenous [IV] and Oral [PO] administration**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Interpreting microbiological results**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Planning to streamline/stop the antibiotic treatment according to clinical evolution and investigations**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$
• **Planning the duration of the antibiotic treatment**	☐$_1$	☐$_2$	☐$_3$	☐$_4$	☐$_5$

19. What influences or guides your prescribing decision?

Tick all that apply

- **Previous experience/knowledge/training** ☐1
- **Seeking advice from a senior colleague** ☐2
- **Seeking advice from an infectious disease specialist** ☐3
- **Seeking advice from a microbiologist** ☐4
- **Seeking advice from a pharmacist** ☐5
- **Use of local/national guidelines/policies/protocols** ☐6
- **Laboratory result** ☐7
- **Not sure?** ☐8
- **Other……..**

Please specify

Perceived importance of the problem of antibiotic resistance

	Yes	No	Unsure
20. Is antibiotic resistance a national problem?	☐1	☐2	☐3
Is antibiotic resistance a problem in your hospital?	☐1	☐2	☐3
Is antibiotic resistance a problem in your clinical practice?	☐1	☐2	☐3

21. How often do you think *E. coli is* resistant to trimethoprim in the community?

<5% ☐1
5-20% ☐2
21-50% ☐3 Not sure ☐5
>50% ☐4

22. How often do you think *S.aureus is* resistant to methicillin in your hospital?

<5% ☐1
5-20% ☐2
21-50% ☐3 Not sure ☐5
>50% ☐4

Antibiotic prescribing practice

23. What proportion of antibiotics prescription do you consider to be unnecessary or inappropriate in your hospital?

<10% ☐1
11-20% ☐2
21-50% ☐3 Not sure ☐5
>50% ☐4

24.in which of the following conditions do you consider antibiotics prescription appropriate?

Malaria fever ☐1
Enteric Fever ☐2
Upper respiratory tract infection (common cold) ☐3
Lower respiratory tract infection ☐4

25. The following scenarios are potential causes of resistance; please identify which, in your opinion, are the most or least important.

	Very important	Important	Neutral	Unimportant	Very Unimportant
• **Too many antibiotic prescriptions**	☐1	☐2	☐3	☐4	☐5
• **Too many broad spectrum antibiotics used**	☐1	☐2	☐3	☐4	☐5
• **Too long durations of antibiotic treatment**	☐1	☐2	☐3	☐4	☐5

• **Too low a dose of antibiotics**	☐1	☐2	☐3	☐4	☐5
• **Excessive use of antibiotics in livestock**	☐1	☐2	☐3	☐4	☐5
• **Poor hand hygiene**	☐1	☐2	☐3	☐4	☐5
• **Not removing the focus of infection (e.g. medical devices or catheters)**	☐1	☐2	☐3	☐4	☐5
• **Paying too much attention to pharmaceutical representatives / advertising**	☐1	☐2	☐3	☐4	☐5

Attitudes about current and potential interventions to evaluate the problem of antibiotic prescription

26. What measures do you think would be the most helpful in improving antibiotic prescription?

	Very helpful	Helpful	Neutral	Unhelpful	Very unhelpful
• **Educational sessions on prescribing**	☐1	☐2	☐3	☐4	☐5
• **Availability of local / national guidelines / policies / protocols**	☐1	☐2	☐3	☐4	☐5
• **Availability of local/national resistance data**	☐1	☐2	☐3	☐4	☐5
• **Computer-aided prescribing**	☐1	☐2	☐3	☐4	☐5
• **Presence of an antimicrobial management team**	☐1	☐2	☐3	☐4	☐5
• **Readily accessible microbiological advice**	☐1	☐2	☐3	☐4	☐5

• **Readily accessible advice from infectious disease [ID] physician**	☐1	☐2	☐3	☐4	☐5
• **Readily accessible advice from a pharmacist**	☐1	☐2	☐3	☐4	☐5
• **Readily accessible advice from infection control team**	☐1	☐2	☐3	☐4	☐5
• **Advice from senior colleagues**	☐1	☐2	☐3	☐4	☐5
• **Speaking to a pharmaceutical representative**	☐1	☐2	☐3	☐4	☐5
• **Restriction of prescription of certain antibiotics**	☐1	☐2	☐3	☐4	☐5
• **Restriction of prescription of all antibiotics**	☐1	☐2	☐3	☐4	☐5
• **Regular audit and feedback on antibiotic prescribing on your ward**	☐1	☐2	☐3	☐4	☐5

27. Are you restricted from prescribing certain class of antibiotic? Yes☐ No ☐ Not sure ☐3

28 If yes, which class? Penicillins ☐1 **Chloramphenicol** ☐2 **Macrolides** ☐3 **Quinolone** ☐4 **Tetracycline** ☐5 **Cephalosporins** ☐6 **others please specify …….**

29. last year, did you receive any training on antibiotic Prescribing? Yes ☐1 No ☐2

30 If yes, how was the training delivered? **Tick all that apply**

Lecture ☐1 Workshop ☐2 Web based learning ☐3

Self directed learning☐ 4 Informal educations in the clinical work place ☐5

Thank you

APPENDIX II

POSTGRADUATE OFFICE

FACULTY OF MEDICINE

AHMADU BELLO UNIVERSITY TEACHING HOSPITAL

SHIKA - ZARIA, NIGERIA

P.M.B. 06 Samaru Zaria
Phone: 069 -551399
Fax: 069 - 555001
E-mail: abuthpg@yahoo.com

*Your Ref:*_____

Our Ref: ABUTH/PGO/COMM/9

Date: 23rd Sept. 2011

Popoola Zakariyya Bashir
Dept of Pharmacology
ABU Teaching Hospital
Zaria

ETHICAL CERTIFICATE

Your application for ethical clearance on your proposal titled" **RATIONAL DRUG USE: KNOWLEDGE ATTITUDE AND PRACTICE OF ANTIBIOTICS PRESCRIPTION AMONG RESIDENT DOCTORS AND MEDICAL OFFICERS IN AHMADU BELLO UNIVERSITY TEACHING HOSPITAL ZARIA, (ABUTH) NIGERIA."** refers.

This is to convey ethical approval for you to commence the study. You are required to update the committee on progress of your work.

Thank you.