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Assessment of Antibiotic Prescribing by General Medical Praticitioners in Health Care Facilities in Okada and Environs

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ABSTRACT

INTRODUCTION: Antibiotics are important medicines that fight infections caused by bacteria. Inappropriate and irrational use of these drugs provides favorable condition for antimicrobial resistance and therefore jeopardizes the positive therapeutic outcome to the society.

OBJECTIVE: This study is aimed at assessing the rational use of antibiotics by general medical practitioners in healthcare facilities in Okada and environs and also to evaluate the frequency of antibiotic prescription in these healthcare facilities.

METHOD:A retrospective method of drug evaluation study was carried out to assess the rationaluse of antibiotics by General Medical Practitioners in Okada and environs.

RESULT: From a population size of 62,000 patients, 34,073 patients were prescribed antibiotics; General hospital Usen having the largest number (12,121) and Primary Health Care Okada having the smallest (3,579). Various classes of antibiotics were administered in the treatment of microbial infections which indicates the level of irrational antibiotic prescription here.

CONCLUSION: This study has shown that very high level of antibiotics is prescribed by General Medical Practitioners in Okada and environs, of which most of the drugs were prescribed irrationally. The hazards of irrational prescribing and antibiotics misuse should be made known to the prescribers and patients.

Keywords: Antibiotics, Antimicrobials, Irrational, Non-responsive, Resistance.

Definition of Terms

Antibiotic: any substance that can destroy or inhibit the growth of bacteria and similar micro-organisms.

Bactericidal: any substance that has the ability to kill bacteria, especially one that is otherwise harmless.

Diagnosis: the identification of the nature and cause of an illness.

Frequency: the rate of occurrence of anything, the relationship between incidence and time period.

General Health Practitioners: practitioners who treat acute and chronic illnesses and provide preventive care and health education.

Healthcare: the prevention, treatment and management of illness or the preservation of mental and physical well-being through the services offered by the medical, nursing and allied health professions.

Hygiene: those conditions and practices that promote and preserve health.

Irrational: not rational, unfounded or not making sense.

Medication: a medicine, or all the medicine regularly taken by a patient for therapeutic benefits.

Micro-organism: an organism that is too small to be seen by the unaided eye; especially a single-celled organism, such as bacterium.

Polypharmacy: the use of multiple drug in a single prescription. The use of multiple concurrent disorders in the same patient, especially the indiscriminate prescription of many drugs to the elderly and younger children.

Prescription: a healthcare program that governs the plan of care for an individual patient and is implemented by a qualified practitioner.

Primary Healthcare: defined by the World Health Organization in 1978 is: essential healthcare; based on practical, scientifically sound and socially acceptable method and technology; universally accessible to all in the community through their full participation; at an affordable cost; geared towards self-reliance and self- determination.

Rational: logically sound, not contradictory or otherwise absurd.

Replication: process by which an object, person, place or idea may be copied, mimicked or reproduced.

Resistance (antibiotic): a form of drug resistance whereby some (or less commonly, all) sub-populations of microorganism are able to survive after exposure to one or more antibiotics.

Self-Medication: the use of medicinal products by individuals to treat self- recognized disorders or symptoms, or the intermittent or continuous use of a medication prescribed by a physician for chronic or recurring diseases or symptoms.

Secondary Healthcare: the general health services available in hospitals. It is an intermediate level of health care that includes diagnosis and treatment, performed in a hospital having specialized equipment and laboratory facilities.

Sensitivity test: the ability of an organism to respond to external stimuli or a chemical substance.

Synergy: the behavior of a system that cannot be predicted by the behavior of its parts; in pharmacology, it is an interaction between drugs where the effects are stronger than their mere sum

1. INTRODUCTION

What Are Antibiotics?

In the strictest sense, antibiotics are antibacterial substances produced by various species of microorganism (bacteria, fungi and actinomycetes) that suppress the growth of other microorganisms. Common usage often extends to the term antibiotics to include synthetic antimicrobial agents such as Sulfonamides and Quinolones. Antibodies differ markedly in physical, chemical, and pharmacological properties, in antimicrobial spectra, and in mechanisms of action. Knowledge of molecular mechanism of bacterial replication has greatly facilitated the rational development of compounds that can interfere with the replication.[1]

Classification and Mechanism of Action: Antimicrobial agents are classified basedon chemical structure and proposed mechanism of action, as follows

(1) Agents that inhibit synthesis of bacteria; cell walls, including the B-lactam class (e.g., penicillins, cephalosporins and carbapenems) and similar agents such as cycloserine, vancomycin and bacitracin;
(2) Agents that act directly on the cell membrane of the microorganism, increasing permeability and leading to leakage of intracellular compounds, including detergents such as polymyxin; polyene antifungal agents (e,g., nystatin and amphotericin B) which bind to cell-wall sterols; and the lipopeptide daptomycin;
(3) Agents that disrupt the function of 30S or 50S ribosomal subunits to reversibly inhibit protein synthesis, which generally are bacteriostatic (e.g., chloramphenicol, the tetracyclines, erythromycin, clindamycin, streptogramins, and linezolid);
(4) Agents that bind to the 30S ribosomal subunit and alter protein synthesis which generally are bactericidal (e.g., the aminoglycosides):
(5) Agents that affect bacterial nucleic acid metabolism, such as the rifamycins (e.g., rifampin and rifabutin), which inhibit RNA polymerase, and the Quinolones, which topoisomerases; and
(6) The antimetabolites, including trimethoprim and the Sulfonamides, which block essential enzymes of folate metabolism.

The precise mechanism of action of some antimicrobial agents is still unknown. Antimicrobial agents are among the most commonly used and misused of all drugs. The inevitable consequence of the widespread use of antimicrobial agents has been the emergence of antibiotic-resistant pathogens, fueling an ever-increasing need for

new drugs. However, the pace of antimicrobial drug development has slowed dramatically, with only a handful of new agents, few of which are novel, being introduced into clinical practice each year. Reducing inappropriate antibiotic use is thought to be the best way to control resistance. Although awareness of the of the consequences of antibiotic misuse is increasing, over prescribing remains widespread driven largely by patient demand, time pressure on clinicians and diagnostic uncertainty. If the gains in the treatment of infectious diseases are to be preserved, clinicians must be wiser and more selective in the use of antimicrobial agents.[1]

Bacterial Resistance to Antimicrobial Agents. The recent emergence of antibiotic resistance in bacterial pathogens, both nosocomially and in the community, is a very serious development that threatens the end of the antibiotic era. Today more than 70% of the bacterial associated with hospital-acquired infections in the United States are resistant to one or more of the drugs previously used to treat them. Penicillin- resistant strains of *pneumococci* account for 50% or more of isolates in some European countries, and the proportion of such strains is rising in the United States.

The worldwide emergence of *Haemophilus* and *genecocci* that produce b-lactamase is a major therapeutic problem. Methicillin-resistant strains of *Staphylococcus aureus* are endemic in hospitals and are isolated increasingly from community- acquired infections. Multiple-drug-resistant strains of S.*aureus* with intermediate susceptibility to antibiotics and high level resistance to

vancomycin have been reported. There now are strains of *enterococci*, *Pseudomonas*, and *Enterobacter* that are resistant to all available antibiotics. Epidemics of multiple-drug-resistant strains of Mycobacterium tuberculosis have been reported in the United States. The rampantspread of antibiotic resistance mandates a more responsible approach to antibiotic use.

For an antibiotic to be effective, it must reach its target in an active form, bind to the target and interfere with its function. Accordingly, bacterial resistance to an antimicrobial agent is attributable to three general mechanisms: (1) The drug does not reach its target, (2) the drug is not active, or (3) the target is altered.[2]

Optimal and judicious selection of antimicrobial agents for the therapy of infectious diseases requires clinical judgement and detailed knowledge of pharmacological and microbiological factors. Antibiotics have three general uses: empirical therapy, definitive therapy, and prophylactic or preventive therapy. When used as empirical, or initial therapy, the antibiotic should cover all the likely pathogens because the

infecting organism(s) has not yet been defined. Either combination therapy or, preferably, treatment with a single broad-spectrum agent maybe employed. However, once the infecting microorganism is identified, definitive antimicrobial therapy should be instituted with a narrow-spectrum, low-toxicity agent to complete the course of treatment. Failure to document the bacterial etiology so that a narrow-spectrum agent can be used and failure to narrow the spectrum when an organism has been identified are two common ways in which antibiotics are misused. The first consideration in selecting an antimicrobial agent is whether it is even indicated.

Initiation of optimal empirical antibiotic therapy requires knowledge of the most likely infecting microorganisms and their susceptibilities to antimicrobial drugs. Selection of an antibiotic regimen should rely on the clinical presentation, which may suggest the specific microorganism, and knowledge of the microorganisms most likely to cause specific infections in a given host. In addition, simple and rapid laboratory techniques are available for the examination of infected tissues. Whenever the clinician is faced with initiating therapy on a presumptive bacteriological diagnosis, cultures of the presumed site of infection and blood, if bacteremia is a possibility, should be taken prior to the institution of drugs therapy. For definitive therapy, the regimen should be changed to a more specific and narrow- spectrum antimicrobial agent once an organism has been isolated and results of susceptibility tests are known.[3]

Pharmacokinetic Factors. In vitro activity, although critical, is only a guide as to whether an antibiotic is likely to be effective for an infection. Successful therapy also depends on achieving a drug concentration that is sufficient to inhibit of kill bacteria at the site of the infection without harming the patient. To accomplish this therapeutic goal, several pharmacokinetic and host factors must be evaluated. The location of the infection to a large extent may dictate the choice of drug and the route of administration. Traditionally, the dose and dosing frequency of antibiotics have been selected to achieve antibacterial activity at the site of the infection for most of the dosing interval.

Knowledge of the status of the individual patient's renal and hepatic function also is essential, especially when excessive plasma or tissue concentrations of the drugs may cause serious toxicity.

Route of Administration- While oral administration is preferred whenever possible, parenteral administration of antibiotics usually is recommended in seriously ill patients in whom predictable concentrations of drug must be achieved.

Host Factor; Innate host factors can be the prime determinants not only of the type of drug selected but also of its dosage, route of administration, risk and nature of untoward effects, and therapeutic effectiveness.

Host Defense Mechanisms: A critical determinant of the therapeutic effectiveness of antimicrobial agents is the functional state of host defense mechanisms. Both humoral and cellular immunity are important. Inadequacy of type, quality, and quantity of the immunoglobulins; alteration of the cellular immune system; or a qualitative or quantitative defect in phagocytic cells may result in therapeutic failure despite the use of otherwise appropriate and effective drugs. In the immunocompetent host, merely halting multiplication of the microorganisms with a bacteriostatic agent frequently is sufficient to cure the infection. If host defenses are impaired, bacteriostatic activity may be inadequate, and a bactericidal agent may be required for cure. Examples include bacterial endocarditis, where phagocytic cells are absent from the infected site; bacterial meningitis, where phagocytic cells are ineffective because of lack of opsonins in CSF; and disseminated bacterial infections in neutropenic patients, where the total mass of phagocytic cells is reduced.

Local Factors: cure of an infection with antibiotics depends on an understanding of how local factors at the site of infection affect the antimicrobial activity of the drug.

Antimicrobial activity may be reduced significantly in pus, which contains phagocytes, cellular debris, and proteins that can bind drugs or create conditions unfavorable to drug action. Low pH, characteristic of the fluid in abscesses and in other confined infected sites (pleural space, CSF, and Urine), and anaerobic conditions can reduce the antimicrobial activity of some agents markedly, particularly the aminoglycosides.

The presence of a foreign body in an infected site markedly reduces the likelihood of successful antimicrobial therapy. Prosthetic material (e.g., prosthetic cardiac valves, prosthetic joints, pacemakers, vascular grafts and various vascular and CNS shunts) promotes formation of a bacterial biofilm that impairs phagocytosis. Certain antibiotics e.g., fluoroquinolones, isoniazid, trimethoprim-sulfamethoxazole, and rifampin penetrates cells well and can achieve intracellular concentrations that inhibit or kill pathogens residing within cells.

Age- The age of the patient is an important determinant of antimicrobial drug pharmacokinetics. Mechanisms of elimination, especially renal excretion and hepatic biotransformation, are poorly developed in the new born, especially the premature infant. Failure to make adjustments for such differences can have

disastrous consequences. Elderly patients' clear drugs eliminated by the kidneys less well because of reduced creatinine clearance. They also may metabolize drugs less rapidly, predisposing them to elevated and potentially toxic concentrations of drugs when compared with younger patients. Elderly patients therefore are more likely to suffer toxicity at otherwise safe concentration of drugs, as is the case for aminoglycoside ototoxicity.

Development factors also may determine the type of untoward response to a drug.

Tetracycline bind avidly to developing teeth and bones, and their use in young children can result in retardation of bone growth and discoloration or hypoplasia of tooth enamel. Fluoroquinolones accumulate in the cartilage of developing bone, affecting its growth. Kernicterusmay follow the use of sulfonamides in new born infants because the class of drugs competes effectively with bilirubin for binding sites on plasma albumin. Achlohydria in young children and in the elderly or antacid therapy may alter absorption of orally administered antimicrobial agents (e.g., increased absorption of penicillin G and decreased absorption of ketoconazole and itraconazole)

Genetic Factors- certain genetic or metabolic abnormalities must be considered when prescribing antibiotics. A number of drugs (e.g., sulfonamides, nitrofurantoin, chloramphenicol, and nalidixic acid) may produce hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency. Patients who acetylate isoniazid rapidly may have subtherapeutic concentrations of the drug in plasma.

Pregnancy- Pregnancy may impose an increased risk of reaction to antimicrobial agents for both mother and fetus. Hearing loss in the child has been associated with the administration of streptomycin to the mother during pregnancy. Tetracyclines can affect the bones and teeth of the fetus. Pregnant women receiving tetracycline may develop fatal acute fatty necrosis of the liver, pancreatitis, and associated renaldamage. Pregnancy also may affect the pharmacokinetics of various antibiotics.

The lactating female can pass antimicrobial agents to her nursing child. Both nalidixic acid and the sulfonamides in breast milk have been associated with hemolysis in children with glucose-6-phosphate dehydrogenase deficiency. In addition, sulfonamides, even in the small amounts received from breast milk, may predispose the nursing child to kernicterus.

Drug Allergy- Antibiotics, especially b-lactams, are notorious for provoking allergicreactions. Patients with a history of atopy seem particularly susceptible to the

development of these reactions. Sulfonamides, trimethoprim, nitrofurantoin, and erythromycin also have been associated with hypersensitivity reactions, especially rash. A history of anaphylaxis (immediate hypersensitivity reactions) or hives and laryngeal edema (accelerated reaction) precludes use of the drug in all but extreme, life-threatening situations. Skin testing, particularly of the penicillin, may be of value in predicting life-threatening reactions. Antimicrobial agents, like other drugs, can cause drug fever, which can be mistaken for a sign of continued infection.

THERAPY WITH COMBINED ANTIMICROBIAL AGENTS

The simultaneous use of two or more antimicrobial agents is recommended in specifically defined situations based on pharmacological rationale. However, selection of an appropriate combination requires an understanding of the potential for interaction between the antimicrobial agents. Interactions may affect either the microorganism or the patient. Antimicrobial agents acting at different targets may enhance or impair overall antimicrobial activity. A combination of drugs also may have additive or super-additive toxicities. For example, Vancomycin given alone usually has minimal nephrotoxicity. However, when vancomycin is given with an aminoglycoside, the toxicity of the aminoglycoside is increased.

Indications for the Clinical Use of Combinations of Antimicrobial Agents-

Use of a combination of antimicrobial agents may be justified (1) for empirical therapy of an infection in which the cause is unknown, (2) for treatment of polymicrobial infections, (3) to enhance antimicrobial activity (i.e., synergism) for a specific infection, or (4) to prevent emergencies of resistance.

Disadvantages of Combination of Antimicrobial Agents- Disadvantages of antimicrobial combination include increased risk of toxicity from two or more agents, selection of multiple-drug-resistant microorganisms, eradication of normal host flora with subsequent super infection, and increased cost to the patient. Although antagonism of one antibiotic by another has been a frequent observation in vitro, well-documented clinical examples of this phenomenon are relatively rare. on the other hand, if achieving a bactericidal effect is critical for cure of the infection (e.g., meningitis, endocarditis, and gram-negative infections in neutropenic patients), such as antibiotic antagonism could adversely affect outcome.

MISUSE OF ANTIBIOTICS

The purpose of this introductory chapter has been to lay the groundwork for the maximally effective use of antimicrobial drugs. Therefore, a brief discussion of the misuse and over use of antimicrobial agents is in order. Organizations such as the Centers for Disease Controls and Prevention have outlined a number of steps to optimize the use of antimicrobial agents and to prevent drug resistance and the transmission of infections.

Treatment of Nonresponsive Infections- A common misuse of these agents is in infections that have been proved by experimental and clinical observation to be nonresponsive to treatment with antimicrobial agents. Most of the diseases caused by viruses are self-limited and do not respond to any of the currently available anti- infective compounds. Thus, antimicrobial therapy of measles, mumps, and at least 90% of infections of the upper respiratory tract and many GI infections is ineffective and, therefore, useless.

Therapy of Fever of Unknown Origin- Fever of undetermined cause may persist for only a few days to a week or for a longer period. Both of these are treated frequently and inappropriately with empirical antimicrobial agents. Fever of short duration, in the absence of localizing signs, probably is associated with undefined viral infections. Antimicrobial therapy is unnecessary, and resolution of fever occurs spontaneously within a week or less. Fever persisting for 2 or more weeks, commonly referred to as fever of unknown origin, has a variety of causes, of which only about one-quarter are infections. Some of these infections (e.g., tuberculosis or disseminated fungal infections) may require treatment with antimicrobial agents that are not used commonly for bacterial infections. Others such as occult abscesses, may require surgical drainage or prolonged courses of pathogen-specific therapy, as in the case of bacterial endocarditis. Inappropriately administered antimicrobial therapy may mask an underlying infection, delay the diagnosis, and by rendering cultures negative, prevent identification of the infectious pathogen.

Improper Dosage- Dosing errors, which can be the wrong frequency of administration or the use of either an excessive or a subtherapeutic dose, are common. Although antimicrobial drugs are among the safest and least toxic of drugs used in medical practice, excessive amounts can result in significant toxicities, including seizures (e.g., aminoglycosides), especially in patients with impaired drug excretion or metabolism. The use of too low a dose may result in treatment failure and is most likely to select for microbial resistance.

Inappropriate Reliance on Chemotherapy Alone- Infections complicated by abscess formation, the presence of necrotic tissue, or the presence of a foreign body often cannot be cured by antimicrobial therapy alone. Drainage, debridement, and removal of the foreign body are at least as important as the choice of antimicrobial agent.

Lack of Adequate Bacteriological Information- Antimicrobial therapy administered to hospitalized patients too often is given in the absence of supporting microbiological data. Bacterial cultures and Gram stains of infected material are obtained too infrequently, and the results, when available, often are discharged in the selection and application of drug therapy. Frequent use of drug combinations or drugs with the broadest spectra is a cover for diagnostic imprecision. The agents are selected more likely by habit than for specific indications, and the dosages employed are routine rather than individualized on the basis of the clinical situation, microbiological information, and the pharmacological considerations.[1,3]

PRESCRIPTION AND USE OF ANTIBIOTICS

In 1894, William Osier wrote 'But know also, man has an inborn craving for medicine…is one feature which distinguishes man the animal, from his fellow creatures. It is really one of the most serious difficulties with which we have to contend … the doctor's visit is not thought to be complete without a prescription.'

We live in a world heavily populated by microorganisms of astonishing diversity. Most of these exist in our external environment but certain classes are normally harbored within our bodies, especially colonizing mucosal surfaces. Depending on the circumstances, infectious disease can arise from organisms living exogenously or endogenously, and a knowledge of common pathogens at specific sites often provides a good basis for rational initial therapy. Therefore, antibiotics are important medicines,

they help fight infections that are caused by bacteria. Antibiotics resistance (when an antibiotic is no longer effective) is a major problem. Antibiotic resistance is driven by overusing antibiotics and prescribing them inappropriately. It is important that we use antibiotics the right way, to slow down resistance and make sure these life-saving medicines remain effective for us and future generations.[4]

If you think antibiotics resistance is not a problem or does not affect you, think again. A prominent example of the dangers of antibiotic resistance is the spread of methicillin-resistant *staphylococcus aureus* **(**MRSA). MRSA was once a concern only for people in the hospital, but newer form of MRSA is causing infections in healthy people in the community. Antibiotic resistance occurs when antibiotics nolonger work against disease-causing bacteria. These infections are difficult to treat and can mean longer lasting illnesses, more doctor visits or extended hospital stays, and the need for more expensive and toxic medications. Some resistant infections can even cause death. Although experts are working to develop new antibiotic and other treatments to keep pace with antibiotic resistant strains of bacteria, infectious organisms can adapt quickly. Hence, antibiotic-resistant bacteria will continue to bea global health concern – and using antibiotics wisely is important for preventing their spread.

Therefore, when is it important to use antibiotics? Antibiotics are effective against bacterial infections, certain fungal infections and some kinds of parasites. Antibiotics don't work against viruses. The list below shows some common illnesses and whether they are caused by bacteria or viruses. Taking an antibiotic when you have a viral infection will not make you feel better- and can contribute to antibioticresistance.

Bacterial infections

- Bladder infections
- Many wounds and skin infections
- Severe sinus infections that last longer than 2 weeks
- Some ear infections
- Strep throatViral infections
- Bronchitis
- Colds
- Flu (influenza)
- Most coughs
- Most ear infections
- Most sore throats
- Stomach flu (viral gastroenteritis)

The development of antimicrobial drugs represents one of the most important advances in therapeutics, both in the control or cure of serious infections and in the prevention and treatment of infectious complications of other therapeutic modalities such as cancer chemotherapy and surgery. However, evidence is overwhelming that antimicrobial agents are vastly overprescribed in outpatient settings in the united

states, and the availability of antimicrobial agents without prescription in many developing countries has-by facilitating the development of resistance-already severely limited therapeutic options in the treatment of life-threatening infections. Therefore, clinician should first determine whether antimicrobial therapy is warranted for a given patient. The specific questions one should ask including the following:

1. Is an antimicrobial agent indicated on the basis of clinical findings? Or is it prudent to wait until such clinical findings become apparent?
2. Have appropriate clinical specimens been obtained to establish a microbiologic diagnosis?
3. What are likely etiologic
4. What measures should be taken to protect individuals exposed to the index case to prevent secondary cases, and what measures should be implemented to prevent further exposure?
5. Is there clinical evidence (e.g., from clinical trials) that antimicrobial therapywill confer clinical benefit for the patient?

Once a specific cause is identified based on specific microbiologic tests, the following further questions should be considered:

1. If a specific microbial pathogen is identified, can a narrower-spectrum agentbe substituted for the initial empiric drug?
2. Is one agent or a combination of agent necessary?
3. What are the optimal dose, route of administration, and duration of therapy?
4. What specific tests (e.g., susceptibility testing) should be undertaken to identify patients who will not respond to treatment?

5. What adjunctive measures can be undertaken to eradicate the infection? For example, is surgery feasible for removal of devitalized tissue of foreign bodies-or drainage of an abscess-into which antimicrobial agents may be unable to penetrate? Is it possible to decrease the dosage of immunosuppressive therapy in patients who have undergone organ transplantation or to give immunomodulatory drugs or antitoxins to patients with preexisting immune deficiency?

Consequences of antibiotic misuse: if antibiotics are used too often for things they cannot treat like colds, flu, or other viral infections- not only are they of no benefit, they become less effective against the bacteria they are intended to treat. When bacteria become resistant to first line treatments, the risk of complications and death

is increased. The failure of first line antibiotics also mean that doctors have to resort to less conventional medications, many of which are more, costly and associated with more serious side effects. For instance, the drugs needed to treat drug-resistant forms of tuberculosis (TB) are much more expensive than the drugs used to treat non-resistant TB. The course of treatment is long (up to 2 years) and the side effects can be severe. Other consequences are the increased costs associated with prolonged illnesses, including expenses for additional tests, treatments and hospitalization and indirect costs, such as lost income.[5]

Empirical treatment: antimicrobial agents are frequently used before the pathogen responsible for a particular illness or the susceptibility to a particular antimicrobial agent is known. This use of antimicrobial agents is called empiric (or presumptive) therapy and is based on experience with a particular clinical entity. The usual justification for empiric therapy is the hope that early intervention will improve the outcome; in the best cases, this has been established by placebo-controlled, double- blind prospective clinical trials. For example, treatment of febrile episodes in neutropenic cancer patients with empiric antimicrobial therapy has been demonstrated to have impressive morbidity and mortality benefits even though the specific bacterial agent responsible for fever is determined for only a minority of such episodes. Conversely, there are many clinical situations in which empiric therapy might be useful or may actually be harmful. For example, neutropenic patients with fever and pulmonary infiltrates may have a wide variety of causes for their clinical illness, including viruses, bacteria, mycobacteria, fungi, protozoa, and noninfectious disorders. In this setting, it may be more prudent to obtain specimens by sputum culture or via bronchoalveolar lavage early to offer narrow-spectrum therapy based on culture results. Lastly, there are many clinical entities, such as certain episodes of community-acquired pneumonia, in which it is difficult to identify a specific pathogen. In such cases, a clinical response to empiric therapy may be an important clue to the likely pathogen. Initiation of empiric therapy should follow a specific and systematic approach.

A. Formulate a clinical diagnosis of microbial infection

   Using all available data, the clinician should conclude that there is anatomic evidence of infection (e.g., pneumonia, cellulitis, sinusitis).

B. Obtain specimens for laboratory examination

   Examination of stained specimens by microscopy or simple examination of an uncentrifuged sample of urine for white blood cells and bacteria may provide important etiologic clues in very short time. Cultures of selected

   anatomic sites (blood, sputum, urine, cerebrospinal fluid, stool) and nonculture methods (antigen testing, polymerase chain reaction, serology) may also confirm specific etiologic agents.

C. Formulate a microbiological diagnosis

   The history, physical examination, and immediately available laboratory results (e.g., Gram stain of urine or sputum) may provide highly specific information. For example, in a young man with urethritis and Gram-stained smear from the urethral meatus demonstrating intracellular gram-negative diplococci, the most likely pathogen is Neisseria gonorrhea. In the latter instance, however, the clinician should be aware that a significant number of patients with gonococcal urethritis have uninformative Gram-stain for the organism and that a significant number of patients with gonococcal urethritisharbor concurrent chlamydial infection that is not demonstrated on the Gram-stain smear.

D. Determine the necessity for empiric therapy

   Whether or not to initiate empiric therapy is an important clinical decision based partly on experience and partly on data from clinical trials. Empiric therapy is indicated when there is a significant risk of serious morbidity if therapy is withheld until a specific pathogen is detected by the clinical laboratory.

   In other settings, empiric therapy may be indicated for public health reasons rather than for demonstrated superior outcome of therapy in a specific patient. For example, urethritis in a young sexually active man usually requires treatment for N gonorrhea and chlamydia trachomatis despite the absence of microbiologic confirmation at the time of diagnosis. Because the risk of noncompliance with follow up visits in the patient population may lead to further transmission of these sexually transmitted pathogens, empiric therapyis warranted.

E. Institute treatment

   Selection of empiric therapy may be based on the microbiologic diagnosis or a clinical diagnosis without available microbiologic clues. If no microbiologic information is available, the antimicrobial spectrum of the agent or agents

chosen must necessarily be broader, taking into account the most likely pathogens responsible for the patient's illness.[1,3]

Hence, this study is to evaluate prescribing patterns of general practitioners to ascertain whether or not antibiotics are properly utilized. So to talk about antibiotics prescribing practices, one must also understand generalprescription patterns in Nigeria.

LITERATURE REVIEWS

Literature reviews have shed better light on the topic of study. For instance, a study in 2011 by Babalola "evaluation of prescription pattern in Osun State, Nigeria". Drug therapy is the most commonly used method of any disease treatment in general practice. However, the patterns of drug prescription are often inappropriate and the need for registration of these patterns is essential in an effort to improve prescribing standards. Drugs play an important role in the health care delivery system, giving it credibility. Availability of drugs is one factor known to improve utilization of health services. The extent of drug use is directly affected by the prescribing behavior of physicians and other healthcare professionals who sometimes stand in the position of being the issuer of drug prescriptions. Rational drug use refers to the prescription of the right drug for the right indication in the right dosage and dosing frequency for the correct duration. The best way to investigate drug use in health facilities is usage of indicators created and validated by the World Health Organization. Drug use indicators are a set of standardized indices used to measure drug use in outpatients' facilities. They provide a measure of the optimal use of these resources and can help in correcting deviations from expected standards and in planning. Drug use indicators include average number of drugs per patient encounter, percentage of patient encounters with prescribed injection, percentage of patient encounters witha prescribed antibiotic, etc.[6]

According to one Igbiks Tamuno 2011, the introduction of the manual, "how to investigate drug use in health facilities ", following the collaborative work of the international network for the rational use of drugs (INRUD) and the WHO essential drugs and medicines policy department (WHO-EDM) provided useful tools for objective and reproducible measures of the effectiveness and efficiency of drug use.[7]

Also, according to another study by Abu-Saeed 2013, Disease prevention, management and treatment require use of different classes of medications. One of the commonest classes of medication used for such purposes are antibiotics. Antibiotics are chemical substances produced by microorganisms which have the capacity, in dilute solutions to inhibit the growth of or to kill other microorganisms. Those that inhibit growth of microorganisms are said to be bacteriostatic and those that kill microorganisms are said to be bacteriocidal. Resistance to antibiotics have been identified as a common problem in world at large.[8]

Furthermore, a study in 2010, states "information about antibiotic use patterns are therefore necessary for constructive approach to problems that arise from indiscriminate use of multiple antibiotics available". Such information on antibiotics use pattern and the illnesses for which they are prescribed are generally lacking in hospitals in developing countries. Hence this study was carried out to evaluate prescribing patterns of general practitioners to ascertain whether or not antibiotics are properly utilized".[9]

In discussing rational drug use, a study in 2004 on drug use indicators at a secondary health care facility in Lagos, Nigeria. Drugs play an important role in the health care delivery system, giving it credibility. Availability of drugs is one factor known to improve utilization of health services. Drugs are expensive, constitute a large percentage of the cost of health care therefore require optimal or rational use. Rational drug use refers to the prescribing of the right drug for the right indication in the right dosage and dosing frequency for the correct duration. Drugs use indicators are a set of standardized indices used to measure drugs use in outpatient facilities. They provide a measure of optimal use of these resources and can help in correcting deviations from expected standards and in planning.[10]

Researches from other countries like Greece, it was noted that antibiotic prescription in primary care rose steadily during the last decade world-wide, in many European countries. Unnecessary antibiotic prescribing remains the cardinal contributing factor to the development of antibiotic resistance. Primary health care practitioners have been shown to account for the majority of antibiotic prescribing. To prevent overprescribing, detailed data on antibiotic utilization should be obtained. The use of markers such as the daily defined doses of antibiotics (DDD), and the daily defined doses for 1000 people/day (DID) for the estimation of antibiotic use has facilitated the comparison of the findings in various countries. Greece is among the European countries with the highest antibiotic prescribing and resistance to bacteria. Information is very limited for Crete, the major island of Greece. The aim of this study was to investigate antibiotic use in primary health care in a region of Crete for a period of 12 months as well as to highlight the important role of the family physicians.[11]

Also similar studies in 2010 on the analysis of drug prescription in primary health care is an essential component of health system research. Determination of the drug use indicators in a country, region or individual health facility allows health planners, managers and researchers to make basic comparison between situation situations in different areas or at different times. Three categories of indicators related to the rational use of drugs in primary care have been described:

pharmaceutical prescribing practices by health providers; key elements of patient care; and availability of facility-specific factors which support rational use. Generally, only a small number of basic or core indicators are recommended for national adoption and are included in any drug use study using indicators. Of these, the prescribing indicators are often used as a starting point in determining the core drug use indicators. The World Health organization (WHO) has developed, standardized and validated a set of indicators to provide an appropriate means to evaluate a country's drug use patterns and to measure the efficacy of interventions.[12]

Another study in Pakistan 2002, examined prescription practices of public and private health care providers in Attock district of Pakistan, and showed that the irrational use of drugs is a major problem of present day medical practice and its consequences include the development of bacterial resistance to antibiotics, ineffective treatment, adverse effects of drugs and the economic burden on the patient and society. Irrational or misuse of drugs refers to the distribution or consumption of drugs in ways that negate or reduce their efficacy or in situations where they are unlikely to have the desired effect. As accepted by the WHO, the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequateperiod of time, and at the lowest cost to them and their community.[13]

Also in Nigeria, a study done in Ilorin showed that appropriate drug utilization has a huge contribution to global reductions in morbidity and mortality with its consequent medical, social and economic benefits. The WHO published its first report on selection of essential drugs in 1977. Essential drugs program was introduced in Nigeria through the promulgation by the Federal Government National Drug Formulation and essential Drug list decree in 1989. One of the objectives of preparation of essential drugs list is to develop and follow a system of rational use of drugs. Expenditures due to irrational use of drugs have been a strain on the meagre health budgets of several developing countries. Despite the Essential drug program in countries, there is some evidence of poor prescribing habits by physicians, including irrational use of drugs, high numbers of drugs per prescription and high use of injectable formulations and antibiotics. Inappropriate prescribing has been identified in many health facilities in developing countries. Misuse of antibiotics, overuse of injections, and under-use of life-extending drugs for illnesses such as HIV/AIDS, heart disease, and other chronic illnesses together constitute a global epidemic of irrational use of medicines. According to figures gathered by surveys presented to WHO, in 2000, about 60% of antibiotics in Nigeria were prescribed

unnecessarily. Irrational use of drugs due to inappropriate prescription can also lead to adverse drug events which cause illness or death. Surveys have shown that doctorsprescribe drugs when they are not indicated.[14]

Worthy of note is the study that was done in Edo State in 2012 on the assessment ofdisease profiles and drugs prescribing patterns of health care facilities in Edo State, Nigeria, that rational use of medicine provides patients with clinically appropriate medications at doses tailored to their individual needs, for an adequate period of timeand at the lowest cost to them and their society. Unfortunately, irrational use of medicines is a major problem worldwide, especially in developing countries. More than half of all medicines are prescribed, dispensed or sold inappropriately and half of all patients fail to take them correctly. Irrational prescribing is reported to negatively impact on health and economics of individuals and the society, leading to wastage of scarce resources and widespread health hazards. Consequently, appropriate use of drugs is recognized as one essential element in achieving qualityhealth or medical care for patients and the community, and has the potential to resultin 50-70% cost-efficiency in medicine expenditure.[15]

In other words, the discovery of compounds with antimicrobial activity was a major advancement in medicine and patient care. These compound provide healthcare professionals with an adjunctive therapy to patients own immune system, the principal and perhaps best defense for fighting infectious diseases. Antibiotics are viewed as the most frequently prescribed drugs among hospitalized patients. Not too long after the first discovery of penicillin, resistance to the drug emerged and as more antibiotics were discovered and used more resistant bacteria evolve.[16] Extravagant use of antibiotics without careful consideration of their appropriate indications leads more rapidly to the emergence of resistant strains. The recent emergence of antibiotic resistance in bacterial pathogens both nosocomial and in the community is a very serious development that threatens antibiotic use. The performance of antibiotics over the years leaves much to be desired, yet the abuse of antibiotic usage plays a significant role in organisms' resistance.[17]

In spite of their advantages in treatment, the problems that occur from the irrational use of antibiotics (IUA) have put them in the health agendas of the countries as a common issue of consideration. Nonetheless it is needed to carry out comprehensiveresearches that make an assessment of the use of antibiotics by various healthcare facilities.[18] There is a gap between official guidelines and

the state of current practices. Excessive and poorly adapted antibiotic prescription favors the disturbing

phenomenon of resistance which is all the more alarming because the emergence ofresistant strains is difficult to predict. An effort should be made to prescribe the mostappropriate active substance at optimal dose and treatment duration to limit the development of micro-organism resistance.[19] Comprehensive education programs can reduce antibiotic prescriptions but the impact on clinical outcomes is unclear. Unfortunately, antibiotics produce side effects and-regardless of whether they are used appropriately or inappropriately- will ultimately lead to a change in the sensitivity of organisms, which can sometimes lead to a reduction in clinicaleffectiveness.[20]

RATIONAL USE OF ANTIBIOTICS

The conference of experts on the rational use of drugs, convened by the WHO in Nairobi in 1985 defined that "rational use of drugs requires that patients receive medications appropriately to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, at the lowest cost to them and their community". Components of antibiotics policy include education, direction, monitoring and evaluation, and an antibiotic committee made up of the hospital pharmacist, microbiologist, clinical doctor, administrative key person, othermembers co-opted as necessary. Antibiotics are the great discovery of the 20th century. But the miracle seems to come to an end. Inappropriate use of these life- saving instruments has resulted in many problems. On the other hand, not many newantimicrobial molecules have been discovered since the 1980s and funding on antimicrobial research is on the decline. Now we gave to fight against the irrational use to save these important discoveries of man from extinction.[21]

The worldwide emergence of antimicrobial resistance is a major public health problem that significantly impacts patient treatment and outcomes. The relationshipbetween antimicrobial use and antimicrobial resistance is complex, with a growing body of data strongly suggesting that higher levels of antimicrobial usage are associated with increased levels of antimicrobial resistance. Patients in hospital nowadays are older, more severely ill, and more immune compromised than was thecase two or three decades ago, and are predisposed to contracting bacterial infectionsrequiring frequent antimicrobial therapy.[22] With the increase in antimicrobial prescriptions, prescribing errors have also become more common. These include treatments of colonization, suboptimal empiric therapy, inappropriate combination therapy, dosing as well as duration errors and mismanagement of apparent antibioticfailures. Studies have shown an inappropriate prescribing of antimicrobials for

prophylaxis as well as treatment.[23] Inadequate consideration of potential antimicrobial resistance, tissues penetration, drug interactions, side effects, and cost are among the factors which influence the prescription pattern and effectiveness of antimicrobial therapy.[24]

In developing countries, antibiotics are prescribed 44-97% of hospitalized patients often unnecessarily or inappropriately.[25] Several socio-economic and behavioral factors are thought to contribute to the inappropriate use of antibiotics and, consequently, to the increased incidence of bacterial resistance in developing countries.[26] The spread of antibiotic resistance in those countries is associated with complex and interconnected factors, such as excessive and unnecessary prescribing of antibiotics, increased self-prescribing by the people, poor quality of available antibiotics, failure to implement simple infection control practices, and the dearth of routine susceptibility testing and surveillance.[27] The lack of funds combines with other factors such as ignorance, inadequate education, inaccessibility to proper health and diagnostic facilities.[28] Though the reported factors are complex, an excessive and inappropriate prescribing of antibiotics is at least partially responsiblefor the increased rates of resistance worldwide. The main reason for self-medicationis the sale of antibiotics without a prescription.[29]

A plethora of drug utilization studies focused on assessing patterns of drug prescribing as a mean of pin-pointing areas for improvement with the aim to rationalize drug use. The health threats that can be caused by improper prescribing cannot be overlooked. Improper prescribing can cause toxicity for patients and will be a waste of money and time. It can also cause therapeutic failure that results in progress of disease conditions and worsening of the patient health condition. The improper prescribing and excessive use of antibiotics can lead to loss of the effectiveness of currently used antibiotics.[30] The World Health Organization (WHO)has repeatedly emphasized the importance of drug utilization studies and developedindicators examine trends of pre-scribing and the health facilities. Once irrational drug use in its various forms is determined, feasible means of intervention are triedwith the hope to improve drug use. The use of antibiotics has been the subject of several studies, because of the globally confirmed trends of under treatment, wrong antibiotic selection and the risk of consequent emergence of bacterial resistant.[31] Guidelines for rational prescribing have been developed but unfortunately, they haveneither been always available nor effectively implemented in many developing countries. However, drug utilization studies in Egypt are scarce and misuse of particularly antibiotics has not been extensively explored.[32]

WHO defines rational use of drug as "Patients should receive medication appropriateto their clinical needs, in doses that meet their

own individual requirements for an adequate period of time, and the lowest cost to them and their community".[33] It has been estimated that fifty percent of medicines being used in India, either on prescription or in over-the-counter sales, are inappropriately or irrationally used. Recently there has been an alarming concern over the injudicious use of many irrational drug worldwide. Amongst them, are important ones are AMAs (antimicrobials), Corticosteriods, Analgesics, Antacids, Acid reducing agents, Vitamins and use of many irrational drugs combinations. The practice of indiscriminating prescribing of AMAs is posing a major problem of ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and harm to the patient as well as an additional burden of an expensive medical cost for the patient and importantly development of drug resistance. Irrational prescription of drugs is of common occurrence in clinical practice, important reasons being lack of knowledge about drugs, unethical drug promotions and irrational prescribing habits of clinicians. Monitoring of prescriptions and drug utilization studies can identify the problems and provide feedback to prescribers so as to create awareness about irrational use of drugs.[34] General Practitioner is the most sought out healthcare provider as has been confirmed by number of studies. Most of the common ailments are managed by medical practitioners or general practitioners (GPs) GPs prescribe major bulk of the drugs sold in the market. Naturally, irrational use of drugs at this level could lead to disastrous consequences. Patients with fever, loose motions, and upper respiratory infections generally are treated by General Practitioners, who are also called as Family Doctors. A GP is a practitioner who treats acute and chronic illnesses and provides preventive care and health education.[35] GPs in Okada and environs are mainly of Bachelor of Medicine Bachelor of Surgery (MBBS), Bachelor of Science Nursing (bSc.N), Community Health Worker (CHWO), Registered Nurse (R.nursing) qualifications though people with other qualifications (like Licentiate of the Court of Examiners in Homeopathy(LCEH) also are found insmall numbers.

Diarrhea diseases (DD), acute respiratory infection (ARI) and malaria cause more than half of childhood mortality in some developing countries and irrational prescribing of drugs has been noted as a major health concern in these countries. In Nigeria, many children under the age of five die from these diseases that are preventable or treatable with low cost drugs and these drugs are usually bought frompatent medicine dealers (PMD) that have constituted the primary source of drugs in

rural and urban Nigeria especially for the poor. The patent medicine dealer has beendefined as "a person without formal training in pharmacy and sells orthodox pharmaceutical products on a retail basis for profit". They dispense drugs most of the time but do not prescribe. Geographical accessibility, free consultation, lower cost, shorter waiting times, drug availability, longer opening hours, friendly staff disposition, greater confidentiality, and flexible payment modes have been adduced as some of the reasons for preferring PMDs. However, it has been noted that these PMDs have poor knowledge of childhood illnesses and dispensing behavior especially with malaria episodes. Rational use of medicines 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". Irrational or non-irrational use is therefore the use of medicines in a way that is not compliant with rational use as defined above. Aspectsof irrational medicine use are found in diagnosis which includes (inadequate examination of patient, incomplete communication between patient and doctor, lack of documented medical history, inadequate laboratory resources; prescribing which includes extravagant prescribing, over prescribing, incorrect prescribing, under- prescribing, and multiple prescribing); dispensing which includes (incorrect interpretation of the prescription, retrieval of wrong ingredients, inaccurate counting, compounding, or pouring, inadequate labeling, unsanitary procedures, packaging, poor quality packaging materials, odd package size, which may require repackagingand unappealing package) and patient adherence which includes (poor labeling, inadequate verbal instructions, inadequate counseling to encourage adherence, inadequate follow-up/support of patients, treatments or instructions that do not consider the patient's beliefs, environment, or culture.[25,26]

Irrational prescribing of drugs is a major health concern in developing countries where half of the childhood mortality is caused by diarrhea, acute respiratory infection (ARI), and malaria. In Nigeria, many under the age of five die from acute respiratory infection (ARI), diarrhea disease (DD), malaria and other diseases that are preventable or treatable with low cost drugs bought mainly from patent dealers (PMD) who are the primary source of drugs in rural and urban Nigeria especially the poor. Free consultation, lower cost, lower cost, geographical accessibility, shorter waiting times, more reliable drug stocks, longer opening hours, friendly staff, greater confidentiality, and flexible pricing policies have been adduced as one of the reasons for preferring PMDs. However, one of the problems associated with treatment by these PMDs is that there is poor knowledge and poor dispensing behavior in relation

to childhood illnesses especially malaria episodes. The patient medicine vendor can be defined as a person without formal pharmacy training, who sells orthodox pharmaceutical products on a retail basis for profit. Irrational prescribing has been noted in some studies to increase the cost of medical treatment, morbidity and mortality. Also, evidence shows that there is increasing trend in prescription of expensive, widely advertised, brand name medication and reduction in the use of generic first line medication thus leading to adverse health and economic effects. A study in Nepal, of primary health care centers showed that 20-52% of drug cost was wasted through irrational prescribing.[36] The wastage was incurred by formally trained health workers and it is expected to be worse with PMDs who have no formaltraining on treatment of common ailments. Therefore, an intervention area is the training and re-training of the PMDs on rational drug prescribing. Also, consumer's information on appropriate drug consumption through community health education is likely to reduce the cost of treatment to care givers. The use of drugs from

the essential drug list should have however be promoted for optimal use of limited financial resources. This is imperative in other to achieve the MDG goal of reducinginfant mortality in Nigeria by the year 2015. [37,40]

The indiscriminate and inappropriate use of antibiotic in outpatient clinic, hospitalized patients and in the food industry is the single largest factor leading to antibiotics resistance (super bugs). In the recent years, the number of new antibiotics licensed for human use in different parts of the world has been lower than in the recent past. In addition, there has been less innovation in the field of antimicrobial discovery research and development. The pharmaceutical industries, large academic institutions or the government are not investing the necessary resources to produce the next generation of newer, safe and effective antimicrobial drugs. In many cases, large pharmaceutical companies have terminated their anti-infective research programs all together due to economic reasons. The potential negative consequences of this events are relevant because they put society at risk for the spread of potentiallyserious MDR bacterial infections.[38]

According to William Osler, a great feature which distinguishes man from animals is the desire to take medicine.[37] self-medication involves the use of medicinal products by the individuals to treat self-recognized disorders or symptoms, or the intermittent or continuous use of a medication prescribed by a physician for chronic or recurring diseases or symptoms. Self-medication thus forms an integral part of self-care, which can be defined as the primary public health resource in the health care system. The increased advertising of pharmaceuticals poses a large threat of

self-medication to the younger population in general. This raises concerns of incorrect self-diagnosis, drug interaction, and use of drugs other than for original indication. A study from Nigeria has observed self-medication as a common practice among group of health workers that included dental, midwifery and nursing students. It has been suggested that self-prescription is also prevalent among practicing physcians.[39]

CHAPTER TWO: METHOD

STUDY DESIGN:

This study was a retrospective evaluation of antibiotics prescribed from January 2010 to May 2014which was studied to assess the rational use of antibiotics by general medical practitioners in health care facilities in Okada and environs.

SAMPLE SIZE:

The population size for this period is about 62,000patients. The number with antibiotics in their prescriptions is about 34,000 patients. Number of patients that had antibiotics in their prescription for each hospital includes

Usen General Hospital (GHU)=12,121 Medical Centre Ogbese (MCO)=7,868 General Hospital Iguobazua (GHI)=9,799 PHC Okada=3,579.

SETTINGS:

This research was carried out in Okada and environs using three Primary Health carecenters and two secondary health care centers.

I. Primary health care center Okada is located in Ovia North Local Government Area of Edo state. This health center has no pharmacy department but has a matron in charge of drug prescriptions and dispensing, with five nurses. The health center is used mainly for delivery and managing paediatric illnesses. Average number of patients is 12 on immunization days and 3 on other days.

II. General Hospital Usenis a secondary health care facility located in Ovia South-west Local Government Area of Edo state. The hospital has oneconsulting room manned by one medical officer. The pharmacy department has one pharmacy-technician with a 300 level student on industrial training. The average number of patients that visit the hospital per day is 30.

III. General Hospital Iguobazua also in Ovia South-west Local Government Area, a secondary health care facility, has two medical officers and one pharmacy-technician with some secretarial staff. Average number of patient per day is 30.

IV. The medical center in Ogbese, a primary health care facility has one medical officer and two pharmacy-technicians. Average number of patients per day is25.

DATA COLLECTION:

Case files or prescription cards were collected from each health facility. Relevant data on socio-demographic data, names of prescribed antibiotics, number of antibiotics prescribed per prescription, class of antibiotics, commonly treated diseases and frequency of prescribed antibiotics were evaluated. Data was filled ina data collection form.

CHAPTER THREE: RESULTS

SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH ANTIBIOTICS

Variables	GHU (%)		MCO(%)		GHI (%)		PHC Okada (%)	
Age (Yrs)								
0-10	1528	(25.5)	1295	(25.1)	3255	(15.8)	2079	(13.9)
11-20	1512	(25.7)	1179	(23.6)	2315	(23.6)	500	(58.1)
21-30	1400	(23.6)	1921	(31.3)	1550	(33.1)	450	(12.6
>31	1486	(25.0)	3438	(20.0)	2699	(27.5)	550	(15.4)
Gender								
Male	30,030	(25)	1958	(25)	4099	(41.8)	1079	(30.2)
Female	9, 091	(75)	5875	(75)	5700	(58.2)	2500	(69.8)
Marital status								
Single	8120	(67.0)	4070	(52.0)	5900	(60.2)	2120	(59.2)
Married	4001	(33.0)	3763	(48.0)	3699	(37.7)	1459	(40.8)
Education Level								
Basic	7821	(64.5)	6381	(81.5)	6,620	(67.6)	2580	(72.1)
Post basic	4300	(35.5)	1452	(18.5)	3,179	(32.4)	999	(27.9)
Occupation								
Employed	8866	(48.4)	3653	(46.7)	3982	(40.6)	1579	(44.1)
Not employed	6225	(51.6)	4180	(53.4)	5617	(57.3)	2000	(55.9)
Tribe								
Edo	1021	(64.5)	5712	(72.9)	7724	(78.8)	2342	(65.4)
Not Edo	1908	(15.7)	2121	(27.1)	2075	(21.2)	1237	(34.6)

Table 3.1 shows the socio-demographic characteristics of patients that visited each hospital and were prescribed antibiotics within Jan 2010-Dec 2013.

PATIENTS VISIT WITHIN JAN. 2010 – DEC. 2013

Hospital	No. of patients Patients with antibiotics 2010 – 2013	2010 - 2013
GHU	25, 095	12,121
MCOGHI	14,333	7,833
PHC Okada	17,093	5,415
	9,799	3,579
TOTAL	66,310	25,038

Table 3.2 shows general patients visit to each hospital including those withantibiotics.

KEY:

GHU= General Hospital Usen MCO= Medical Centre Ogbese GHI= General Hospital Iguobazua PHC= Primary Healthcare Okada

Class	No. of times prescribed	Percentages
Penicilline	6429	39.7
Tetra-cycline	1510	9.3
Macrolide	1996	12.3
Sulphonamide	1678	10.3
Quinolones	1198	7.4
Imidazole derivative	3436	21.0

Table: 3.3 MOST PRESCRIBED CLASS OF ANTIBIOTICS

Drugs from different classes of antibiotics are normally used to treat different diseases. But a few are frequently used.

Table 3.3 shows the different classes of antibiotics that are most frequently prescribed in each

Commonly prescribed antibiotics in the four health facilities include amoxicillin, amoxicillin/clavulanic acid, ampicillin, ampicillin/cloxacillin, azithromycin, cefuroxime, cephalexin, ciprofloxacin, chloramphenicol, clarithromycin, clotrimazole, co-trimoxazole, doxycycline, erythromycin, fluconazole, gentamicin, ketoconazole, levofloxacin, lincomycin, metronidazole,ofloxacin, pefloxacin, secnidazole, tinidazole.

Table 3.4 COMMONLY PRESCRIBED ANTIBIOTICS

These are the top-most prescribed antibiotics others were excluded from this table.

Antibiotic	**Number of times prescribed**	**Percentages (%)**
Amoxicillin	2320	18.14
Amox/clav	353	19.27
Ampicillin	1951	12.18
Metronidazole	2090	2.87
Amp/clox	1805	5.68
Azithromycin	922	8.28
Cotrimoxazole	1678	16.29
Ciprofloxacin	1198	13.67
Doxycycline	1510	1.17
Erythromycin	1074	0.89
Fluconazole	1346	1.89
Total	**3431**	**100**

This table shows the total number of times antibiotics were prescribed from January2010 to December, 2013.
Diseases that are frequently treated in Okada and environs are typhoid, ulcer, upper respiratory tract infections, lower respiratory tract infections, sexually transmitted infections, urinary tract infections, candidiasis, diarrhea, measles, chicken pox, eye/ear-nose and throat infections, malaria, burns, accident, surgery etc.

TABLE 3.5 COMMONLY TREATED DISEASES

Disease	Number of times presented	Percentage (%)
Typhoid	1032	28.83
Ulcer	354	9.89
RTI	835	23.30
Diarrhoea	342	9.60
Skin infect.	129	3.60
STI	806	22.51
Candidiasis	82	2.24
Total	**3580**	**100**

Table 4 shows the number of times each disease was treated from January, 2010 to December,2013.

CHAPTER FOUR: DISCUSSION

This study was carried out to draw attention to the rational use of antibiotics by General Medical Practitioners. This was carried out three Secondary Healthcare facilities and one Primary Healthcare facility in Okada and environs. The results collected were represented in statistical tables. The population size was 62,000 patients out of which a sample size of 34,000 was used which cut across all age ranges. Children (0 – 10 years) are a population of particular concern because they have the highest rates of antibiotic use and are the ones also at increased risk of infection with antibiotic – resistance micro-organisms of any age group.[25]Also froma study, it has been shown that children (0-5 yrs) that are given antibiotics are more likely to develop eczema. About 2.4million of the UK's 12million children have been diagnosed with the disease, caused by an over-active immune system and resulting in dry and itchy skin. Also the antibiotics use in children expose them to the drug's potential side effects and also contributes to the overuse of the drugs in the community.[26,27]

Different types and classes of antibiotics were prescribed but about 11 were frequently prescribed within the period of study. The most prescribed antibiotics were Amoxycillin (2320;14.3%), Metronidazole (2090;12.7%) and ampicillin (1951;12.0%).This study carried out in Okada and environs proved that the patients between 0 and 10years of age received more antibiotics (78.2%) as compared to other age groups. They are said to be vulnerable to all sorts of infections possibly because of their low immunity. The proportion of antibiotic prescription was 78.2% in this present study as against the World Health Organization (WHO) recommendation of 20% antibiotic use for these common childhood illness.[28]

All prescription sheets used in this study were those from General Medical Practitioners. From table 3.4, it will be observed that only one antifungal drug

(Fluconazole) was frequently used. This may be an indication that the prevalence of diagnosed fungal infections among patients visiting the hospital was low. Amoxicillin happened to be the most prescribed antibiotic. This may be as a result of it being readily available and cheap. In addition, Amoxicillin is a broad spectrum antibiotic that covers a very wide range of organisms

(Gram positive and Gram negative bacteria). Metronidazole was next in frequency of prescribed antibiotic to amoxicillin. Metronidazole is one of the few antibiotics that is effective against anaerobic and amoebic organisms in addition to being cheap, readily available and exhibiting high efficacy against susceptible organisms. Similar study carried out in Nigeria showed that Metronidazole and Ampicillin/Cloxacillin were the highest prescribed (19%) - drugs which were also among the most commonly prescribed in this study[29]. In addition, a study carried out in Southern Nigeria and in Egypt also revealed that the most commonly used antibiotics were the Penicillins[30,31]. This result also is in agreement with the result British Journal of Pharmaceutical Research, 3(4): 940-947, 2013945 obtained from its study as the Penicillins were themost prescribed antibiotics.

The trend of prescription of antibiotics may vary from region to region depending largely on the common types of infections predominant in the area, another study carried out in Ibadan showed that Cotrimoxazole was the most commonly used- a drug with a medium frequency in the present study [32].

The result obtained from this study also showed that more than half of the prescription containing two antibiotics and close to half also contained just one antibiotic. This shows very low level of unnecessary polypharmacy in antibiotic usage. The combination of two antibiotics may be to reduce the incidence of resistance to a particular antibiotic and may also be able to cover a wider range of organisms which may be necessary sometimes when commencement of treatment is

done before obtaining laboratory results. For example, the combination of Amoxicillin and Metronidazole to cover wide range of both gram positive and gramnegative organisms. It is worthy to note that many of the patients received more thanone antimicrobial in order to prevent resistance and also for its synergistic advantages (e.g. Penicillin G/ ampicillin in combination with gentamicin or streptomycin). When used in combination, penicillin G/ ampicilin facilitates the intracellular uptake of the aminoglycoside which then causes the subsequent bacteriodical effect against the enterococci. In the absence of these agents, there is little intracellular uptake of aminoglyclosides. The sulfonamides are used in combination with trimethoprim, pyrimethamines. This combination blocks two distinct steps in folic acid metabolism and prevents the emergence of resistant strains.

In contrast, majority of antibiotics prescribed by these medical practitioners were inbranded names which does not conform to the objectives of the National Drug Policy. One of the reasons for this observed trend may be as a result of the activities of the sale representatives of various pharmaceutical companies who strive at ensuring that their brands are prescribed by the medical practitioners. Another possible reason is that of the experience of the medical practitioner in respect to the efficacy of a particular brand for treatment of infections. Studies have shown that generic prescription has got special importance for rationale use of drug as regards to cost, safety and efficacy by permitting the identification of the products by its scientific name[33].

Looking at the dosage form, almost all antibiotics (98.4%) prescribed was in oral form. This could be an indication that most infections treated may be systemic and not local. The low level of eye/ear drop and ointments also buttresses this point. Although it should be noted here that certain antibiotics comes in certain dosage

forms. For example, Clotrimazole isusually a topical antibiotic used for skin infections although it may also come as pessaries.

Another good trend observed in this study was that all antibiotics being used in thisfacility were found in the Essential Drug List. This is another indication that the General Medical Practitioners adhered largely to the National Drug Policy. Most drugs were available at the pharmacy for dispensing as at the time they were prescribed. This also goes to show that the pharmacy department were maintaining a good drug revolving fund program that promotes availability of drugs at all times.This will help the patient in obtaining required drugs promptly that can aid in promptreduction in morbidity and mortality resulting from the various infections. A study carried out in Lokoja is in agreement with this study as it showed that almost all thedrugs under study were found in the Essential drug list and in the Pharmacy department as the time the drugs were being prescribed[34].

From the population size of 62,000 patients, 25038 patients took antibiotics with GHU having the highest number. This result is proportional to the total number of patients that attended the health facility per year. Also from this study, the female gender has been found out to have received more antibiotics than male. Pregnant women (who are immunosuppressed), and other female – related infections such as vaginal infections, might have contributed to the increase. The latest study by Dr. Maya Saleh, of the Research institute of the McGill University Health Centre and McGill University, shows that women have a more powerful immune system than men. In fact, the production of estrogen by females could have a beneficial effect onthe innate inflammatory response against bacterial pathogens. This surprising result were published May 2009 in the proceeding of the National Academy of Science.[35] Although, women are more prone to infections of the urinary tract, men above 50 years of age are also highly susceptible to these infections, thus this claim has been

found to be based on the type of infection. UTIs are most common in sexually active women and increase in diabetics and people with sickle cell diseases or anatomical malformations of the urinary tract. Since bacteria can enter the urinary tract through the

urethra (an ascending infection), poor toilet habits (such as wiping back to front for women) can predispose to infection, but other factors (pregnancy in women, prostate enlargement in men) are also important and in many cases the initiating events is unclear. Women are more to the UTIs than in males, and they lack the bacteriostatic properties of prostatic secretions. Among the elderly, UTI frequency is in roughly equal proportions in women and men.

Researchers show how estrogen protect women from the gastric inflammation that can lead to cancer. Several types of Cancer, including stomach, liver and colon, are far more common in men than in women. Some scientists have theorized that differences in lifestyle, such as diet and smoking, may account for discrepancy, but growing evidence suggests that the differences are rooted in basic biological differences between men and women.[36]

Commonly treated infections during this period were typhoid, ulcer, upper and lower respiratory tract infections, diarrhea, vaginal candidiasis, sexually transmitted infection, skin infections and malaria. The common drugs used for these infections for this period were ampicillin, cotrimoxazole, amoxicillin, ampicillin/cloxacillin, metronidazole, gentamicin, doxycycline, artemisinin-based combination therapy, erythromycin, azithromycin, fluconazole, ofloxacin, ciprofloxacin, cefuroxime, clotrimazole etc. Based on this study the most common of these infections is typhoid(28.83% from table 3.5) as the most commonly prescribed drug is amoxicillin (14.3% from table 3.4). It could because this is a rural area where their major source of water is a small river, there is limited education on the use of orthodox medicine to treat the infection therefore they engage in all manner of herbs which may lead to

deterioration of the infection, and most preventive measures like the use of boiled and filtered watered are not taken. Also, poor hygiene encourages the perching of flies on foods. In addition, another commonly treated disease is malaria. There are estimated 300-500 million clinical cases each year with more than 90% of these occurring in sub-Saharan Africa. Malaria causes up to 2.7 million deaths per year with the vast majority of these among young children in Africa, especially in remote rural areas with limited or no access to medical care. In fact, in some parts of Africa, malaria kills 3000 children under 5 years of age each day. Based on WHO recommendation for malaria treatment, artemisinin – based combination therapy was the basis for malaria therapy. Malaria in pregnant women was seen in large numbers because of their immunosuppressive status. Several studies have demonstrated that patterns of antibiotic usage greatly affect the number of resistance organisms.

This study also show that most antibiotics are also prescribed for respiratory tract infections (23.3%). The Havard Report on "improving Hong Kong's Health Care system" in 1999 had also commented on the overuse of antimicrobials by primary care doctors for treatment of upper respiratory tract infection. In U.K., 80% of antimicrobials prescription was irrational or inappropriate. Withhold antibiotics in situations where by they are not likely to benefit the patient for self – limited viral infections such as "the common cold" symptomatic treatment and supportive measures are the most appropriate care and antibacterial agents are not indicated. Since this study was conducted in a rural area, it may be safe to assume that exposure to infection was more as a result of poor hygiene, etc. It was noticed as well that most of the ailments were treated with antibiotics without considering their spectrum of activities. This could be verified by conducting sensitivity test for the most appropriate antimicrobial against that infection. Sexually transmitted infections like

syphilis, gonorrhea, chlamydia, trichomoniasis, pelvic inflammatory disease also accounts for a high percentage of prescribed antibiotics.

Almost as soon as drugs were taken, bacteria responded by manifesting various forms of resistance. As antimicrobial usage increased, so did the level and complexity of the resistance mechanisms exhibited by bacteria pathogens. The struggle to gain the upper hand against infections continues to this day, although the number of scientist who are developing new antibacterial agents is beginning to dwindle, even as bacteria evolve ever cleverer mechanisms of resistance possibly because the more the development, the more the misuse thereby giving room for emergence of resistance. Resistance occurs when wide spectrum antimicrobials is prescribed for a condition that can be treated with narrow spectrum. The increased rate and widespread of indiscriminate use of antimicrobials through self-medication or recommendation by health care provider shown in this study are major factors that could lead to the development of microbial resistance to antimicrobials resulting in therapeutic failure, and hence high morbidity and mortality.

CHAPTER FIVE: CONCLUSION AND RECOMMENDATION

CONCLUSION:

Antibiotic resistance poses a serious threat to human health and welfare and undermines national economies worldwide. Annual losses stemming from antimicrobial resistance are estimated to range from 21 000 million to 34 000 million dollars in the United States of America1 and about 1500 million euros in Europe.[37]There is a positive correlation between antimicrobial resistance and the consumption of antibiotics. Unnecessary use of antibiotics is seen among both health professionals and the public. In European

countries, systemic antibiotics are prescribed in the greatest volumes to ambulatory patients, mostly for respiratory tract infections.[38]Increasing awareness of antimicrobial resistance and promoting the rational use of antibiotics among prescribers and the general public are key to combating the unnecessary use of these drugs.[39] Some important programmes have been launched in developed countries. They include Strama in Sweden;[40] the Get Smart: know when antibiotics work programme of the US Centers for Disease Control and Prevention.[41]

Antibiotics Smart Use (ASU) was introduced in 2007 as an innovative model to promote the rational use of medicines and counteract antimicrobial resistance. It was established for two major reasons. First, few resources were available for the fight against the irrational use of antibiotics, which was rampant. Using these few resources to empower health professionals and the public was seen as an expedient and efficient way to galvanize improvements by inducing individual behaviour change while creating a critical mass of people who could conduct advocacy and promote the rational use of antibiotics. Second, the rational use of medicines as a concept was not always getting translated into practice, and the ASU model was felt to be useful in bridging this gap.[42]

Conceptual framework of the Antibiotics Smart Use (ASU) model;Individual level

- Correct misunderstanding and attitudes and increase confidence in diagnosis and non-antibiotic treatment• Reduce perceived pressure from patients' expectation that they will be prescribed antibiotics (Reinforcing factors) E.g. patient's expectations, social approval, mutual recognition, peer pressure, drug promotion (Enabling factors)E.g. hospital formulary, availability of treatment guidelines and medical equipment, social support

Organizational level

- Build compelling and supportive climate for rational use of antibioticsNetwork level
- Develop collaborative, decentralized networksPolicy level
- Integrate ASU into national policiesSocial level
- Create social norms on rational use of antibiotics. Sources: Adapted from Green &Kreuter30

Antibiotic resistance among pathogenic microorganisms is a matter of worldwide concern. Selective pressures by antimicrobial drugs are by far the most important driving force for the development of such resistance. This present study on antibiotic use, under the circumstances tested, provides four characteristics of antibiotic prescribing:

(1) in the majority of cases treatment was empirical, with antibiotic prescription based on a clinical suspicion of infection without objective criteria of infection;
(2) all antibiotics were administered orally and parenteral administration never occurred,
(3) irrespective of the site of infection and the most likely pathogen causing that infection, a single broad-spectrum antibiotic, usually amoxicillin or amoxicillin- clavulanic acid, was prescribed and in most cases, brand names were used in prescribing;
(4) Most of the drugs prescribed were drugs in the essential drug list, however, treatment was not in accordance with standard prescribing guidelines.

The trend that emerges from these observations is that antibiotic use is nonrestrictive. This study has revealed significant flaws in the prescribing pattern of general medical practitioners in Okada and environs. The findings of this study suggest that there is wide difference between defined recommendations in standard treatment guidelines and the clinical use of antimicrobial agents. Establishing an appropriate and restrictive guide for antibiotic use should therefore be a high priority to this hospital. A standard treatment guideline should be established in the hospital for antibiotic prescription and a drug utilization program should be setup alongside as a means of checking the practices of physicians on a regular basis.

There is a high level of use of antibiotics in Okada and environs especially in 0 – 10 years of age as represented in the results above. This may be as a result of poor hygiene and undeveloped immune system. Many of the patients received more than one antimicrobial in order to prevent resistance and also for its synergistic advantages (e.g. penicillin G/ Ampicillin in combination with gentamicin or streptomycin as discussed in chapter 4). In Okada and environs antimicrobial

resistance is inevitable as long as prescriptions are written blindly i.e. without conduction of laboratory tests required and this could be the reason for high antibiotic consumption (a medical laboratory scientist is needed for this purpose). Microbial resistance remain a global health problem and public efforts today focus on controlling it.

According to the set out objectives, the rational use of antibiotics by general practitioners in Okada and environs has been examined and it has been found out that larger number (25,038) of patient went home with an antibiotic. Poverty as a factor could be responsible for antibiotic resistance as the regimen might not be completed. Prescribers only made use of the available

medications and so wide spectrum antibiotics were used where unnecessary. Thus, inadequate antibiotic medication could contribute to its resistance. Illiteracy could be an additional factor as patients might not get the necessary information correctly. Other factors that contribute to incorrect use of antibiotics are lack of skills and knowledge, inappropriate unethical promotion of medicines by pharmaceutical companies, profits from selling medicines (by retailers), unrestricted availability of medicines, overworked health personnel, unaffordable medicines, lack of coordinated national pharmaceutical policy. The common problems include poly pharmacy (use of too many drugs at once), overuse of antibiotics and injections, failure to prescribe in accordance with clinical guidelines, inappropriate self-medication.[43]

What then can be done to improve rational use of antibiotics?

- Evidence-based clinical guidelines for training, supervision and supportingdecision-making about antibiotics
- A national body to coordinate policies on antibiotic use and monitor theirimpact
- List of essential antibiotics for procurement and insurance reimbursement
- Public education about antibiotics and their misuse
- Adequate funding to ensure availability of medicines and health personnel
- Withhold antimicrobials that are not likely to benefit patients
- Use the narrowest spectrum possible to treat infections
- Use of broad spectrum should be based on severity and sensitivity of theinfection
- Educate patients in order to achieve therapeutic and preventive goals
- Emphasis should be made on hygieneWorld Health Organization response

To improve rational medicine use, WHO;

- Monitors global medicines use and pharmaceutical policy
- Provides policy guidance and support to countries to monitor medicines useand to develop, implement and evaluate
- Develops and delivers training programs to national health professionals on how to monitor and improve drug use at all levels of the health system.[44]

RECOMMENDATION:

It is better to support a system, protecting it from deterioration than to strive to repair that system. Therefore, recommendation for potential interventions for rational use of antibiotics in order to prevent resistance in these healthcare facilities is necessary. The importance of hygiene cannot be overemphasized as some of these infections (typhoid fever, diarrhea, malaria, candidiasis, etc.) could be caused or even potentiated by poor hygiene.

The practice of use of a combination of antibiotics for infections in order to preventresistance should be continued. This has to be done with care to avoid possible drug
– drug interaction.

Conditions of sensitivity test (like widal tests for diagnosing typhoid) is also recommended as means of preventing resistance as this enables the use of the most sensitive antibiotics to fight against infections (rational drug use). This can be achieved by involving a medical laboratory scientist in the hospitals and clinics.

More health professionals (like the nurses, doctors, medical laboratory scientists, pharmacists, etc.) should be recruited. Health education and sufficient information of the drugs given to them should be provided by these professionals as resistance could occur as a result of drug misuse which happens when patients do not understand their medications.

Complete socio-demographic information, information about their ailments, and medications given (including the dosage, duration of use, etc.) should be included intheir case files as this will make it easier for researchers to draw accurate conclusionfrom their results.

Antibiotic use should be given to the patient using the dialect he understands as this will also help the rational use (patient education).

In order to change their prescription behavior, it might be important that GPs are aware of their motives for prescribing antibiotics when there is insufficient medicalreason for it. What then can be done to improve rational use of antibiotics?

- A national body to coordinate policies on antibiotic use and monitor theirimpact
- List of essential antibiotics for procurement and insurance reimbursement
- Public education about antibiotics and their misuse
- Adequate funding to ensure availability of medicines and health personnel
- Withhold antibiotics that are not likely to benefit patients

- Use the narrowest spectrum possible to treat infections
- Use of broad spectrum should be based on severity and sensitivity of infection
- Emphasis should be made on hygiene.

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APPENDIX:

Data collection form

1. AGE: 0-10yrs[ ] 11-20yrs[ ] 21-30yrs[ ] 31 - 40yrs[ ]>40yrs

2. WEIGHT: 1-9KG[ ] 10-19KG[ ] 20-29KG[ ] 30-39KG[ ] >40KG[ ]

3. GENDER: Male[ ] Female[ ]
4. MARITAL STATUS: Single[ ] Married[ ]
5. LEVEL OF EDUCATION: Basic[ ] Post basic[ ]
6. OCCUPATION: Employed[ ] Not employed[ ]
7. TRIBE: Edo[ ] Non Edo[ ]
8. NUMBER OF PATIENT(S) ASSESSED PER YEAR: 2010[ ] 2011[ ] 2012[ ] 2013[ ]
9. NUMBER OF PATIENTS WITH ANTIBIOTICS IN THEIR PRESCRIPTION PER YEAR: 2010[ ] 2011[ ] 2012[ ] 2013[ ]
10. NUMBER OF PATIENTS WITH ANTIBIOTICS IN THEIR PRESCRIPTION BY GENDER: Male[ ] Female[ ]
11. TOTAL NUMBER OF PATIENTS THAT USED ANTIBIOTICS FROMJANUARY 2010 TO MAY 2014: [ ]
12. COMMONLY PRESCRIBED ANTIBIOTICS PER MONTH:……

    ……

    ……

    ……
13. GENERALLY PRESCRIBED ANTIBIOTICS PER

YEAR:……

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14. COMMONLY PRESCRIBED ANTIBIOTICS WITHIN JAN. 2010-MAY 2014:……

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15. MOST COMMONLY TREATED DISEASES PER MONTH:……

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16. MOST COMMONLY TREATED DISEASES WITHIN JAN. 2010-MAY 2014:……

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17. CLASS OF ANTIBIOTICS COMMONLY USED……

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