THE USE OF ANTIBIOTICS AND THE PATTERN OF ANTIMICROBIAL RESISTANCE AT S.D.A HOSPITAL, KUMASI, GHANA

BY

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DECLARATION

This document is my own work and all sources of information have been fully acknowledged by means of reference or quotation marks. This work has not been submitted by any other for the award of a degree.

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DEDICATION

To my wife Lydia and kids Antwiwaa and Aseda

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ABSTRACT

Objectives of Study

To assess the current antibiotic prescribing and use pattern and the extent of microbial resistance to antibiotics at the Seventh-Day Adventist (SDA) Hospital in Kumasi. Also to obtain data that will serve as a basis for designing intervention to improve the quality of antibiotic prescribing and use at the hospital.

Methods

All the patients who were admitted between 1st March to 15th April 2013 and consented to participation in the study were included. Total number of patients involved was 176.

Data on antibiotic prescribing and use was extracted from the medical notes, nursing notes and medication sheets of the patients followed by interviews with prescribers, other health professionals or the patients when necessary. Also laboratory data on antibiotic susceptibility testing was analyzed to assess the extent of antimicrobial resistance at the hospital.

Results

The average number of drugs per prescription for the patients in this study was 5. In all 82% of the prescriptions given to the patients contained antibiotic. Average number of antibiotics per prescription was 1.6.

Ciprofloxacin was the most commonly prescribed antibiotic followed by cefuroxime and ceftriaxone. With regards to combination therapy, ciprofloxacin and metronidazole was the most prescribed and also used by the patients. Out of the 145 patients who received antibiotics during the study, none of the prescriptions was informed by culture and sensitivity results.

Analysis of the culture and sensitivity data obtained from the lab indicated that *Esherichia coli*, *Staphyllococcus aureus* and *Salmonella* were the most pathogenic organisms isolated for patients at the hospital. All the three isolates (*Esherichia coli, Staphyllococcus aureus and Salmonella*) were mostly susceptible to gentamicin, cefotaxime, and ceftriaxone but resistant to ampicillin, chloramphenicol, cotrimoxazole, tetracycline and erythromycin and to some extent cefuroxime.

Conclusion

Polypharmacy practice was high at the hospital, and the use of antibiotics which were mostly given empirically was also too high. In addition, the study suggested widespread microbial resistance to many common antibiotics including a second generation cepholosporins. There is the need to establish protocols to guide the prescribing and judicious use of antibiotics in the hospital, and thus minimize waste and the risk of spread of microbial resistance to effective and life saving antibiotics currently available in the Ghanaian health system.

1.0 INTRODUCTION

Selman Waksman and his collaborators were the first to use the term antibiotics in their journal articles to describe any substance produced by a microorganism that is antagonistic to the growth of other microorganisms in high dilution (Waksman S.A, 1973). Their definition did not include other agents like gastric juices and hydrogen peroxide that were able to kill bacteria but did not originate from bacteria. Most antibiotics currently in used are semisynthetic modifications of various natural compounds and thus the term antibiotics include all of these substances.

The discovery of antibiotics has been said to be one of the biggest breakthrough in the medical world. This is not just because of their use in the management of bacterial infections but also for their role in some other diseases like viral infections, in the management of cancer and even in some cardiovascular diseases and for immunosuppression.

Antibiotics are life saving instruments that can be compared to other practices like mechanical ventilation, dialysis and other life support devices and thus they should be used with care and caution.

Although antibiotics has now come to save a lot of lives who at first could not be saved, over use and inappropriate use of antibiotics has led to development of resistance against these agents.

The first agents to be used as chemotherapeutic agents were the sulphonamides in 1937 although Sir Alexander Fleming had discovered the Penicillins in 1928 it was until the 1940s when penicillins were produced commercially. Streptomycin was introduced in 1944 for the management of tuberculosis, since then a lot more antibiotics have been rapidly produced by scientist. 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. (Chambers HF, 2006)

1.1 EXTENT OF ANTIBIOTIC USE

Antibiotics are mostly useful in the management of bacterial infections, but now are being given for almost every condition and its applied to almost every part of the body.

Fever is one major cardinal sign of infection, but not all fevers are of infectious origin and even not all infections are due to bacterial. Most of the infections seen in general practice are of viral origin and antibiotics can neither treat viral infections nor prevent secondary bacterial infections in these patients.

In circumstances where bacterial aetiology is even established, an antibiotic may not always be necessary as many bacterial infections are self limiting.

The evaluation of the quality of prescriptions with antibiotics in the Government Hospitals of Yemen by Abdulkareem M. et al indicated that the average percentage of prescriptions with antibiotics was 51.0% (Abdulkareem M et al, 2011). A similarly high percentage was reported in Sudan (30 to 60%) (Sachs L, Tomson G., 2009) Similarly, a study which was carried out in Cambodia showed that the percentage of antibiotics which was used ranged from 10.0% to 66.0% (Chareonkul *et al, 2002)*. However, the average percentage of the antibiotics which was used in Malaysia was lower (23.2%) (Saleh K, 2004) and even lower percentages of antibiotic use were reported in Mongolia (20.6%) (WHO, 2003).

Average percentage of prescription encounters containing antibiotics was 50.10% in a studies conducted in Osun state in Nigeria (Babola et al, 2010). Average value of 43.1% obtained from

previous studies from developing countries like Malawi (34%), Indonesia (43.1%), Bangladesh (25%), and Tanzania (39%) (Slobodan et al., 2006; Massele et al. 2001).

Antibiotic prescribing patterns was studied from 700 retrospective outpatient clinical records from seven government health facilities in the Wassa West district of Ghana showed a higher value of 60.7% (Bosu WK, Ofori-Adjei D 2000). Another study conducted at public health facility dispensaries and public health facilities in Ghana in 2008 also showed a value 43.3% (Arhinful K.D, 2009).

1.2 PATTERN OF USE OF ANTIBIOTICS

Assessment of drug use pattern using WHO prescribing indicators at a Teaching Hospital in south Ethiopia showed that the most commonly prescribed antibiotics were amoxicillin, ampicillin (15%), gentamicin and chloramphenicol.(Desalegn AA, 2013)

A study conducted at Korle Bu Teaching Hospital in 2009 revealed Ciprofloxacin and Metronidazole as the most prescribed antibiotics. (Acheampong F.,2009). In the study conducted by Bosu and Ofori Adjei in seven government health facilities in the Wassa West district of Ghana in the year 2000, the commonest antibiotics prescribed were procaine penicillin, cotrimoxazole, benzyl penicillin, metronidazole and amoxycillin. (Bosu WK, Ofori-Adjei D 2000)

1.3 SELECTION OF AN ANTIBIOTIC AGENT

Antibacterial agents have three major uses; empirical uses, definitive use, and prophylactic or preventive uses. Clinical judgment and a detailed knowledge of both the pharmacological and microbiological factors are required in the rational use of antibacterial agents.

1.3.1 EMPIRICAL USES OF ANTIBIOTICS

Empirical Antibacterial therapy is the use of antibacterial agents before the aetiological agent is known due to the fact that culture and sensitivity test results are not readily available. This use of antibiotics is based on experience with a particular clinical entity and guided by the clinical presentation.

The usual explanation for empiric therapy is the hope that early intervention will improve the outcome. For example, diverse studies have confirmed that the prompt institution of antimicrobial therapy active against the causative pathogen is life saving in patients with severe sepsis. (Ferrer R, et al 2009) (Garnacho-Montero J, et al 2003). The surviving sepsis campaign strongly recommends initiating antibiotic therapy within the first hour of recognition of severe sepsis, after suitable samples have been obtatined for cultures (Dellinger RP, et al 2008)

Septic shock is present in 10% of intensive care unit (ICU) patients with a mortality rate of nearly 60% (Ferrer et al, 2009). Early and adequate introduction of antibiotics improve survival in severe sepsis and septic shock patients (Torres A, Aztar R et al, 1990). Leibovici L. et al in their research on the benefit of appropriate empiric antibiotic treatment in patients with bloodstream infection concluded that appropriate empiric antibiotic treatment was associated with a significant reduction in fatality in patients with bloodstream infection .(Leibovici L, Shraga I, Drucker M et al, 1998)

1.3.2 SELECTING ANTIBIOTICS FOR EMPIRICAL USES.

Broad spectrum antibiotics or a combination of antibiotics are normally used for empirical therapy. Guidelines recommend that physicians first combine broad-spectrum antibiotics followed by a reappraisal of the therapy as soon as bacteriological data and susceptibility tests

are available in order to eventually reduce the number and the spectrum of the antibiotics (Niederman MS) (Dellinger RP, Levy MM et al, 2008). For example, in the management of community-acquired pneumonia, a macrolide is used for atypical organisms such as *Mycoplasma,* and cefuroxime is used for Pneumococci and gram-negative pathogens.

1.3.3 INAPPROPRIATE EMPIRICAL THERAPY

Various studies have suggested the importance of appropriate empirical studies, but inappropriate empiric antibiotic therapy can be detrimental to the health of the patient. It can lead to increased morbidity and mortality, and can also increase bacterial resistance. (Goldmann DA, Weinstein RA, Wenzel RP et al, 1996). Leibovici L. et al in their research on the benefit of appropriate empiric antibiotic treatment in patients with bloodstream infection concluded that appropriate empiric antibiotic treatment was associated with a significant reduction in fatality in patients with bloodstream infection However, the same study also found out that 20–50% of patients are given inappropriate empirical antibiotic treatment.(Leibovici L, Shraga I, Drucker M et al, 1998).

One of the major causes of inappropriate initial antimicrobial therapy was the underrecognition of the infections with antimicrobial-resistant organisms (Pazos Anon R, Fernandez Rodriguez R, Tinajas A et al. 2004).

From a report by Kang et al in 2005, Inappropriate empiric antimicrobial therapy was notably higher in the gram-negative bacteria group than the gram-positive bacteria group, resulting in the increasing of mortality in gram-negative bacteremia, especially drug-resistant organisms. (Kang CI, Kim SH, Park WB et al, 2005).

Drug resistant gram-positive bacteria, such as the most frequent MRSA, also significantly associated with the inappropriateness of empirical antimicrobials. Paul et al. demonstrated that inappropriate antimicrobials in MRSA septicemia obviously increased a risk for mortality (M. Paul, G. Kariv, E. Goldberg et al, 2010)

Some patients with symptoms and signs of a serious infection do not, in fact, have an infection at all. Examples include patients with pulmonary edema or hemorrhage with radiologic appearances similar to those of ventilator-associated pneumonia (VAP) (Chastre J, Luyt CE et al, 2006) (, as well as patients with cerebral hemorrhage, advanced cirrhosis, severe burns, malignancy, or autoimmune conditions with fever or hypotension (symptoms that normally would be expected in a severe infection). In these situations, antibiotic therapy creates an increased risk of disturbance of endogenous flora, potentially leading to ***Clostridium difficile*** infection or colonization with antibiotic-resistant bacteria . (Muto CA, Pokrywka M et al, 2005) (Donskey CJ, 2006)

Habitual use of the same antibiotic regimen for all patients with suspected significant bacterial infection may lead to increased resistance (Bonhoeffer S et al 1997) and/or increased rates of inadequate coverage. As described by Kollef, in this situation, inadequate initial empirical therapy is associated with increases in adverse patient outcomes. (Kollef MH, 2000)

1.3.4 DEFINITIVE ANTIMICROBIAL THERAPY

Due to the increasing incidence of resistance to antibiotic therapy by most bacterial, it is always advisable to identify the exact pathogen causing infection before initiating treatment as antimicrobial resistance is strongly associated with adverse patient outcomes and increased resource utilization. The first consideration in selecting an antimicrobial agent is whether it is

even indicated. Each antibiotic use, whether appropriate or inappropriate, affects the bacterial natural balance by exerting selective pressure and thereby driving resistance. Thus, all antibiotic use has possible public health cost and, in this way, differs from the use of all other classes of pharmaceutical agents.

Bacterial strains, even from the same species, may vary widely in sensitivity to antibiotics. Information about the antimicrobial susceptibility of the infecting microorganism is important for appropriate drug selection.

When initially faced with a patient with a serious infection, the clinician mostly do not have any specific knowledge of the aetiologic pathogen and therfore must choose antibiotics empirically.

Once microbiology results have helped to identify the etiologic pathogen and/or antimicrobial susceptibility data are available, every attempt should be made to taper the antibiotic spectrum. This is a significant factor of antibiotic therapy because it can reduce cost and toxicity and prevent the emergence of antimicrobial resistance in the community.

1.3.5 INTERPRETATION OF ANTIBIOTIC SUSCEPTIBILITY TEST

Successful antimicrobial therapy of an infection depends on the concentration of antibiotic at the site of infection. This concentration must be adequate to inhibit growth of the offending microorganism. If host defenses are intact and active, a minimum inhibitory effect, such as that provided by bacteriostatic agents may be sufficient. On the other hand, if host defenses are impaired, bactericidal effect may be required to exterminate the infection. The concentration of drug at the site of infection not only must inhibit the organism but also must remain below the level that is toxic to human cells. If this can be achieved, the microorganism is considered

susceptible to the antibiotic. If an inhibitory or bactericidal concentration exceeds that which can be achieved safely *in vivo*, then the microorganism is considered resistant to that drug.

Antimicrobial susceptibility testing measures the ability of a specific organism to grow in the presence of a particular drug in vitro and is performed using guidelines established by the Clinical and Laboratory Standards Institute, a nonprofit global organization that develops laboratory process standards through extensive testing and clinical correlation.

The purpose of Antimicrobial Susceptibility Test is to predict the clinical success or failure of the antibiotic being tested against a particular organism. Data are reported in the form of minimum inhibitory concentration (MIC), which is the lowest concentration of an antibiotic that inhibits visible growth of an microorganism, and are interpreted by the laboratory as "susceptible," "resistant," or "intermediate," according to Clinical and Laboratory Standards Institute criteria. A report of "susceptible" indicates that the isolate is likely to be inhibited by the usually achievable concentration of a particular antimicrobial agent when the recommended dosage is used for the particular site of infection. For this reason, MICs of different agents for a particular organism are not directly comparable. For example, MICs of 1 (susceptible) for ciprofloxacin and 2 (susceptible) for ceftriaxone against *Escherichia coli* do not imply that ciprofloxacin is twice as active as ceftriaxone. Instead, it indicates that concentrations achieved by giving recommended doses of both drugs are likely to be active against the organism. Although AST results are generally quite useful in narrowing the antibiotic regimen, AST has some limitations that should be kept in mind. First, it is important for both clinicians and laboratory personnel to be aware of the site of infection. For example, an isolate of *S aureus* could be reported as susceptible to cefazolin in vitro; however, if this particular isolate was

obtained from the cerebrospinal fluid (CSF), cefazolin would not be an optimal therapeutic choice because it does not achieve therapeutic concentrations in the CSF. Clinical laboratories may provide different AST interpretations for different sites of infection (eg, meningitis and nonmeningitis AST results for *S pneumoniae*). In addition, some organisms carry enzymes that, when expressed in vivo, can inactivate antimicrobial agents to which the organism shows in vitro susceptibility. Although their presence is not immediately apparent from AST results, certain AST "patterns" can provide a clue to their existence. For example, extended-spectrum β-lactamases (ESBLs) in *Enterobacteriaceae* are enzymes that mediate resistance to almost all β-lactam agents except carbapenems (eg, meropenem or imipenem). Extended-spectrum β-lactamases can be difficult to detect because they have different levels of in vitro activity against various cephalosporins. In clinical practice, susceptibility to cephamycins (cefoxitin, cefotetan) but resistance to a third-generation cephalosporin (eg, cefpodoxime, cefotaxime, ceftriaxone, ceftazidime) or aztreonam should alert one to the possibility of ESBL production. The production of ESBL should also be suspected when treatment with β-lactams fails despite apparent in vitro susceptibility. This should lead to additional testing, which usually involves growing the bacteria in the presence of a third-generation cephalosporin alone and in combination with clavulanic acid (a β-lactamase inhibitor); enhanced bacterial inhibition with the addition of clavulanic acid indicates ESBL. When detected by the laboratory, these bacteria should be considered resistant to all β-lactam agents except the carbapenem class.

In general, it is good practice to communicate directly with the microbiology laboratory when antimicrobial susceptibility patterns appear unusual. It is also useful to be aware of the limitations of AST at the local laboratory, particularly in smaller hospitals (eg, testing of

relatively newer agents [such as daptomycin for gram-positive cocci] might not be routinely performed or reported but could be available on request). (Surbhi leekha et al 2011)

1.3.6 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. In addition, patients initially managed with parenteral therapy can be carefully switched to oral antibiotics when they become clinically stable. When using oral therapy for invasive infections such as pneumonia, pyelonephritis, or abscesses, clinicians are advised to select an agent that has excellent absorption and bioavailability (Surbhi leekha et al 2011). Examples of antibiotics with excellent bioavailability are fluoroquinolones, cotrimoxazole, and metronidazole. For more serious infections, such as meningitis, in which high serum or Cerebrospinal Fluid drug concentrations are preferred, a change to oral therapy is less dependable and not generally recommended. (Baddour LM, Wilson WR, Bayer AS, et al. 2005)

1.4 THERAPY WITH COMBINED ANTIBIOTIC AGENTS

The simultaneous use of two or more antibiotics is sometimes 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 superadditive 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 (Rybak *et al.*, 1999).

1.4.1 INDICATIONS FOR THE CLINICAL USE OF COMBINATIONS OF ANTIBIOTICS.

Use of a combination of antibiotics may be considered for empirical therapy of an infection in which the cause is not known, for treatment of polymicrobial infections, to enhance antimicrobial activity (*i.e.*, synergism) for a specific infection, or to prevent emergence of resistance.

i. **Empirical therapy of an infection in which the cause is unknown;** Empirical therapy of infection perhaps is the most common basis for using a combination of antibiotics. Combination therapy is used in this situation to ensure that at least one of the administered antibiotics will be active against the suspected organism(s). For example, in the treatment of community-acquired pneumonia, a macrolide is used for atypical organisms such as *Mycoplasma*, and *cefuroxime* is used for pneumococci and gram-negative pathogens. Prolonged administration of empirical broad-spectrum coverage or multiple antibiotics, however, should be avoided; it often is unnecessary (e.g., when the infection is caused by a single pathogen or no infection is documented) and unnecessarily expensive. Moreover, toxicity, superinfection, and selection of multiple-drug-resistant microorganisms may result. Inappropriately broad spectrum often is continued because adequate cultures were not obtained before the commencement of therapy or because of the false impression that a broad-spectrum regimen is superior to a narrow-spectrum regimen. Although unwillingness to change antibiotics is understandable when a positive clinical response has occurred, the goal should be to use the most selectively active drug that gives the fewest adverse effects, which includes adverse affects on host normal flora.

ii. **Treatment of Polymicrobial Infection;** sometimes there might be more than one likely pathogens for an infection, in such situations a combination regimen may be preferred because it would extend the antibiotic coverage beyond that achieved by a single agent. Most infections of the intra-abdominal, hepatic and brain are typically mixed aerobic –anaerobic infections and thus may require the use of a drug combination. These and other mixed infections may be caused by two or more microorganisms that are different in antimicrobial susceptibility such that no single agent can provide the required coverage.

iii. **Enhancement of Antibacterial Activity in the Treatment of Specific Infections.** Antibiotics given together may produce a synergistic effect. Synergy between antimicrobial agents means that, when studied in vitro, the combined effect of the agents is greater than the sum of their independent activities when measured separately. (Pillai SK, Eliopoulos GM et al 2010). Synergistic combinations of antibiotics have been shown to be better than single-agent therapy in some few conditions. For example, the combination of certain β-lactams and aminoglycosides exhibits synergistic activity against a variety of gram-positive and gram-negative bacteria (Drusano GL, 1990) and is used in the management of serious infections, for which rapid bactericidal effect is needed. Example is seen in the treatment of endocarditis caused by ***Enterococcus*** species with a combination of penicillin and gentamicin. In this setting, the addition of gentamicin to penicillin has been shown to be bactericidal, whereas penicillin alone is only bacteriostatic and gentamicin alone has no significant activity.

iv. ***Prevention of the Emergence of Resistant Microorganisms.*** The emergence of resistant mutants in a bacterial population is generally as a result of selective pressure from antibiotic therapy. Given that the mechanisms of resistance to two antibiotics are different, the chance of a mutant strain being resistant to both antibiotics is much lower than the chance of it being resistant to either one. In other words, the use of combination therapy would give a better chance that at least one drug will be effective, thereby preventing the resistant mutant population from emerging as the dominant strain and causing therapeutic failure. This is why combination drug therapy is used as the standard for treatment of infections such as tuberculosis and the human immunodeficiency virus (HIV) when treatment duration is likely to be prolonged, resistance can emerge relatively easily, and therapeutic agents are limited.

1.4.2 DISADVANTAGES OF COMBINATIONS OF ANTIMICROBIAL AGENTS.

Drawbacks to antibiotic combinations include increased risk of toxicity from two or more agents, selection of multiple-drug-resistant microorganisms, eradication of normal host flora with subsequent superinfection, and increased cost to the patient.

1.5 THE DURATION OF ANTIBIOTIC THERAPY

The duration of antibiotic therapy needs to be adequate to control the bacterial infection and prevent relapse. When optimizing therapy for an infection it is very important to consider the person's immune status, the infecting agent and the focus of infection. The optimal duration of antibiotic therapy for many infections is well defined, such as for UTIs and pneumonia (Therapeutic Guidelines limited, 2010) However, it may be surprising to learn there is a lack of randomised clinical trials to establish the course of therapy for many common infections

(Horsburgh CR, et al 2013). It is difficult to change prescribing practices to shorten antibiotic courses without strong evidence supporting the safety and efficacy (Rice LB, 2008).

Several studies have shown that when antibiotics are given for a longer than normal duration it leads to the development of of antibiotic resistant organisms. For example in one study penicillin resistance risk increased by 4% for each day of beta-lactam antibiotic taken in the preceding 6 months (Nasrin D, et al, 2002). Another trial also demonstrated that a low daily dose and a long duration of treatment with oral beta-lactam correlated with penicillin-resistant pneumococcal carriage in children (Guillemot D, et al, 1998).

Compliance to antibiotic therapy is also another factor that is of great concern to the medical world. The least complied regimens are those of longer duration with higher frequencies. In patients given a prescription for respiratory symptoms, a recent study demonstrated that > 41% did not take them and only about 44% took the prescribed course (Francis NA et al, 2012). For some infections, such as *Staphylococcus aureus* bacteraemia, enterococcal endocarditis or tuberculosis, clear evidence favours prolonged treatment to prevent relapse (Paul J, 2006)

It is therefore advisable to keep duration of therapy as short as possible, unless otherwise indicated, as this may lower the selection pressure and help prevent resistance in the individual.

Shorter course of antibiotic therapy have been very successful in treating some infections, such as a 3-day course for uncomplicated UTIs in women(Therapeutic Guidelines limited, 2010)(Rice LB, 2008)

1.6 ASSESSMENT OF RESPONSE TO TREATMENT

Response to treatment of an infection with antibiotic is normally assessed using both clinical and microbiological indicators. Clinical indicators of progress include symptoms and signs (eg, a decrease in fever, tachycardia, or confusion), laboratory values (eg, decreasing white blood cell count), and radiologic findings (eg, decrease in the size of an abscess). Although radiologic criteria are commonly used in assessing response to infectious disease therapy, radiologic improvement can normally lag behind clinical improvement, and routine radiographic follow-up of all infections is not always necessary. For example, in a study of clinical and radiographic follow-up of patients with community-acquired pneumonia, (Bruns AH et al, 2010) clinical cure was observed in 93% of patients after 10 days of follow-up, whereas radiographic resolution was noted in only 31% of patients. In fact, several weeks or even months may be required before chest radiography or computed tomography shows complete resolution of an infiltrate.

Bacteremia is the most common setting in which microbiological response is closely assessed as clearance of the bloodstream is as significant as clinical improvement. Persistent bacteremia is often the only evidence to the presence of an ineffectually treated source or to the existence or development of endovascular infection (such as endocarditis or an intravascular device infection). Persistent bacteremia can also be associated with the emergence of antimicrobial resistance and should always be investigated. (Bennet JW et al, 2008)

1.7 MISUSES OF ANTIBIOTICS

The use of antibiotics can be said to be inappropriate in some scenarios. Examples of these scenarios are been given

i. **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 (Nyquist *et al.*, 1998). Many noninfectious, inflammatory, or neoplastic syndromes can present with symptoms and signs that resemble infectious diseases. Examples include adult-onset Still disease and other connective tissue disorders that can present with high fever, some fever can also be induced by some drugs, the fever associated with pulmonary embolism, and recurrent sinusitis. Most clinicians also tend to manage some viral infections with antibiotics which is not necessary. Thus, antibiotic therapy of measles, mumps, and at least 90% of infections of the upper respiratory tract and many Gastrointestinal infections is ineffective and, therefore, useless.

ii. **Treatment of fever of unknown origin;** Fever of uncertain cause may last for only a few days to a week or for a longer duration. These type of fever are frequently and inappropriately treated with empirically with antibiotics. Fever of short duration, unaccompanied by localizing signs, probably is associated with undefined viral infections. Antibiotic therapy is therefore irrelevant, 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 (de Kleijn *et al.*, 1997). Noninfectious causes, including regional enteritis, lymphoma, renal cell carcinoma, hepatitis, and drug fever, do not respond to antimicrobial agents at all. Rather than embarking on a course of empirical antimicrobial therapy for fever of unknown origin, the physician should search for its cause.

iii. **Improper Dosage.** Errors in dosing, which can be in the form of wrong frequency of administration or the use of either an excessive or a subtherapeutic dose, are common. Although antibiotics are among the safest and least toxic of drugs used in medical practice, overdosage can lead to significant toxicities, including seizures example as seen in penicillin, vestibular damage and renal failure in aminoglycosides, especially in patients with impaired drug excretion or metabolism. Under dosing may also result in treatment failure and is most likely to select for bacterial resistance.

iv. **Inappropriate Reliance on antibiotics alone.** Infections complicated by abscess formation, the presence of necrotic tissue, or the presence of a foreign body often cannot be cured by antibiotic therapy alone. Drainage, debridement, and removal of the foreign body are at least as important as the choice of antibiotic. For example, the patient with pneumonia and emphysema is often unresponsive to administration of large doses of an effective drug unless the infected pleural fluid is drained. The patient with *S. aureus* bacteremia owing to an intravascular device will continue to have fevers and positive blood cultures and is at risk of dying unless the device is removed. As a general rule, when an appreciable quantity of pus, necrotic tissue, or a foreign body is present, the most effective treatment is an antimicrobial agent given in adequate dose plus a properly performed surgical procedure.

v. **Lack of Adequate Bacteriological Information.** Antibiotics given to hospitalized patients is most often given without any supporting microbiological data. Bacterial cultures and Gram stains of infected patients are not frequently obtained, and the results, even when is available, is often disregarded in the selection and administration of drug therapy. Frequent use of drug combinations or drugs with the

broadest spectra is a cover for diagnostic ambiguity. The agents are selected more likely by habit than for specific indications, and the dosages prescribed are routine rather than individualized on the basis of the clinical state.

vi. **Treatment of a Positive Clinical Culture in the Absence of Disease.** Sometimes there can be colonization with potentially pathogenic organisms without any associated sign of disease is normally seen in certain populations, examples are colonization of the urinary tract in women of advanced age or in the presence of an indwelling urinary catheter, colonization of endotracheal tubes in mechanically ventilated patients, and colonization of chronic wounds. Appropriate management in these situations involves obtaining cultures from these sites only when indicated and avoiding treatment of a "positive" culture result when symptoms and signs of active infection are absent as in asymptomatic bacteriuria.

vii. **Failure to Narrow Antibiotic Therapy When a Causative Organism Is Identified.** For most infections encountered in most hospitals, initial therapy is often empiric and relies on broad-spectrum agents until culture or other tests help to determine the aetiological pathogen. Once culture and susceptibility data are available, an antibiotic with the narrowest possible spectrum should be selected for continuation of therapy. Most of the time, however, this does not occur, particularly if the patient has improved while receiving empiric therapy, and the physician is uncomfortable about changing therapy in the face of clinical improvement.

viii. **Prolonged Prophylactic Usage of Antibiotics.** At times antibiotics are used prophylactically to prevent some infections especially before and after surgical procedures. However, in most cases, guidelines support the use of a single,

preoperative dose of an antimicrobial agent. Prolonged “prophylaxis” simply sets the stage for the emergence of antimicrobial resistance. For example, the common practice of prolonging antimicrobial therapy until the removal of surgical drains is not supported by any evidence.

ix. **Excessive Use of Certain Antibiotics.** Some prescribers are most of the time stack to one particular antibiotic or class of antibiotic because they see it to be very effective and this can result in selection of organisms that are resistant to that particular antibiotic. For example, the increased use of fluoroquinolones during the past decade is thought to be, in part, responsible for the epidemic of a fluoroquinolone-resistant strain of *Clostridium difficile*, (Pepin J, et al, 2005) the most common cause of nosocomial infectious diarrhea. More recently, an increase in levofloxacin use as initial therapy for UTI as a result of policy change at a single institution was found to have led to a rapid increase in fluoroquinolone resistance among outpatient urinary ***E coli*** isolates at that institution (Johnson L, et al, 2008). For this reason, those involved in antimicrobial stewardship should avoid the excessive prescribing of a single class of antibiotic.

1.8 BACTERIAL RESISTANCE TO ANTIMICROBIAL AGENTS

The indiscriminate use of antibiotics has led to most bacterial developing resistance against the available antibiotics. Certain bacterial infections now defy all antibiotics. Antimicrobial drug resistance is a global issue that affects health, economic, and social development. 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. The rise in antibiotic resistance by bacterial can be attributed to the various misuses of antibiotics as

discussed earlier i.e. treatment of nonresponsive infections, treatment of fever of unknown origin, improper dosage inappropriate reliance on antibiotics alone, lack of adequate bacteriological information, treatment of a positive clinical culture in the absence of disease**,** failure to narrow, antibiotic therapy when a causative organism is identified**,** prolonged prophylactic usage of antibiotics and excessive use of certain antibiotics

The following studies on antibiotic resistance was taken from a fact sheet by Action on Antibiotic Resistance (ReAct) an independent global network for concerted action on antibiotic resistance.

ESBL-producing bacteria are frequently causing infections in newborns. In an Indian hospital, Klebsiella and E-coli were the most common Gram-negative bactria among infants with BSIs. About 33% of ESBL-infections were deadly in spite of available newer antibiotics and other supportive care.

In a study from Pakistan, 37 of 78 newborns (less than 6 days old) with infections due to Actinobacter died within a short time frame. 71% of the bacteria were resistant to all antibiotics.

In an outbreak in india caused by NDM-1 E-coli, four newborn babies contracted blood stream infections. All four died.

Three premature babies in a German neonatal ward died due to an outbreak of ESBL-producing *Klebsiella pneumonia* from an unknown source.

In a study of Tanzanian children, the BSI rate was as high as 13.9%. one third of these children died. The death rate from Gram-negative BSI (43.5%) was more than double that of malaria

(20.2%). One significant risk factor for death was treatment with ineffective antibiotics due to antibiotic resistance.

In Spain, among 416 patients undergoing transplantations of kidneys, 58 were infected with multi drug resistant bacteria, most often Gram-negative BSIs occurred in 14% of those. Death or graft loss was significantly more frequent among those with MDR infections (19% vs. 8 %).

In egpyt, children contracting a BSI while treated for cancer were followed. Among 239 episodes of BSI, 385 were multidrug resistant. Twenty five children died and among those, 72% were infected with multidrug resistant bacteria.

The above studies show that antibiotic resistance poses threat to human health across the globe. The rampant spread of antibiotic resistance mandates a more responsible approach to antibiotic use.

A prospective quantitative study set in various hospitals including two teaching hospitals, seven regional hospitals, and two district hospitals in Ghana from December 2002 to December 2003 indicated that The most prevalent organism in the country was *Escherichia coli***,** followed by ***S. aureus*****,** *Klebsiella* spp, and *Pseudomonas aeruginosa* (Mercy J.N et al 2011)**.** High percentage of resistance was observed for tetracycline, cotrimoxazole, ampicillin , and chloramphenicol. Another study conducted by Duredoh Freeman George et al in 2010 to determine the antibiotic resistance patterns of Escherichia coli isolated from Kumasi-South, Tafo and Suntreso Hospitals, Kumasi, Ghana also showed that Majority of the E. coli isolates (90.7%) exhibited resistance to ampicillin while 6.2 and 3.1% showed intermediate and sensitive respectively. Co-trimoxazole, 78.4% of the isolates were resistant while 9.3 and 12.4% exhibited

intermediate and sensitive responses respectively. E. coli isolates (28.6 to 46.4%) were resistant to gentamicin, ciprofloxacin and ceftriaxone while 14.4 to 47.4% gave intermediate responses.(Duredoh F.G. et al 2012).

1.8.1 PREVENTING THE APPEARANCE OF ANTIBIOTIC RESISTANCE

The single most important cause for the emergence of drug resistance as already said is the erratic and inappropriate use of these life saving agents. Prior antibiotic exposure has been shown to be the most frequent risk factor for the development of community-acquired respiratory infections caused by drug-resistant *S pneumonia*. (Levine OS, et al 1999) This is not surprising because acute upper respiratory illnesses account for the highest proportion of ambulatory antibiotic prescriptions, (McCaig LF, Hughes JM, 1995) with most being dispensed in situations in which antibiotics were not even indicated (Gonzales R, et al 2001). The emergence of antimicrobial resistance can be prevented or delayed through careful prescribing, which can be characterized as follows: avoidance of antibiotic treatment for community-acquired, mostly viral, upper respiratory tract infections; use of narrow-spectrum antibiotics when possible; and use of antibiotics for the shortest duration that is effective for the treatment of a particular clinical syndrome.

In the past few years, interest has been increasing in the development of rapid and accurate diagnostic tests for detection of viral respiratory pathogens with the ability to differentiate between viral and bacterial infections, such as measurement of procalcitonin levels and nucleic acid tests. Although not yet widely available in clinical practice, these tests have the potential to stop the use of antibacterial agents for clinical syndromes that are clearly caused by viruses.

1.9 AIMS AND OBJECTIVES OF THE STUDIES

1.9.1 AIMS

This survey sought to describe the current antibiotic use pattern and the extent of antimicrobial resistance and also gather baseline data that will serve as a basis for designing intervention to improve the antibiotic use profile in the institution

1.9.1 OBJECTIVES

1. To determine the extent and pattern of antibiotic use in the hospital.
2. To determine whether the use of antibiotics in the hospital is empirical or definitive.
3. To determine how patients respond to antibiotic therapy in the hospital.
4. To determine the extent of antimicrobial resistance in the hospital.

Among the key areas that the project will look at are:

- The average number of drugs per prescription.
- The number of prescriptions with an antibiotic.
- The types of antibiotics commonly used in the hospital.
- Data on the appropriateness of choice, where available.
- Available results from susceptibility tests done in clinical microbiology laboratory on pathogens isolated from patients visiting the hospital will be collated and analysed.

CHAPTER 2

2.0 RESEARCH METHODOLOGY

2.1 SETTING

S.D.A Hospital , Kumasi, is an eighty two (82) bed mission hospital established by the Central Ghana Conference of the Seventh – Day Adventist Church. The hospital is situated at Kwadaso along the main Kumasi – Sunyani road.

The hospital has a male and female medical wards, a paediatric ward, male and female surgical wards and a recovery ward. The hospital is a member of the Christian health association of Ghana under the Ministry of Health and it is also accredited to provide primary level health care to members registered under the National Health Insurance scheme and other private insurance bodies.

2.2 SAMPLE

Patients included in the study were patients admitted at the male and female medical wards and paediatric of the Seventh-Day Adventist Hospital in Kwadaso, Kumasi between the study period of 1st March to 15th April 2013. Patients excluded from the studies were; out-patients, and patients at the surgical and recovery wards.

A total of 176 patients who were on admission during the study period and consented to participate were included in the analysis.

Laboratory data on antibiotic susceptibility testing between January and March 2013 was also obtained from the Laboratory and analysed.

2.3 DATA COLLECTION METHODS

A questionnaire was designed to assess the use of antibiotics in the hospital. It was then used to develop a data collection form, on which particulars of the patient and he relevant clinical information on antibiotic use were documented. The required information was extracted from the medical notes, nursing notes and medication sheets followed by interviews with the patients and prescribers where necessary.

The existing laboratory data on antibiotic susceptibility testing of the laboratory unit was also collected and analysed.

2.4 TREATMENT OF DATA

The data obtained was analysed using IBM SPSS version 21 and Microsoft Excel 2007.

Frequencies, graphs, and charts, as well as in depth analysis of the outcomes, extent of use and resistance was used.

CHAPTER 3

3.0 RESULTS

The total number of patients involved in the study was 176. One hundred and four were females (59.1%) and 72 males (40.1%) (Table 1)

3.1 AGE AND GENDER DISTRIBUTION OF RESPONDENTS

Table 1: AGE AND GENDER DISTRIBUTION OF RESPONDENTS

Age range of respondents	Gender of Respondent		Total
	Female (n)	Male (n)	n (%)
0-11	36	25	61(34.7)
12-25	20	8	28(15.9)
26-40	11	17	28(15.9)
41-60	16	19	35(19.9)
61-75	0	3	3(1.7)
76-85	21	0	21(11.9)
Total	**104**	**72**	**176**

The largest group of patients were children between the ages of 0-11 years n= 61 (representing 34.7%) while patients between the ages of 61 -75 years were the least, n=3 (1.7%).

3.1 AVERAGE NUMBER OF DRUGS PER PRESCRIPTION

The average number of drugs per prescription is 5, with a range of 2 to 16 (table 2).

Table 2: Total number of drugs prescribed per prescription

Number of drugs prescribed per prescription	**n (%)**
2	16(9.1)
3	37(21)
4	25(14.2)
5	38(21.6)
6	28(15.9)
7	16(9.1)
8	5(2.8)
11	6(3.4)
16	5(2.8)
Total	**176(100)**

3.3 THE EXTENT AND PATTERN OF USE OF ANTIBIOTICS USE AT THE HOSPITAL

One hundred and forty five (145) of the patients studied (82.4%) received one or more antibiotics as part of their medication while 31 patients (17.6%) had no antibiotics (fig 1).

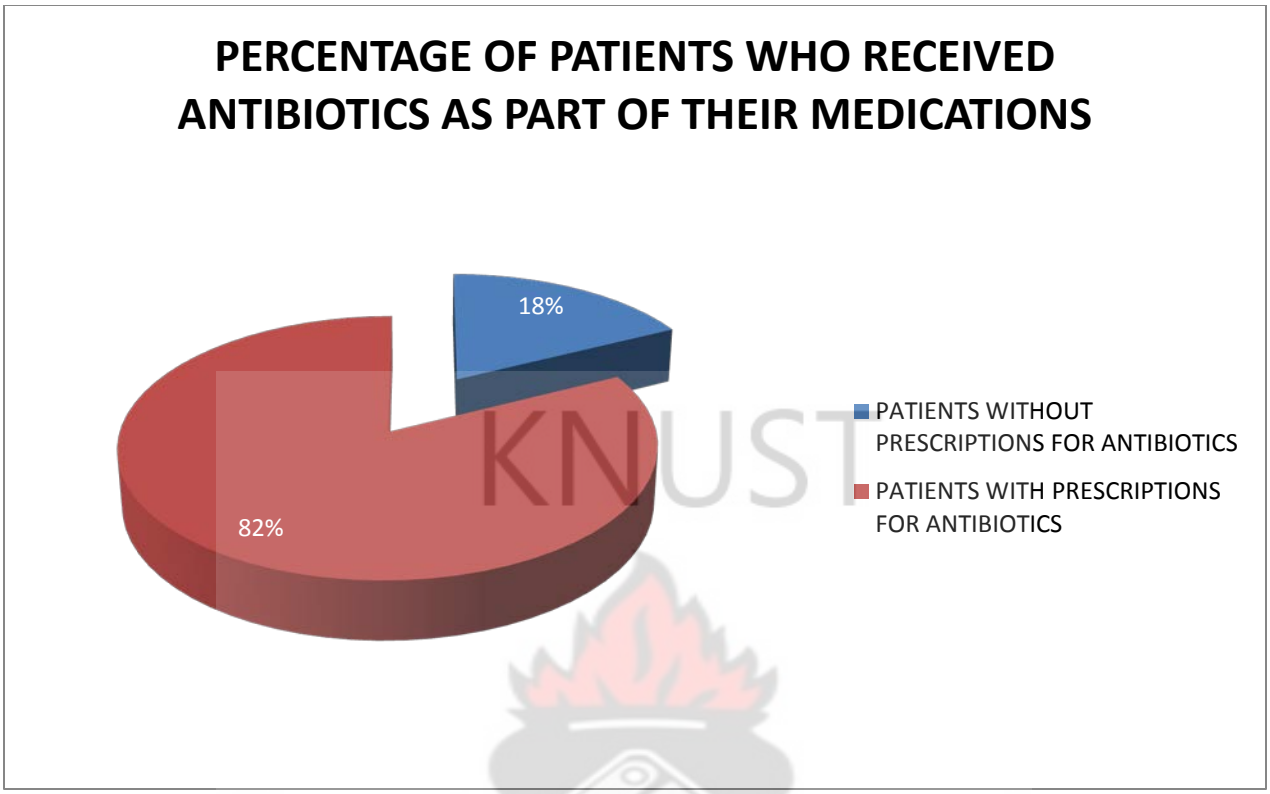

Fig 1.

Out of the 145 patients who received antibiotics as part of their medication, 57% (n=82) received one antibiotic, 30% (n=44) had 2 antibiotics, 12% (n=17) had 3 antibiotics while 2 patients (1 %) had 4 antibiotics (figure 2).

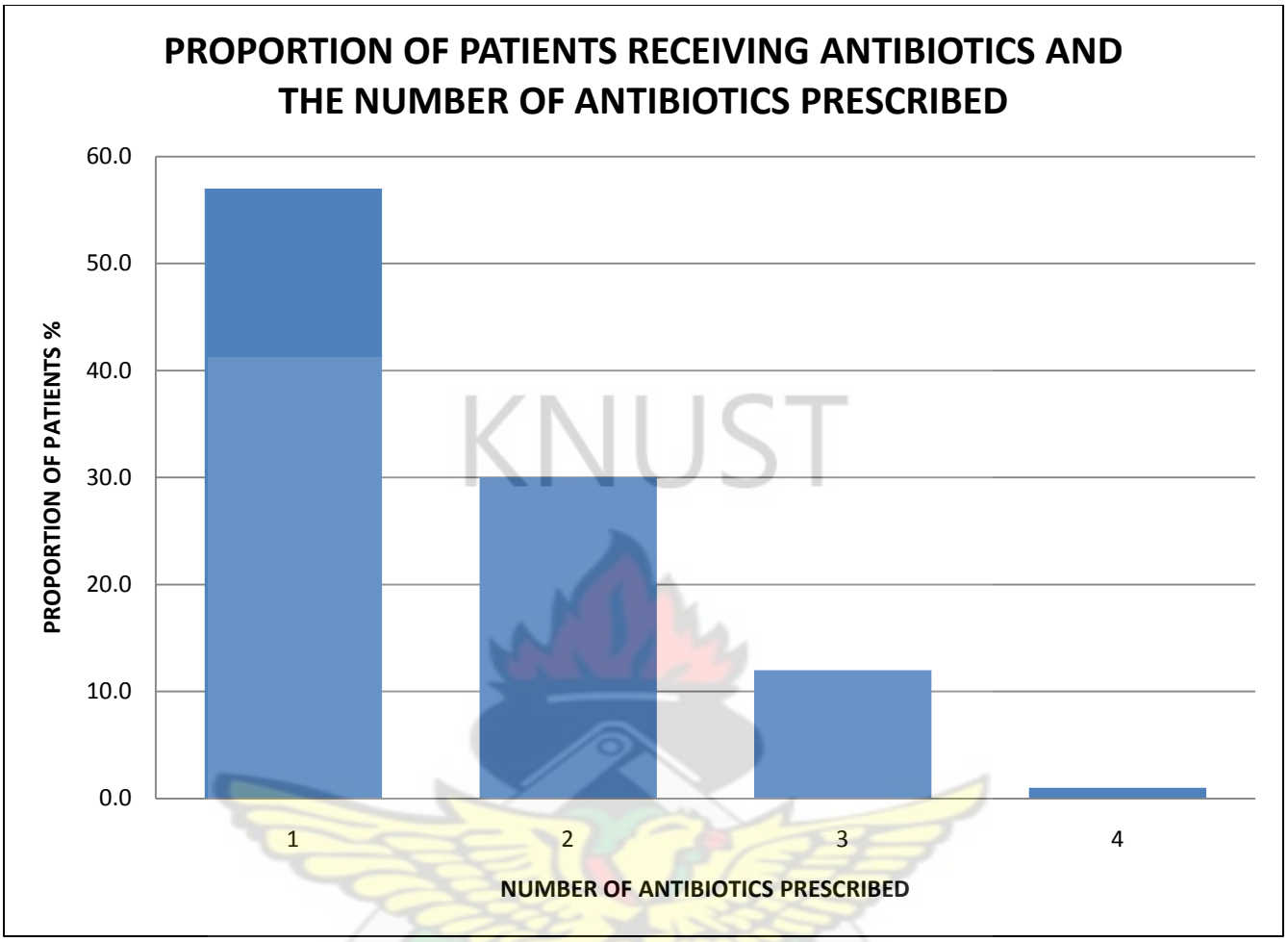

Fig 2.

Ciprofloxacin was the most prescribed antibiotic as monotherapy. This was given to 20% of the patients followed by cefuroxime, ceftriaxone, metronidazole, Amoxicillin/ clavulanic acid, benzyl penicillin, flucloxacillin and cotrimoxazole. The most prescribed combination drugs were ciprofloxacin/metronidazole, ceftriaxone/gentamicin and ciprofloxacin/ceftriaxone. Other combinations that were not common were cefuroxime/metronidazole, ceftriaxone, cefuroxime, gentamicin and azithromycin and ceftriaxone/cefuroxime/azithromycin (Fig. 3).

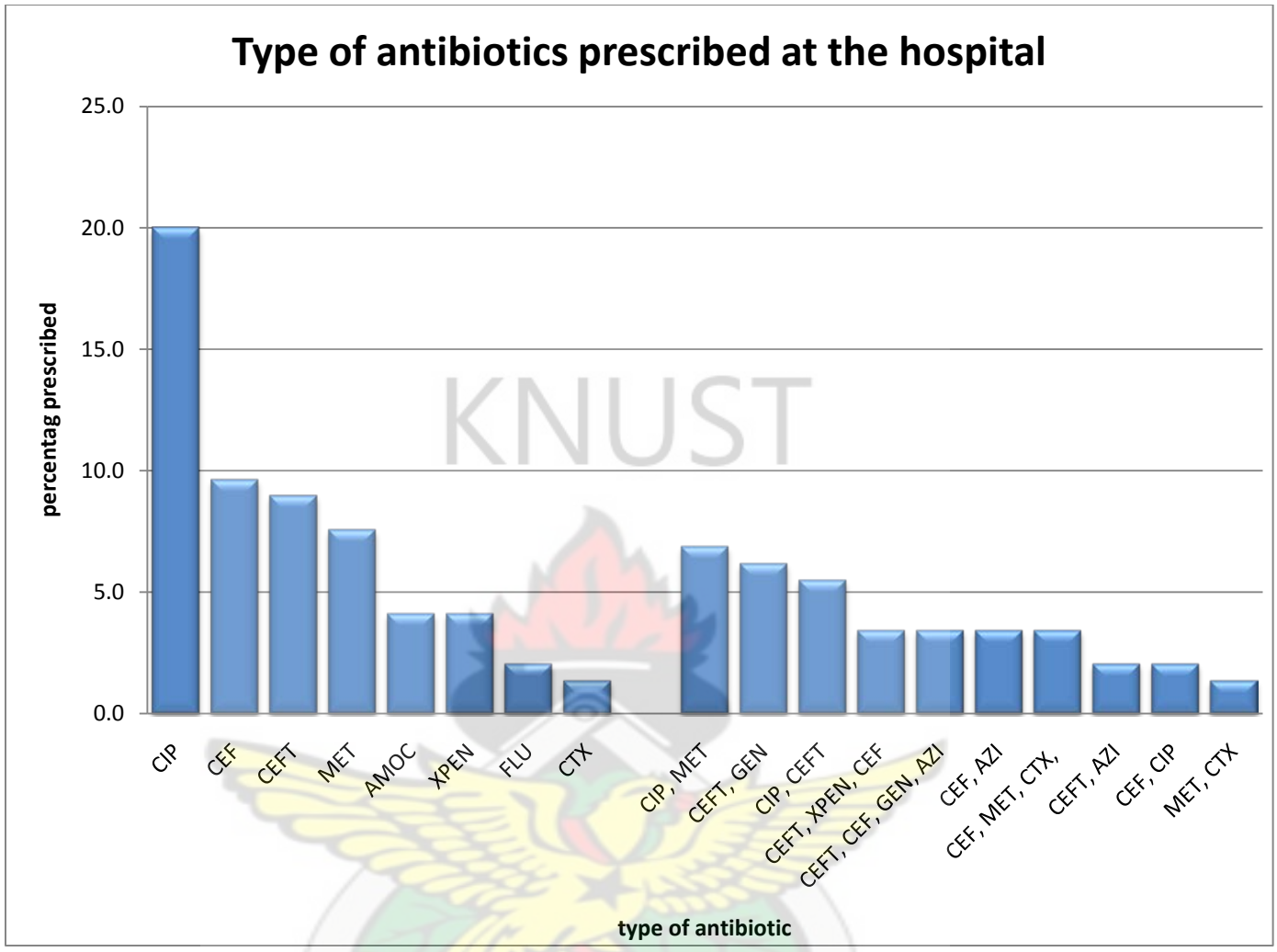

Fig. 3

KEY : AMOC = Amoxyclav, XPEN = Benzyl Penicillin, CEFT = Ceftriaxone, AZI = Azithromycin, CEF = Cefuroxime, GEN = Gentamycin, CIP = Ciprofloxacin, MET = Metronidazole, CTX = Cotrimoxazole, FLU = Flucloxacillin

3.4 EMPIRICAL USE OFANTIBIOTICSAND REASONS FOR ANTIBIOTIC PRESCRIBING

Out of the 145 patients who received antibiotics during the study, culture and sensitivity test was not done for any of them .

Fifty four percent of the patients who received antibiotics had raised WBC count, 28% had hyperpyrexia and raised WBC count, 16% had only hyperpyrexia and only 2% were diagnosed as having neutropenic sepsis (figure 4)

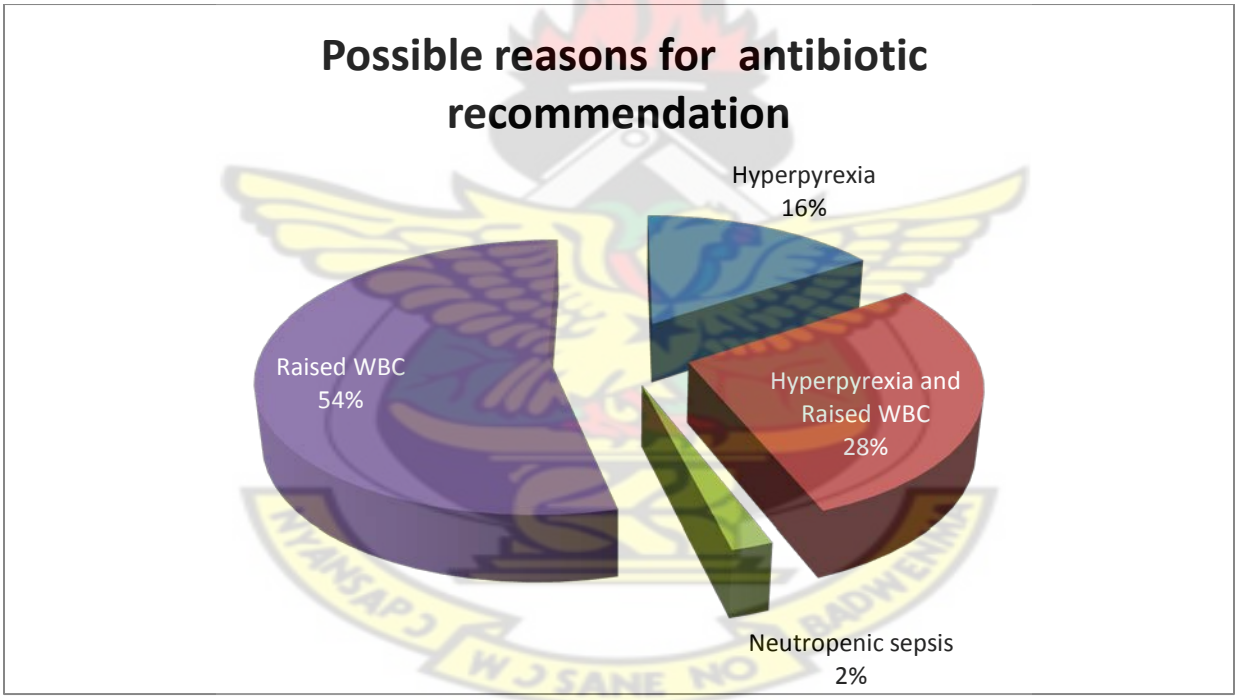

Fig 4

3.5 PATIENTS RESPONSE TO ANTIBIOTIC THERAPY

93% of the patients were discharged two days after empiric treatment with antibiotics with 7% not responding appropriately to the antibiotics. Patients with hypertension, vertigo and snake bite as co-morbidity were those who did not respond favorably to the empirical antibiotic treatment

3.6 ANTIBIOTIC RESISTANCE PATTERN FROM LABORATORY DATA

Data on culture and sensitivity results obtained from the laboratory between the period of January 2013 to March 2013 indicated that the three most common pathogenic organisms at the hospital were *Esherichia coli* 50% (n=21), *Staphylococcus aureus* 19% (n=8) and Salmonella (n=4) 12% (Fig. 5)

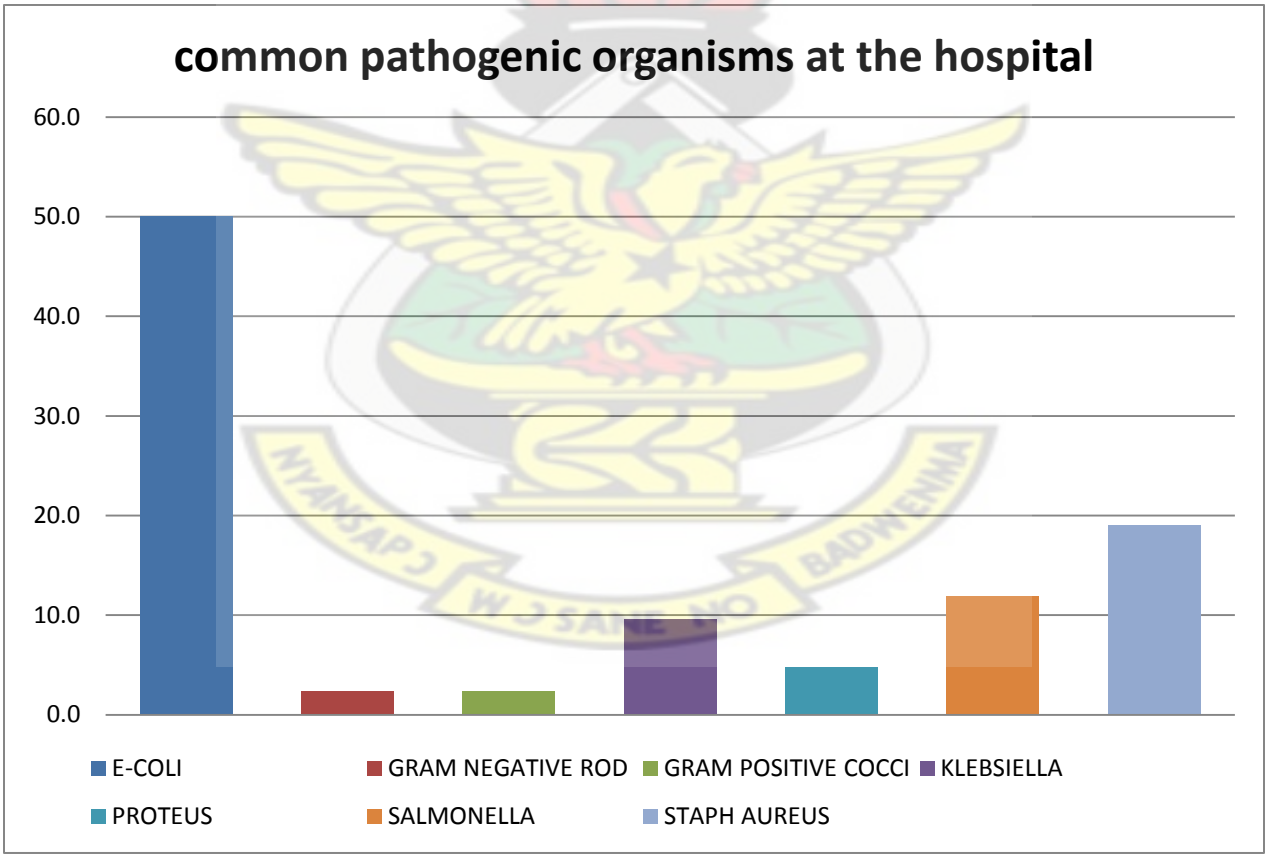

Fig. 5

Urine sample constituted the most used culture sample 40.5% (n=17) followed by vaginal swab 26.2% (n=11), stool 11.9% (n=5), blood sample, ear and wound swabs were the least used for culture and sensitivity (7.1%) (Fig 6)

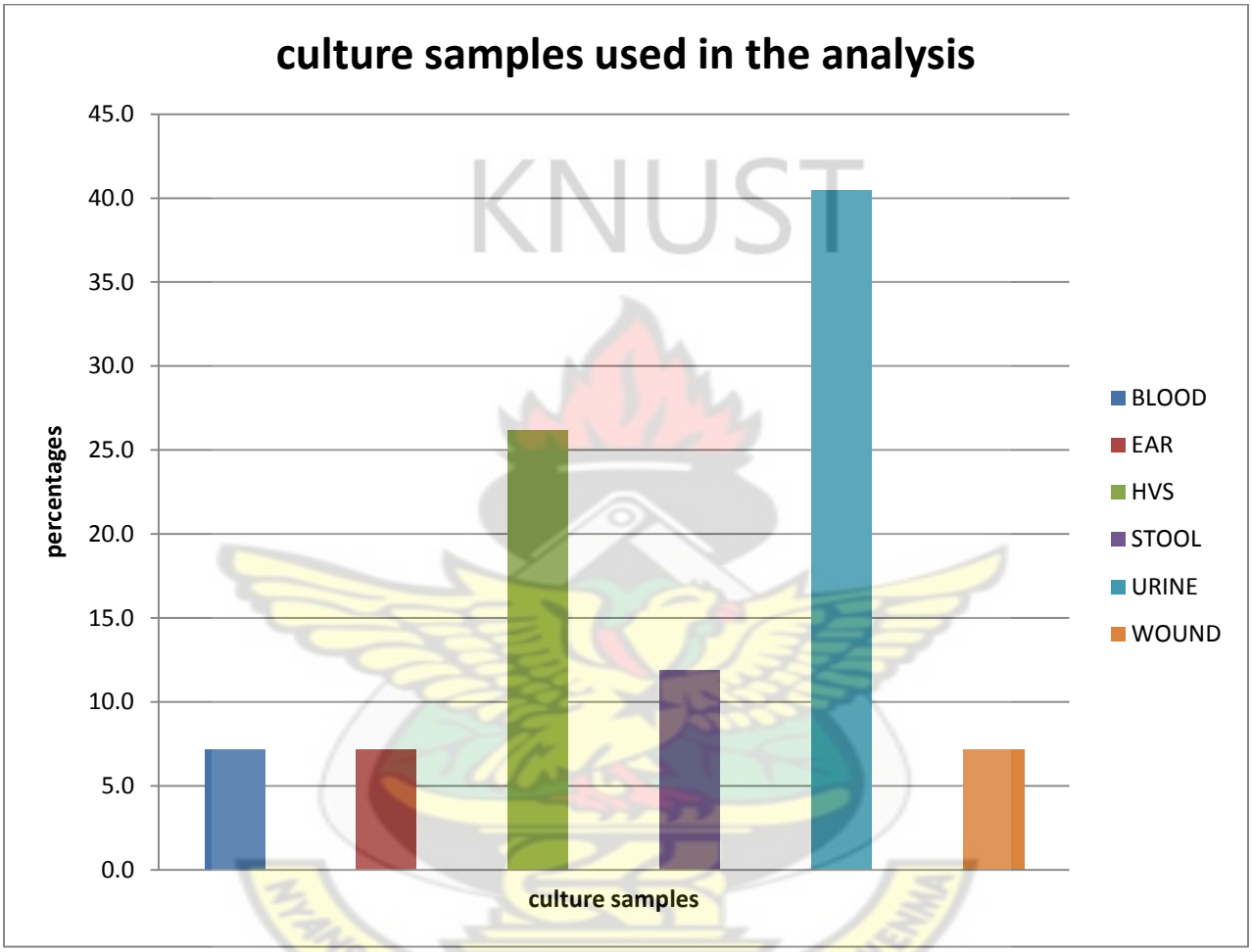

Fig. 6

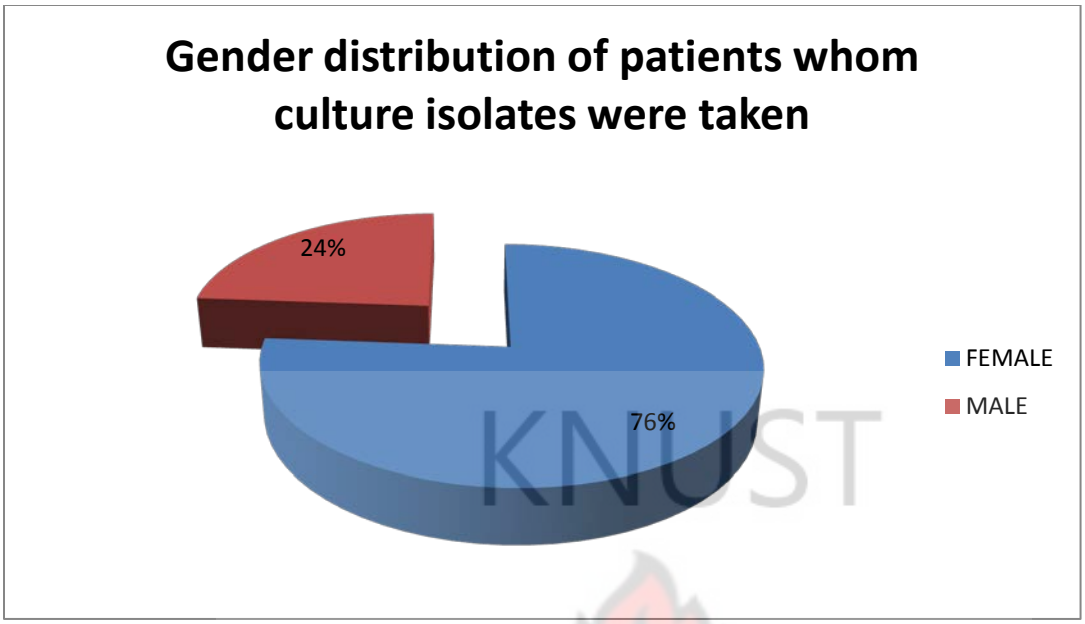

Fig. 7

These samples were mostly taken from females (76%) with 24% from males fig 9.

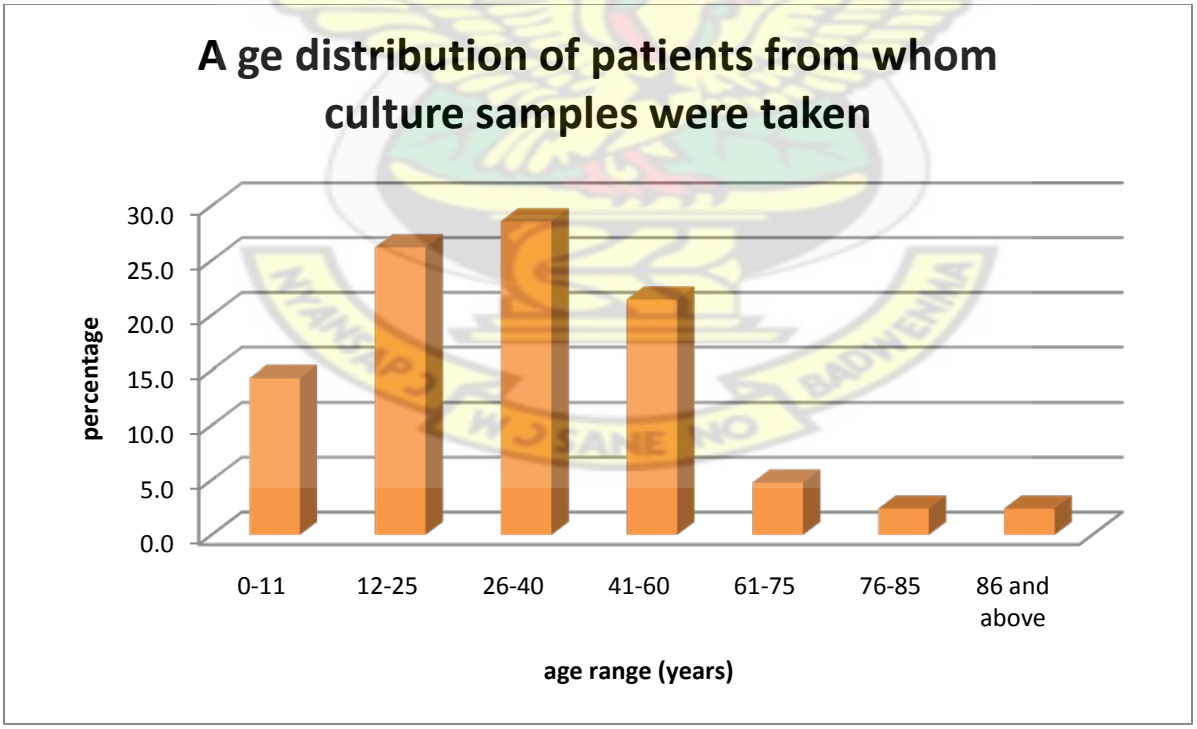

Fig 8.

Patients between the age range of 26-40 years were the largest (28.6%) followed by patients between 12 and 25 years (26.2%), patients between the ages of 76-85 and 86 and above were the least encountered (2.4% for each) (fig. 8)

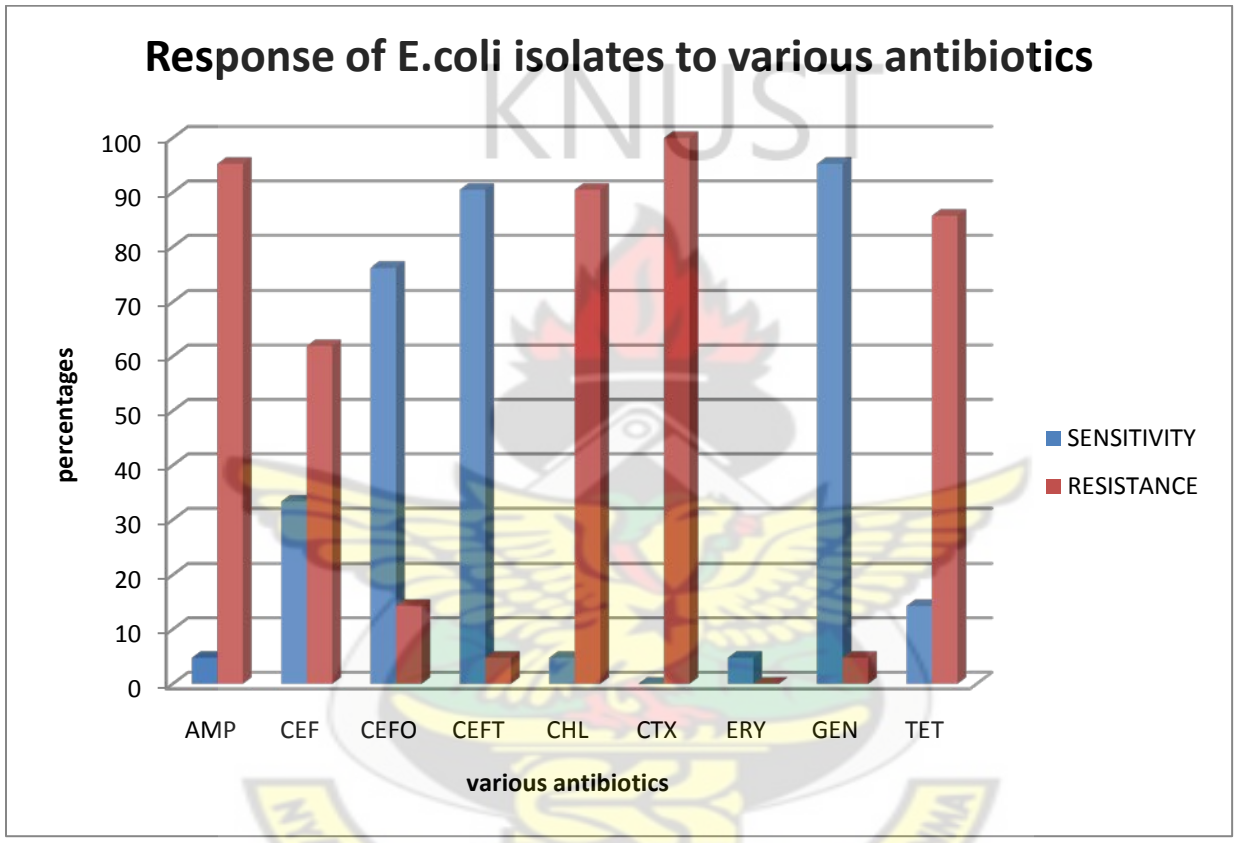

Fig 9

KEY: AMP = Ampicillin, CEF = Cefuroxime, CEFO = Cefotaxime, CEFT = Ceftriaxone, CHL = Chloramphenicol, CTX = Cotrimoxazole, ERY = Erythromycin, GEN = Gentamicin, TET = Tetracycline.

The E-coli isolates were most sensitive to Gentamicin (95.2%) followed by ceftriaxone (90.4%), cefotaxime (76.1%). cefuroxime (33.3%), tetracycline (14.2%), erythromycin (4.7%), ampicillin

(4.7%) and chloramphenicol (4.7%) in descending order, were least sensitive. None of the e-coli isolates was sensitive to cotrimoxazole and only one isolates each were sensitive to chloramphenicol, ampicillin and erythromycin.

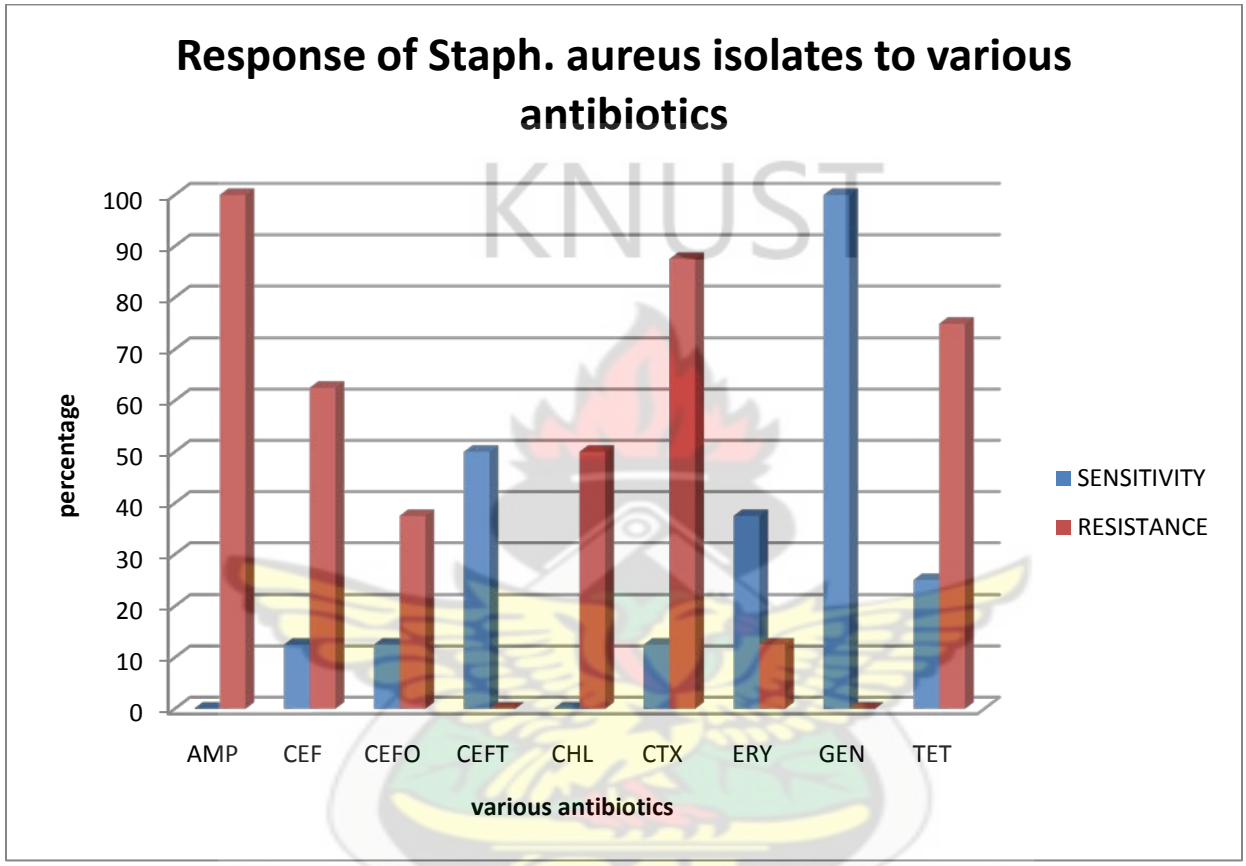

Fig. 10

The *Staph aureus* isolates were all sensitive to gentamicin (100%). 50% of the *Staph* isolates were sensitive to ceftriaxone.Erythromycin (37.5%), tetracycline (25%), cefuroxime (12.5%), cotrimoxazole (12.5%) and cefotaxime (12.5%) in descending order were least sensitive. None of the staph aureus isolates were sensitive to chloramphenicol and only one of each were sensitive to cefuroxime, cefotaxime, and cotrimoxazole.

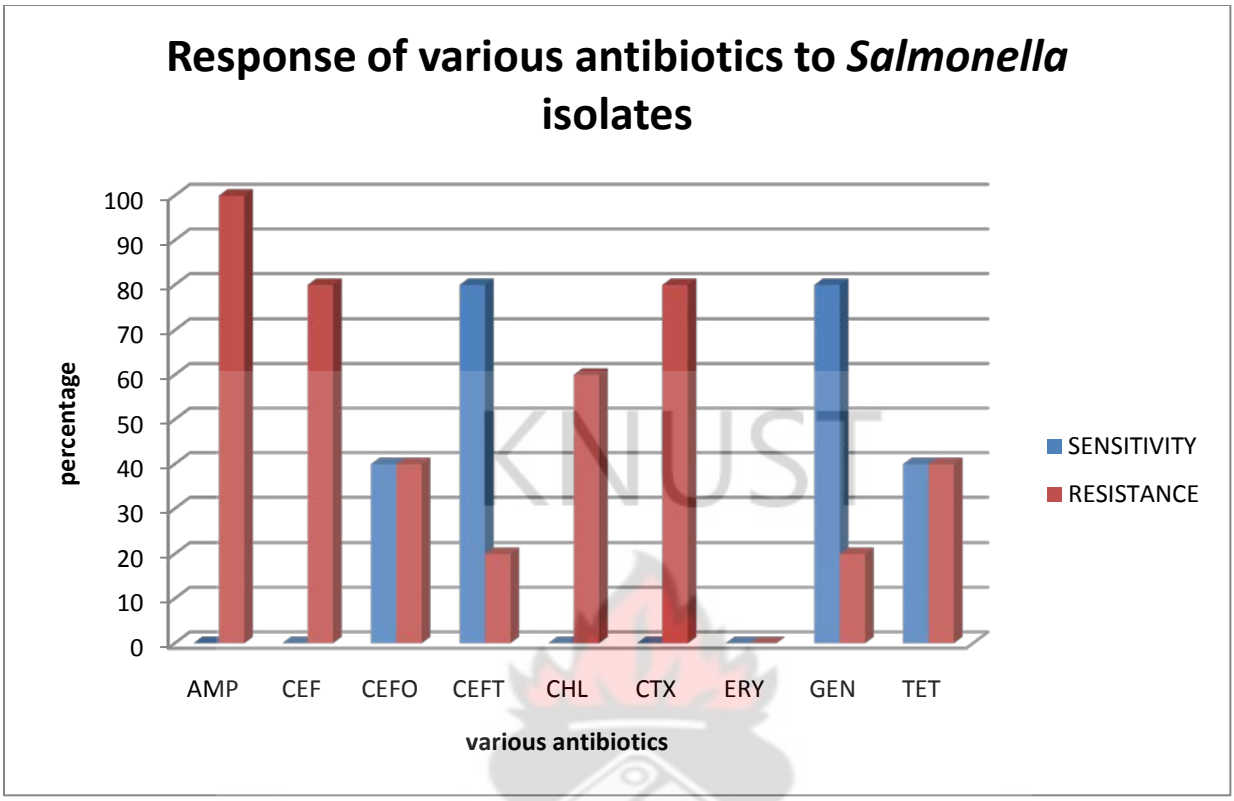

Fig 11

The culture isolates of salmonella were mostly sensitive to gentamicin (80%) and ceftriaxone (80%.) Cefotaxime (40%) and tetracycline (40%) were not very sensitive against salmonella isolates. Also none of the isolates were sensitive to ampicillin, cefuroxime, chloramphenicol and cotrimoxazole.

CHAPTER 4

4.0 DISCUSSION

One hundred and seventy six (176) patients were involved in the study from 01/03/2013 to 15/04/2013.

Males accounted for 40.9% and 59.1% females. The majority of the patients (34.7%) were children between the ages of 0 to 11 years with patients between the ages of 61 to 75 years in the minority (1.7%).

In prescribing antibiotics for patients it is necessary to consider the age of the patient as many antibiotics are contraindicated in some of the age groups. Example; in infants Chloramphenicol (can cause grey baby syndrome) and sulphur (can cause kernicterus) are contraindicated. Below the age of 8 years Tetracyclines are contraindicated because they are known to discolour the teeth. In children and adolescents all fluoroquinolones are contraindicated because they are known to cause arthropathy by damaging the growing cartilage. In the elderly, achlorhydria may affect absorption of antibacterial agents. Drug elimination is slower, requiring dose adjustments. Ototoxicity of aminoglycosides may be increased in the aged.

4.1 AVERAGE NUMBER OF DRUGS PRESCRIBED PER PRESCRIPTION

The average number of drugs per prescription encountered was 5. This value was slightly higher than a similar research conducted from seven government health facilities in the Wassa West district of Ghana which was 4.8 (Bosu and Ofori-Adjei, 2000). A higher average was reported in Nigeria (6.11) (Babola et al, 2007). But this was higher than the values obtained in majority of previous studies from developing countries: Yemen 1.5, Uganda 1.9, Sudan 1.4, Tanzania 2.3 (Odunsanya, 2004), and 1.44 in Bangladesh (Bosu and Ofori-Adjei, 2000). Besides the value is

higher than the one obtained at public health facility dispensaries and public health facilities in Ghana in 2008 which was 3.6 (Arhinful K.D, 2009)

Thus the higher average number of medicines for prescription in this study is a pointer to the high level of poly pharmacy which in turn may have serious negative effects on the therapeutic outcome in patients.

4.2 THE EXTENT OF USE OF ANTIBIOTICS AT THE HOSPITAL

Average percentage of prescription encounters containing antibiotics was 82.4%. This is extremely higher than the WHO recommended average (20 -26.8%) (WHO, 2008) and higher than the average value obtained from previous studies from developing countries like Nigeria (50.1) (Babola et al, 2007) Malawi (34%), Indonesia (43.1%), Bangladesh (25%), Yemen (51%), Sudan (60%) and Tanzania (39%) (Slobodan et al., 2006; Massele et al. 2001). Reports from other studies are 25% (Guvon et al., 1994), 61.9% (Moghadamnia et al., 2002), 72.8% (Hazra et al., 2000) and 60.9% (Otoom et al., 2002). Besides it was higher than the values obtained by Bosu and Ofori Adjei (60.7%) in seven government health facilities in the Wassa West district of Ghana and was also higher than the one Obtained at public health facility dispensaries and public health facilities in Ghana in 2008 which was 43.3% (Arhinful K.D, 2009).

The average number of antibiotics prescribed per patient was 1.6, this was almost similar to the value obtained by Bosu and Ofori Adjei (1.4) in seven government health facilities in the Wassa West district of Ghana. This value was slightly higher than that obtained in similar studies in other developing countries like Yemen (1.22) but lower than a similar research than in northern india (2.09) (Aparna W. et al, 2011)

This result establishes over prescribing and overuse of antibiotics at the hospital.

4.3 PATTERN OF USE OF ANTIBIOTICS AT THE HOSPITAL

Ciprofloxacin was the most prescribed antibiotic as monotherapy followed by cefuroxime and ceftriaxone. With regards to combination therapy ciprofloxacin and metronidazole was the most prescribed.

A study conducted at Korle Bu Teaching Hospital in 2009 also revealed Ciprofloxacin and Metronidazole been the most prescribed antibiotics. (Acheampong F.,2009). In the study conducted by Bosu and Ofori Adjei in seven government health facilities in the Wassa West district of Ghana in the year 2000, the commonest antibiotics prescribed were procaine penicillin, cotrimoxazole, benzylpenicillin, metronidazole and amoxycillin.

Ciprofloxacin and metronidazole has been the drug of choice for first line 'blind' treatment in both prophylaxis and treatment. This practice is of great concern to many health care professionals in the hospital because of the development of resistance. It is recommended that ciprofloxacin be reserved for the indications that it is specific for and not for 'blind' prophylaxis use (WHO 2006).

From the study some patients above 60 years received ciprofloxacin. Patients above 60years of age are more prone to tendon damage which has been reported rarely in patients receiving quinolones (BNF 61).

4.4 EMPIRICAL USE OFANTIBIOTICS AND REASONS FOR ANTIBIOTIC PRESCRIBING

Out of the 145 patients who received antibiotics during the study, culture and sensitivity test was not done for any of them.

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. Early and adequate introduction of antibiotics improve survival in severe sepsis and septic shock patients. Therefore, therapy such as broad-spectrum antibiotics and/or a combination of antibiotics must be started empirically.

Conversely, there are many clinical situations in which empiric therapy may not 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.

There are also 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.

It has been shown that inadequate therapy for infections in critically ill, hospitalized patients is associated with poor outcomes, including greater morbidity and mortality as well as increased length of stay.

In Ghana, antimicrobial therapy constitutes a major form of treatment. It is mainly empirical due to a relative lack of appropriate laboratory facilities for culture and susceptibility testing of bacteria in several health facilities. Even where laboratory facilities are available, culture and

susceptibility tests may not be requested due to the fact that this is an extra cost to be paid by the patient

Fifty four percent of the patients who received antibiotics had raised WBC count, 28% had hyperpyrexia and raised WBC count, 16% had only hyperpyrexia and only 2% were diagnosed as having neutropenic sepsis.

In the absence of culture and sensitivity data most prescribers normally use other parameters like raised WBC count, hyperpyrexia and neutropenic sepsis as an indication for antibiotic therapy. The presence of acute infection normally leads to raised WBC count and hyperpyrexia but conditions like inflammation, tissue necrosis, metabolic disorders, poisoning, acute haemorrhage, leukemias and myeoproliferative disorders, stress, menstruation and strenuous can all be causes of raised WBC count and hyperpyrexia so one cannot not rely solely on raised WBC count and hyperpyrexia to prescribe antibiotics to a patient.

4.5 PATIENTS RESPONSE TO ANTIBIOTIC THERAPY

Ninety three percent (93%) of the patients were discharged two days after empiric treatment with antibiotics with 7% not responding appropriately to the antibiotics. Patients with hypertension, vertigo and snake bite as co-morbidity were those who did not respond favorably to the empirical antibiotic treatment because these conditions are not of bacterial aetiology and thus will not respond to antibiotic therapy.

Response to treatment of an infection can be assessed using both clinical and microbiological parameters. Clinical parameters of improvement include symptoms and signs (eg, a decrease in fever, tachycardia, or confusion), laboratory values (eg, decreasing leukocyte count), and radiologic findings (eg, decrease in the size of an abscess)

4.6 ANTIBIOTIC RESISTANCE PATTERN FROM LABORATORY DATA

Data on culture and sensitivity results obtained from the laboratory indicated that the three most common pathogenic organisms at the hospital were E-coli (50%), staph aureus (19%) and salmonella. This is results is almost similar to a prospective quantitative study set in various hospitals including two teaching hospitals, seven regional hospitals, and two district hospitals in Ghana from December 2002 to December 2003 which indicated that The most prevalent organism in the country was *Escherichia coli*, followed by *S. aureus*, *Klebsiella* spp, and *Pseudomonas aeruginosa* (Mercy J.N et al, 2011).

The susceptibility test performed for the three most common culture isolates showed that the three isolates were mostly susceptible to gentamicin, cefotaxime, ceftriaxone and cefuroxime but resistant to ampicillin, chloramphenicol, cotrimoxazole, tetracycline and erythromycin. The study conducted by Neuwmann et al in the two teaching hospitals and seven regional hospitals in Ghana showed High percentage of resistance was observed for tetracycline (82%), cotrimoxazole (73%), ampicillin (76%), and chloramphenicol (75%). Another study conducted by Duredoh Freeman George et al in 2010 to determine the antibiotic resistance patterns of Escherichia coli isolated from Kumasi-South, Tafo and Suntreso Hospitals, Kumasi, Ghana also showed that Majority of the E. coli isolates (90.7%) exhibited resistance to ampicillin while 6.2 and 3.1% showed intermediate and sensitive respectively. Co-trimoxazole, 78.4% of the isolates were resistant while 9.3 and 12.4% exhibited intermediate and sensitive responses respectively. E. coli isolates (28.6 to 46.4%) were resistant to gentamicin, ciprofloxacin and ceftriaxone while 14.4 to 47.4% gave intermediate responses.(Duredoh F.G. et al 2012).

4.7 LIMITATIONS TO THE STUDY

Not all patients receiving antibiotics in the hospital were covered in the studies as outpatients and patients admitted at the surgical wards were not included.

Laboratory values were not taken from any of the patients to confirm or deny positive response to antibiotic therapy. Most patients were also discharged few days after empiric treatment and thus could not monitor the patients well to assess the response to antibiotic therapy.

4.8 CONCLUSION

This study showed that Poly pharmacy practice was high at the hospital, and the use of antibiotics which are mostly empirical was also too high. The study further confirmed widespread microbial resistance to many antibiotics and therefore call for every effort to ensure the judicious and rational prescribing and use of antibiotics in the hospital, to preserve the lifespan of the existing safe and effective antibiotics, including the third generation cephalosporins.

4.9 RECOMMENDATIONS

1. When possible culture and sensitivity results for patients diagnosed with infection should be available before initiating antibiotic therapy. Prescribers are also to use laboratory data, interpret it right to select antibiotics for patients
2. The existing laboratory capacity including human resource, infrastructure and equipments should be further strengthened to support quality improvement in antimicrobial therapy.

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APPENDIX 1 - QUESTIONNAIRE

THE USE OF ANTIBIOTICS AND THE EXTENT OF ANTIMICROBIAL RESISTANCE AT S.D.A HOSPITAL –KUMASI

DATA COLLECTION FORM

FOLDER NO…….. WARD …… BED NO…….

PATIENT DETAILS

Age 0 – 11❑ 12 – 25❑ 26 – 40❑ 41 – 60❑ 61 -75❑ 76 – 85❑ 86 + ❑

GENDER Male❑ Female ❑

WEIGHT…… DATE OF ADMISSION ……/……/…… DATE OF DISCHARGE ……/……/…….

Type of infection (diagnosis / impression)

……
……
……

Total number of drugs prescribed for the patient at the facility ……

ANTIBIOTIC USE IN HEALTH FACILITY

Antibiotic prescribed for the patient Yes❑ No❑

Number of antibiotics per prescription:……

Culture and sensitivity done before selection of antibiotics Yes❑ No❑

EMPIRIC ANTIBIOTIC USE

TYPE OF ANTIBIOTIC	DOSAGE	FREQUENCY	DURATION

REASONS FOR EMPIRIC ANTIBIOTIC USE

INDICATION	PRESENT	ABSENT
Neutropenic sepsis		
Hyperpyrexia		
Raised WBC		
Raised ESR		
Other		

CULTURE AND SENSITIVITY RESULTS

SAMPLE	CULTURE ISOLATE	SENSITIVE TO	RESISTANT TO

ANTIBIOTICS PRESCRIBED AFTER CULTURE AND SENSITIVITY

TYPE OF ANTIBIOTIC	DOSAGE	FREQUENCY	DURATION

OUTCOMES TO ANTIBIOTIC THERAPY (EMPIRIC)

CURE

Resolution of symptoms Yes ❑ No ❑ Improvement of patient condition Yes ❑ No ❑

TREATMENT FAILURE

(Failure to respond to therapy two days after starting therapy)

Death from infection Yes ❑ No ❑ Resistance Yes ❑ No ❑

OUTCOMES TO ANTIBIOTIC THERAPY (DEFINITIVE)

CURE

Bacteriological cure Yes ❑ NO ❑ No Test Done ❑

Resolution of symptoms Yes ❑ No ❑

Improvement of patient condition Yes ❑ No ❑

TREATMENT FAILURE

(Failure to respond to therapy two days after starting therapy)

Death from infection Yes ❑ No ❑ Resistance Yes ❑ No ❑