ASSESSMENT OF THE RATIONAL USE OF SELECTED ANTIBACTERIALS DRUGS (AMOXICILLIN, COTRIMOXAZOLE AND METRONIDAZOLE) IN KAMPALA INTERNATIONAL UNIVERSITY TEACHING AND KITAGATA HOSPITALS.

BY

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DECLARATION

I hereby declare that all the work in this dissertation is original unless otherwise acknowledged and has not been submitted for another degree in this or any other university or institution of higher learning.

Signed.....

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(Researcher)

This dissertation has been submitted for examination with the approval of my supervisor.

Signed..... Date.....15/06/2011.....

Twinomujuni Silvano Samba

DEDICATION

To my father, Mr. Charles Tumwesigye for his never waning love, support and guidance. May the Lord Almighty continue bestowing his blessings on you.

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I am immensely indebted to the following people for their assistance and support, which have enabled me to get this research to what it is today;

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LIST OF ACRONYMS

AMT	Antimicrobial treatment
KIU-TH	Kampala International University Teaching Hospital
UCGs	Uganda Clinical Guidelines
RUM	Rational Use of medicines
STGs	Standard Treatment Guidelines
WHA	World Health Assembly
WHO	World Health Organization
INRUD	International Network for the Rational Use of Drugs
EML	Essential medicines list
ATC	Anatomical Therapeutic Chemical
DDD	Defined Daily Dose
DOTs	Days of Therapy

OPERATIONAL DEFINITIONS

Antibacterials

Refers to amoxicillin, cotrimoxazole and metronidazole

Appropriatness of antibacterial

The most clinically acceptable or first drug of choice in the treatment of a bacterial infection

Guidelines

Refers to the Uganda clinical guidelines for treatment of common infections (UCGs) by the Ministry of Health Uganda.

Hospitals

Kampala International University Teaching hospital and Kitagata –Bushenyi district hospital

Prescribers

Refers to doctors, dentists and clinical officers.

Rational use

An antibacterial appropriately chosen, in the correct dose, correct duration, appropriate combination and in accordance with the UCGs

ABSTRACT

Background:

More than 50% of all medicines are irrationally used in the world. Rational use of medicines (RUM) means that the right patient receives the right drug, in the right dose, for the right duration, and at the lowest cost for him/her and the community. In a nutshell treatment must follow the standard treatment guidelines of that area. In this case Uganda, the Uganda Clinical Guidelines for treatment of Common Infections is used. The problem of rational use is even most dire with antibacterial drugs, especially commonly used ones where resistance is ever growing.

Purpose of study:

To assess whether amoxicillin, cotrimoxazole and metronidazole are rationally used in KIU-TH and Kitagata hospital

Methods:

Prescriptions from each hospital containing the above antimicrobial therapy were analysed to find frequency of adherence to STGs by prescribers as a measure of rational use. Other indictors of rational use such as generic name use and definitive diagnosis such as laboratory testing were measured. Questionnaires were used to assess knowledge and frequency of use of STGs.

Results:

From KIU-TH 72.4 % of prescription were in accordance with STGs, KITAGATA recorded 57.1% of these drugs were prescribed in accordance with STGs. 9.2% of respondents from KIU used Laboratory diagnosis always, from Kitagata only 2% reported this.

Conclusions:

KIU-TH had higher rates of rational use of antibiotics compared to Kitagata hospital. Cotrimoxazole had the highest rates of rational use. STGs play an important role in promoting rational use of antibacterials.

CHAPTER ONE

1.0 INTRODUCTION

The first antimicrobials were discovered in the mid-20's and many new molecules were discovered between 1960 and 1980. This 'golden era of antibiotics' saw a dramatic fall in the mortality and morbidity from infections. But the miracle seems to be short lived. Irresponsible and erratic use of these life-saving instruments has resulted in the development of drug resistance in many organisms. This has led to untreatable infections and consequently a rise in mortality. It appears that our complacency is leading us into bigger problems in the millennium that has just dawned. (Srinivas Kakkilaya, 2008)

Rational use of medicines (RUM) means that a patient's condition is diagnosed correctly; the most appropriate medicine is prescribed in the right dose and formulation for this particular patient, and that the patient (and the health system) can afford this medicine and assure that it is taken for an adequate time. It also means that the patient is well informed about the medicine, understands the importance of the prescribed treatment and takes the medicines as required. Irrational use occurs when one (or more) of these conditions is not met. (WHO, 2005) Common examples of irrational drug use are:

- Many medicines are prescribed per patient (polypharmacy)
- Injections are used where oral formulations would be more appropriate
- Antimicrobial medicines are prescribed in inadequate doses or duration or antibiotics prescribed for non-bacterial infections, thereby contributing to the growing problem of antimicrobial resistance.
- Prescriptions do not follow clinical guidelines
- Patients self-medicate inappropriately or do not adhere to prescribed treatment.

The scope of this problem involves both developed and developing countries such as Uganda. The epidemic of HIV/AIDS, with over 30 million cases in developing countries, has greatly enlarged the population of immune-compromised patients. The disease has left these patients at great risk of numerous infections and even greater risk of acquiring highly resistant organisms during long periods of hospitalization if the problem of irrational antibiotic use is not addressed soon (Byarugaba, 2004). In Uganda, just as the rest of the world resources must be geared towards the assessment and promotion of rational antibiotic use.

In light of this WHO in 1977 launched the 1st Model List of Essential Drugs, designed to help countries formulate their own national lists. In 1989, the International Network for the Rational Use of Drugs (INRUD) was formed to conduct multidisciplinary intervention research to promote the rational use of medicines. In 1993, WHO and INRUD developed and published a standard methodology or selected drug use indicators in health facilities. It is in line with the above methodology that this study was carried out.

The core drug indicators used are divided into 4 types:

- Prescribing indicators: average number of medicines prescribed per patient encounter; percentage of medicines prescribed by generic name; percentage of encounters with an antibiotic prescribed; percentage of encounters with an injection prescribed; percentage of medicines prescribed from an EML or formulary;
- Patient care indicators: average consultation time; average dispensing time; percentage of medicines actually dispensed; percentage of medicines adequately labeled; percentage of patients with knowledge of correct dose;
- Facility indicators: availability of essential medicines list or formulary to practitioners; availability of clinical guidelines; percentage of key medicines available;
- Complementary drug use indicators: average medicine cost per encounter and the percentage of prescriptions in accordance with clinical guidelines.

Amoxicillin was chosen on the basis that it is the most used penicillin in KIU-TH based on a pre-study of prescriptions received by the pharmacy. Cotrimoxazole was chosen due its wide use alongside antiretroviral therapy (this makes the evaluation of this antibacterial uniquely important). Metronidazole was chosen due the unique specificity, it has for anaerobic microorganisms, placing it as a very important drug in various infections. Despite these drugs uniqueness their resistance prevalence keeps souring.

An estimated two-thirds of global antibiotic sales occur without any prescription, and studies in Indonesia, Pakistan and India show that over 70% of patients were prescribed antibiotics.

In most countries, the problem runs deep. A handful of countries currently monitor inappropriate use of medicines partly due to a lack of awareness of the repercussions. Decision-makers if aware, often lack knowledge of the most cost-effective ways to tackle this problem. Meanwhile, some countries lack the resources needed to promote more accurate diagnostic

procedures, to implement effective regulation of prescribing and dispensing behaviour and to promote compliance to treatment by patients, in both the public and private sectors. In addition, the high cost of medicines contributes to low adherence levels by patients: in some studies, an estimated 90% of consumers buy three days' supply, or less, of antibiotics, making compliance with the recommended dosage impossible. Institutions, health professionals and patients all have roles to play in promoting more rational use of drugs. Effective regulation, clear clinical guidance, supportive incentive structures, training, education and management, are key components of an effective policy in this area. Much greater use of evidence-based diagnostic and treatment guidelines by health professionals is needed. More effective monitoring and regulation of medicines, and public education and information are important components of a strategy for increased rational use.

1.1 PROBLEM STATEMENT

The use of antibiotics has been shown to be associated with the development of antibiotic resistance (Goossens et al, 2005). Antibiotic use has also been shown to lead to additional morbidity, mortality and an extended length of stay in hospital (Gums, 2002). In addition, there is evidence that some antibiotic use in hospitals is inappropriate (Emmer and Besser, 2002).

Unpublished data relating to expenditure on antibiotics in the West Midlands Strategic Health Authority for 2006/7 showed an average expenditure of £860,000 per trust across a sample of 17 hospital trusts.

Clearly each of these reasons is a powerful driver for the need to assess the use of antibiotics within the healthcare system especially in hospitals. The urgency is greatest for commonly used antibacterial agents such as amoxicillin, cotrimoxazole and metronidazole.

1.2 JUSTIFICATION

The irrational use of pharmaceutical drugs specifically antibacterial agents has contributed to the increase in multi-drug resistant strains of microbes. This has become one of the world's most serious public health problems (WHO, 2006). This has left an unprecedented risk of increased morbidity and mortality (Acar, 1997). Logically when coupled with the current HIV/AIDS pandemic in sub-Saharan African countries like Uganda the situation is dire. As all infections are potential threats to life, antibiotics are life-saving. They are largely responsible for improved quality of life and increased life expectancy. Being weapons of such importance, they should be used with all the care and caution. This study therefore aimed at coming up with suggestions on how to improve antibacterial use.

1.3 GENERAL OBJECTIVE

To assess whether chosen antibiotics; amoxicillin, cotrimoxazole and metronidazole are rationally used in KIU-TH and Kitagata hospital

1.4 SPECIFIC OBJECTIVES

- To determine the prevalence of adherence to standard treatment guidelines of infectious diseases in a hospital setting by prescribers.
- To measure the level of rational use of amoxicillin, cotrimoxazole and metronidazole by prescribers.
- To find out the level of these antibacterial drugs' knowledge among prescribers.
- To come up with recommendations on how to promote rational use of antibiotics.

1.5 HYPOTHESIS

Commonly used antibiotics; amoxicillin, cotri-moxazole and metronidazole are irrationally used in KIU-TH and Kitagata hospitals.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Prescribers' adherence to standard treatment guidelines

A number of definitions for what constitute 'guidelines' have been made, perhaps the simplest and most succinct of these was from the UK National Audit Office (NAO), which in 2000 defined antibiotic policies as 'written guidance on treating and preventing specific infections'. In Uganda the Uganda Clinical Guidelines for the Treatment of common Infections is used.

At a meeting held in London in July 2005 organized by the Specialist Advisory Committee on Antimicrobial Resistance in conjunction with the UK National Prescribing Centre and UK Department of Health, R. T. Mayon-White of the department of Primary Healthcare, University of Oxford, UK presented a paper which stated that; Adherence to guidelines has the potential to bring a number of desirable outcomes for patients, among these are: a better chance of effective treatment; less inequality (eliminating unnecessary variations in practice and so-called 'postcode' prescribing); clarity as to how and why treatment decisions have been reached; and improved safety. From the healthcare provider viewpoint they can also facilitate audit and result in a decrease in costs. However, guidelines can have negative effects if: it later proves that the evidence base was incorrect or inadequate; they are misapplied; they are applied too inflexibly; they are not frequently reviewed and updated; and they inhibit further research.

In a study to find out the effect of national standard treatment guidelines on rational drug use in Uganda, it was revealed that the provision of national standard treatment guidelines alone does not result into behaviour change in rational drug use. Support supervision does not necessarily increase the effects of training unless it is well conceived and focused (Kafuko JM et al, 2004). This study does not give knowledge on specific drug use and how to assess use of antibiotics out of a health institution.

D. Raveh et al (2006) concluded that the vast majority of courses with broad spectrum antibiotics are empirically selected and continued, underlying the importance of an optimal initial choice. Antibiotic guidelines, in conjunction with formal infectious disease consultation, can contribute to more appropriate use of these drugs. The study gives a wealth of information

in regards to the intervention of local guidelines. There is a lack of emphasis on the role played by existing national guidelines.

2.2 Rational use of antibacterial drugs (amoxicillin, cotrimoxazole and metronidazole) by prescribers

An April 2005 WHO policy paper on "Containing anti-microbial resistance" said that anti-microbial resistance is one of the world's most serious public health problems. Emergence of resistance is a natural phenomenon that follows use of anti-microbials but it is being accelerated by inappropriate anti-microbial use, and higher consumption is associated with higher resistance, says the paper. According to the paper, WHO country data 2002-03 show the following anti-microbial resistance global prevalence rates; gonorrhoea (5-98% penicillin resistance); pneumonia and bacterial meningitis (0-70% penicillin resistance in streptococcus pneumonia); diarrhoea: shigellosis (10-90% ampicillin resistance, 5-95% cotrimoxazole resistance); hospital infections (0-70% resistance of staphylococcus aureus to all penicillins.

Ina Willemsen et al carried out a study; Appropriateness of Antimicrobial Therapy Measured by Repeated Prevalence Surveys between 2001 and 2004 and discovered that in a setting with a low use of AMT, there are few patients who inadvertently do not receive AMT. On the other hand, a substantial number of the patients are treated inappropriate. In the univariate analysis, the use of quinolones and co-amoxicillin-clavulanic acid were statistically significantly associated with more frequent inappropriate use of AMT. The use of cephalosporines, small-spectrum penicillins, meropenem, metronidazole, and rifampin were significantly associated with more frequent appropriate use of AMT. However, nothing was mentioned about cotrimoxazole in this study.

Excessive clinical use (a form of misuse) is at least partially responsible for the escalating rates of resistance, especially in hospital settings, worldwide (Davey, 2005).

In Uganda antibiotics can be purchased without prescription, even when the practice is not legal. Antibiotics are readily available on demand from hospitals, pharmacies and drugstores. (Calvin M, 2006) Therefore, one would expect that drugs more commonly affected by bacterial resistance in developing countries are generally inexpensive and popular antibiotics.

In most developed countries, research on medicines use is routine in health care facilities and numerous studies have demonstrated its effectiveness. However, most developing countries do not have data on this at the national level. (WHO, 2002)

From 1988 to 2002, WHO through their sister agency International Network for the Rational Use of Drugs (INRUD) carried out studies in 35 countries (mostly low income economies) to evaluate their medicines use situation using the WHO standard methodology for assessing medicines use. The selected WHO/INRUD drug use indicators for health care facilities, patient care, prescribers and complimentary drug use factors can be used to identify problems in general prescribing, assess prudent drug use and quality of care at these facilities. Most countries, Uganda included, were found wanting. This study borrowed this as its principle methodology in assessing rational use of amoxicillin, cotrimoxazole and metronidazole.

2.3 Antibacterial drug knowledge among prescribers.

Professor R. Finch of the Division of Microbiology and Infectious Diseases, City Hospital and University of Nottingham, UK presented a paper in London on July 2005 organized by the Specialist Advisory Committee on Antimicrobial Resistance. It stated that, "that rational use of antibiotics requires rational prescribing and evidence-based recommendations. Rational prescribing is a lifelong process that requires core knowledge, skills and behaviour within a culture of continuous learning".

A telephone survey was conducted in Hong Kong and Sydney by S.S. Lee et al to identify factors associated with appropriate antibiotic use in the community concluded that "proper use of antibiotic requires not just good knowledge".

Medical knowledge by care givers may serve as a benchmark for the assessment and improvement of antibiotic prescribing, a study carried out in Taiwan revealed (Nicole Huang et al, 2000). This can only be of significance if it has been established that the population of study is of high literacy level, or even majorly involved in any health care profession.

2.4 Promotion of rational use of antibiotics

G. Werner and S. Bronzwaer (2001) carried out a study on behalf of the European Commission, Public Health Directorate, European Food Safety Authority (EFSA) and the Robert Koch-Institute to come up with recommendations on the prudent use of antibiotics in human medicine. It was cited that, the overuse and misuse of antibiotics posed a serious danger to public health by contributing to the development of bacteria resistant to treatment. It was, therefore, concluded that all countries should have nationally accepted guidelines in place recommending appropriate antibiotic treatment, at least for the most common human infections and interventions, and the impact of these guidelines on prescribing practices should be assessed regularly. However the study did not reveal what checks should be in place to assess the prudent use of antibiotics.

Public antibiotic campaigns have been reported to be effective in improving prudent antibiotic use (Cliodna A. M. McNulty et al, 2010). The study does not reveal whether public campaigns improve rational antibiotic use when used as the only tool or together with other tools. In addition the element of how to assess whether this benefit is long term is missing.

WHO reported at the WHA in 2005 that countries have done little to promote rational use of medicines and this has now become a very serious global public health problem, with serious health and economic implications. There is increasing anti-microbial resistance, with resistance of up to 70-90% to original first-line antibiotics for dysentery (shigella), pneumonia (pneumococcal), gonorrhoea, and hospital infections (staph. Aureus) (WHO, 2005)

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

This study was cross-sectional study design in nature, employing both quantitative and qualitative method of data collection from prescribing clinicians and prescriptions from 2 hospitals.

3.2 Study area

The study was carried out at Kampala international University Teaching Hospital and Kitagata District Hospital in Bushenyi district. Bushenyi district consists of Igara county which is divided into 5 sub-counties. Bushenyi gets its name from its major town, Bushenyi. It is in the western part of Uganda at 360 kilometers away from Kampala. Busheyi District is located in Western part of Uganda. It borders with Sheema district in the East, Rukungiri District in the West, Kasese District in the North, Ntungamo District in the South and Kamwengye District in the North-East. It covers a total area of about 3949Km^2. Its main town is Bushenyi town. (Wikipedia, 5th May, 2010). It's estimated to be inhabited by 823,100 people according to 2002 Uganda National Census.

3.3 Study population

At the time of research, Kampala International University Teaching Hospital prescribers collectively wrote 100 prescriptions daily (KIU-TH Records, 2010). It is the only teaching hospital in the district. Kitagata hospital prescribers collectively wrote 300 prescriptions daily. Kitagata hospital is the district hospital of Bushenyi. Therefore the total number of prescriptions written was 400 daily. This study was carried out within a period of two weeks and data was collected until the expected sample size was reached. The number of prescribing clinicians (doctors and clinical officers) in the following departments; General medicine, Pediatrics, Surgical, Outpatient and Obstretics and Gynaecology was collectively 50 in both hospitals.

3.4 Eligibility criteria

Prescribers above 18 years but below 70 years were included in this study. Only those who voluntarily offered to take part were included in this study. Prescribers from only the said

locations were allowed to take part in this study. Patients' records of only the said institutions were used. Patients' records before October 2009 were not used. Only prescriptions involving antimicrobial therapy of amoxicillin, cotrimoxazole or metronidazole were included in this study.

3.5 Sampling Procedure

Quantitative data

Prescriptions containing AMT of amoxicillin, cotrimoxazole and metronidazole were used. The first prescription was randomly chosen, and the rest were consecutively sampled until the required sample size was completed.

Qualitative data

Prescribing clinicians (doctors and clinical officers) in the following departments; General medicine; Pediatrics; Surgical; Outpatient and Obstretics and Gynaecology were used from both hospitals. Random sampling was used considering the prescribers present during data collection days.

3.6 Sample size determination

To determine the sample size, the formula used by Krejcie & Morgan (Appendix 3) in their 1970 article "Determining Sample Size for Research Activities" was employed. The total number of prescriptions written daily by both hospitals was 400. Therefore, the sample size was 196 prescriptions for a confidence level of 95%. This was the number of prescriptions that were analyzed.

The number of prescribing clinicians (doctors and clinical officers) in the following departments; General medicine; Pediatrics; Surgical, Obstretics and Gynaenocology; Outpatient was collectively 50 in both hospitals. Considering a confidence level of 95% the sample size of clinicians was 44. This was the number of clinicians who were required to take part in this study.

3.7 Measurements

These variables used included; Adherence to STGs; Use of UCGs; Use of generic names during prescribing; Knowledge about an EML;Knowledge about the antibacterials (amoxicillin, cotrimoxazole and metronidazole)

3.8 Data collection and analysis

Pre-testing

The researcher conducted a one day data collection test using 10 questionnaires in KIU-TH to check on the efficiency of the study instruments, the mistakes found in the questionnaire were corrected immediately before carrying out the research. The questionnaire was then corrected and then used for the data collection.

Data collection tools

Interviewer administered questionnaires were used as tools for a prescriber survey. Both open and closed questions were used in the questionnaire. The questionnaire(Appendix 2) was designed to include some of the 1993 WHO and INRUD drug use indicators in health facilities indicators regarding patients, facility, prescribing patterns and complementary drug use. This questionnaire was directed to 44 prescribers. The following data was collected; Correct knowledge about amoxicillin, cotrimoxazole and metronidazole in regards to indications, dose and dosing regimens; Correct knowledge about UCGs and level of it use; Correct Knowledge about an EML; Level of use of laboratory diagnosis of conditions treated by these antibacterials and knowledge about the presence of a therapeutics board.

196 previous prescriptions which included AMT involving the chosen antibacterial drugs (amoxicillin, cotrimoxazole and metronidazole) were analyzed from both hospitals for a prescription audit. The use of antibiotics was judged according to the UCGs (2003). Indicators used included; correct choice, correct dose, correct duration, appropriate combination, accordance with UCGs. A score of accordance with STGs was only given if all other indicators were found present. This was subsequently used as a score of rational use. The collection of information took place between the period of November 2010 and January 2011.

Collection

A letter of introduction from the Dean of the School of Pharmacy was obtained, and used to obtain permission to use information from the above mentioned hospitals in this research. The questionnaires were then issued to the respondents who voluntarily consented to participating in this study. After being filled these questionnaires were then analyzed. No further attempts were used to confirm what was reported. The questionnaire was used to check the level of knowledge about the antibacterials, knowledge about the presence of a therapeutics board, use of laboratory diagnosis, knowledge about what an EML is, as well as use of UCGs. From each hospital, 98 AMT prescriptions including the selected antibacterials (amoxicillin, cotrimoxazole and metronidazole) were randomly selected, recorded and later analyzed.

Data analysis

The data was entered using Epidata (3.0 version) and then exported to SPSS, Statistical Package for Social Sciences software (SPSS, version 12.0). The data was analyzed as percentage frequencies. The percentage frequency results obtained were then entered in Excel 2007 to produce bar graphs.

3.9 Ethical considerations

A permission letter collected from the Dean of the School of Pharmacy Kampala International University-Western Campus was presented to the administrators in the hospitals of interest. Before enrolment in the study, all the respondents were requested to consent without any material benefits or allowances. The respondents were then be properly informed upon this subject and asked to cooperate voluntarily. Anonymity was exercised. The National Guidelines for Research Involving Humans as research participants were followed.

3.10 Study limitations and their solutions

- Financial predicaments occurred, however ends were met
- There were few unwilling prospective respondents met during this study
- The researcher laboured to explain instructions to respondents, so as to avoid misunderstanding of questions. Hence all questionnaires were completely and correctly answered.
- Bureaucracies encountered during the period of this study were overcome by being patient.

CHAPTER FOUR

4.0 RESULTS

A prescription audit carried out in KIU-TH and Kitagata hospital produced the following findings; Amoxicillin was the most prescribed in KIU-TH, and it was indicated for mixed bacterial infections, cotrimoxazole was prescribed mostly for upper respiratory tract infections and metronidazole was used mostly for infections where anaerobic bacteria was suspected.

A prescriber survey carried out produced various results, notably the use of UCGs and knowledge about these antibacterials. Below are the results obtained.

4.1 Prescribers' adherence to standard treatment guidelines

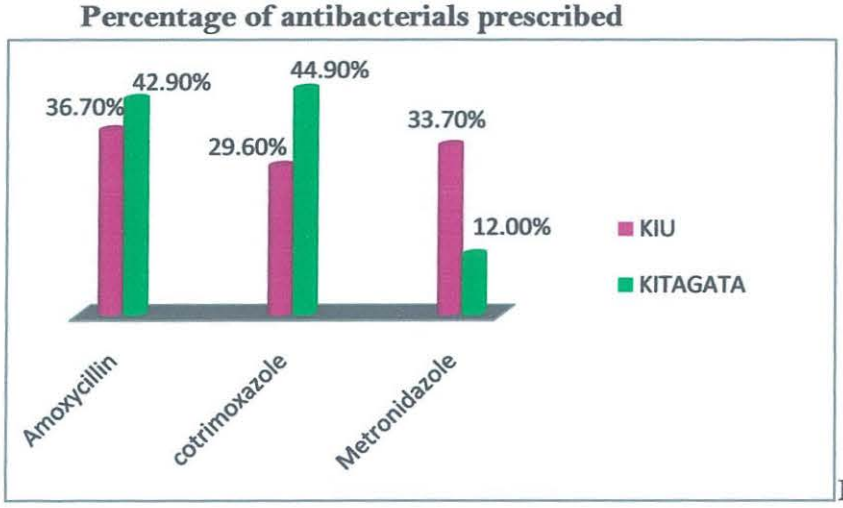

Fig 1

In Kitagata cotrimoxazole was the most prescribed antibiotic while in KIU-TH amoxicillin was most prescribed. These were obtained as frequencies from the prescription audit.

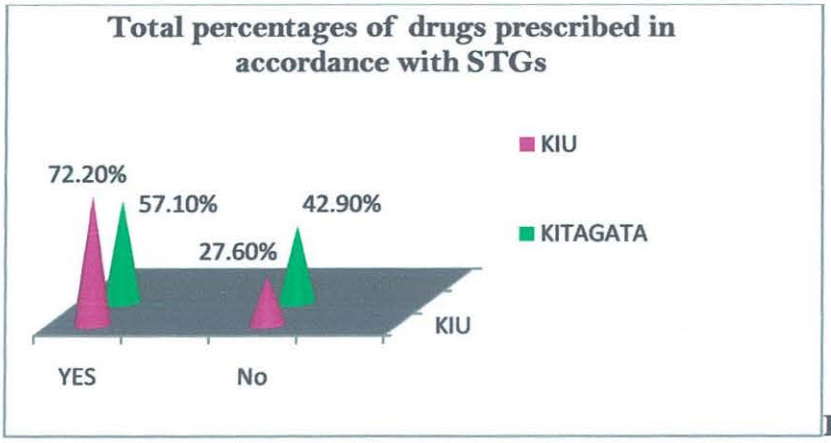

Fig 2

KIU-TH had higher percentages of drugs prescribed in accordance with STGs.

4.2. Rational use of antibacterial drugs (amoxicillin, cotrimoxazole and metronidazole) by prescribers

Percentage of drugs prescribed in accordance with STG

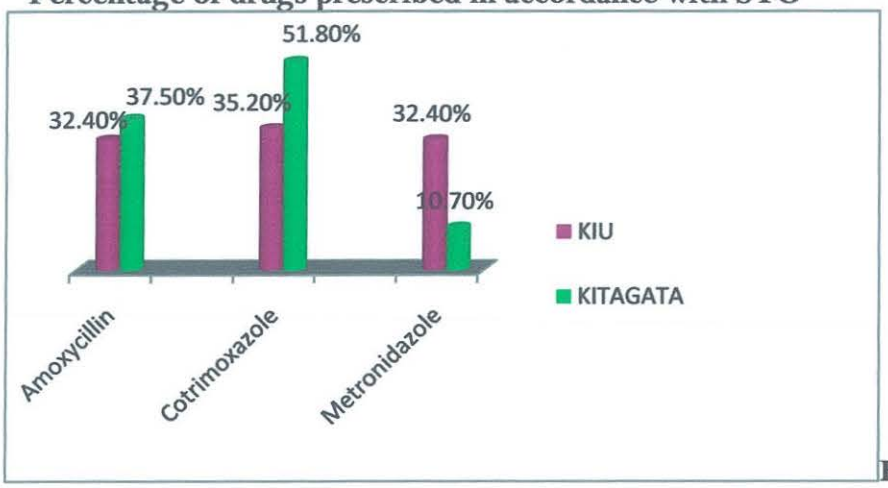

Fig 3

In both KIU-TH and Kitagata hospitals Cotrimoxazole was the drug most prescribed in accordance with STGs. This was followed by amoxicillin as lastly metronidazole.

Percentage of drugs prescribed by generic name

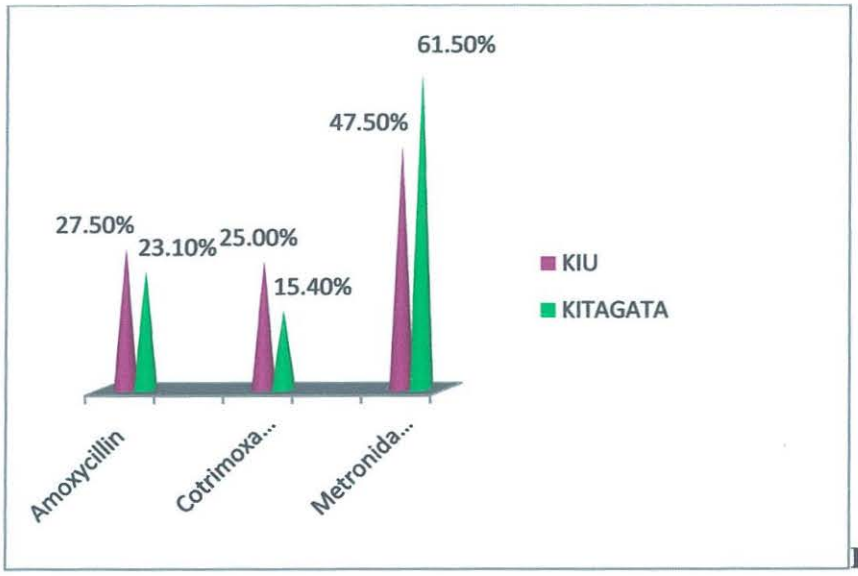

Fig 4

Metronidazole was the drug most prescribed by generic name in both hospitals. Cotrimoxazole was the least antibacterial prescribed by generic name.

4.3 Antibacterial drug knowledge.

Percentage of correct knowledge about antibacterials

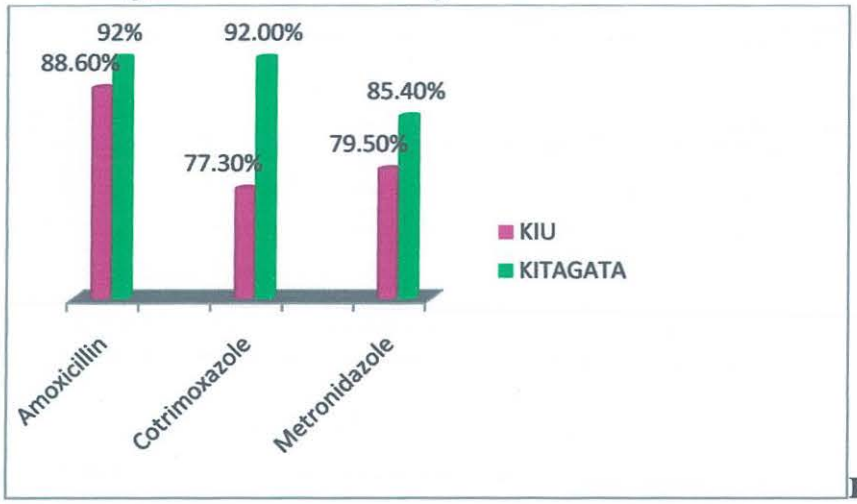

Fig 5

Amoxicillin was the drug most prescribers had correct knowledge about in both hospitals. Metronidazole was the least in terms of knowledge.

4.4 Interventions for promotion of rational use of antibiotics

Percentages of use of UCGs, Lab tests and Knowledge of EML in KIU and Kitagata hospitals

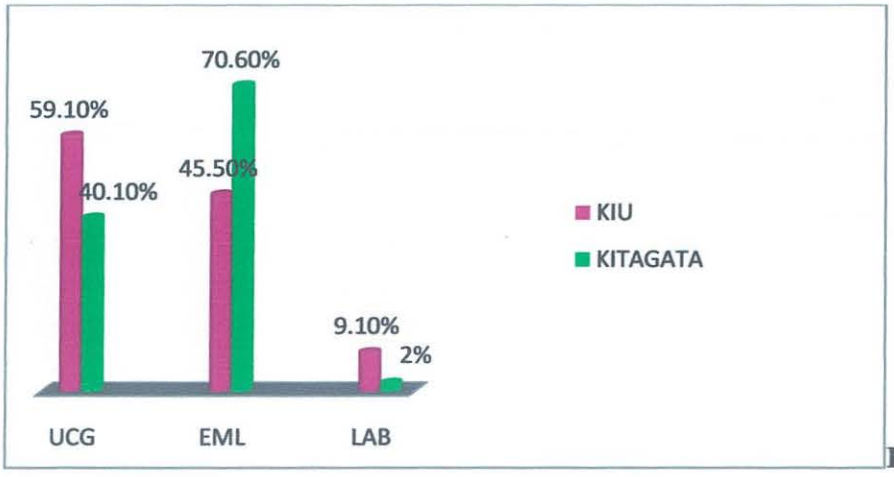

Fig 6

Percentages of Knowledge about the presence of a therapeutic/formulary committee in hospital of practice.

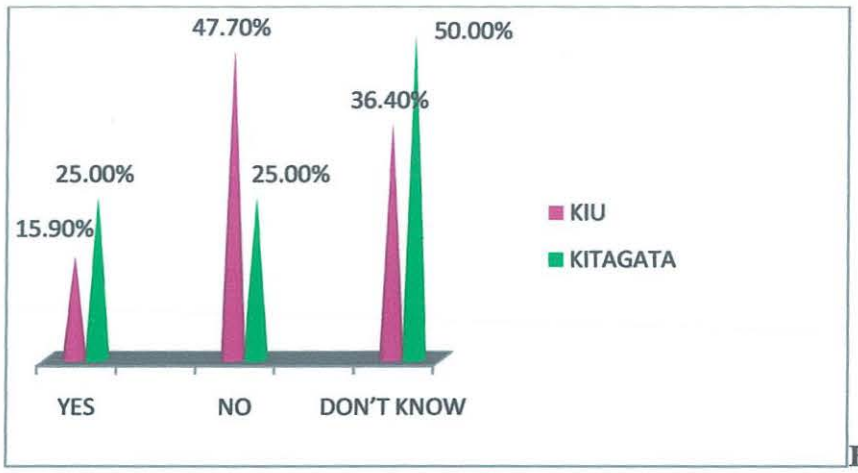

Fig 7

In both hospitals knowledge about the presence of a therapeutics board was very low.

CHAPTER FIVE

5.0 DISCUSSION

This study was conducted in order to assess the rational use of amoxycillin, cotrimoxazole and metronidazole, three of the most commonly prescribed antibacterial drugs. Together, these agents consume a significant proportion of most hospitals' outlay on antimicrobial agents. In this study the following methods were employed; the standard methodology for selected drug use indicators in health facilities developed by INRUD in conjunction with WHO (1993) and the Gyssens et al (1992) methodology.

5.1 Prescribers' adherence to standard treatment guidelines in a hospital setting.

From KIU-TH; a private-government partnership teaching hospital, the following findings were obtained. The total percentage of rationally used (prescribed) antibacterials was 72.4%. This level could be due to the higher percentage of prescribers who use UCGs (59.10%). In addition the patient to prescriber ratio is small allowing proper patient interaction and care.

Kitagata had a percentage of 57.1.% This lower level of rational use of antibacterials could be due to multiple factors, such as high patient turn up (since services are free) with low prescriber number. At the time of doing this research, only 6 prescribers (2 doctors and 4 clinical officers) were present, every day, yet patient turn up remained high (approximately 300) daily. In addition the level of use of UCGs was low (40.10%).

These findings agree with those from the studies by Kafuko JM et al(2004) and D. Raveh et al (2006) which concluded that adherence to guidelines may increase rational use of medicines.

5.2 Rational use of antibacterial drugs (amoxicillin, cotrimoxazole and metronidazole) by prescribers.

The rational use of AMT was measured as the use of any of these drugs in accordance with STGs. These results were used in this study as the most important indication of rational use of these agents; amoxicillin, cotrimoxazole and metronidazole. Cotrimoxazole registered the highest percentages; 35.2% in KIU-TH and 51.8% in Kitagata.

In relation to the Gyssens et al, 1992 study, where more frequent appropriate use of AMT from the use penicillin (amoxicillin) and metronidazole was obtained compared to quinolones; this

study differed in that a sulphonamide (cotrimoxazole) was used instead, it was found that the sulphonamide was more associated with appropriate use. Why this was so remains unexplained. In the case appropriatness of antibacterial prescribed, Fig 4.2.2, it was found that the more appropriate the choice of antibacterial the better the level of rational use.

Ina Willemsen et al (2004) and Davey (2005) agree that more frequent use of a drug was associated with inappropriate use (irrational use), however, in this current study this was not the case with results from Kitagata. Taking Fig 4.1.1 where cotrimoxazole was the most prescribed antibacterial in Kitagata and was also the most rationally used (at 51.8%) drug of the three antibacterials. The findings from the afore mentioned studies however agreed in the instance of KIU-TH; Fig 4.1.1 where amoxicillin is the most prescribed of these drugs in KIU-TH yet least rationally used.

5.3 Level of antibacterial drug knowledge

"Knowledge about a drug at times may be used as a benchmark in the assessment of rational prescribing of antibacterials" (Nicole Huang et al, 2000), however, this was not found to be so in this study. The knowledge about these antibacterials was tested for in the questionnaire and the following findings obtained; Amoxicillin is the drug most prescribers had correct knowledge about in both hospitals (88.6% in KIU-TH, and 92% in Kitagata). It may be expected that amoxicillin would be the most rationally used antibacterial. However as earlier mentioned, cotrimoxazole was the most rationally used drug of the three.

It appears that S.S Lee et al were right after all to conclude that "proper use of antibiotic requires not just good knowledge".

Rational use of antibacterials therefore, requires more than just knowledge but evidence-based recommendations, core skills and behavior as well, as Prof R.Finch of the Division of Microbiology and Infectious Diseases, City Hospital and University of Nottingham, UK suggested.

5.4 Promotion of rational use of antibiotics

The level of knowledge about what an EML was moderate among prescribers (45.5% in KIU-TH and 70.6% in Kitagata), no substantial relation to rational use of the antibacterials could be established.

However, the use UCGs (59.1% in KIU-TH and 40.1%) cannot be underestimated. According to Fig 4.1.2, it was obvious that KIU-TH had a higher rate overall of rational use of these antibacterials. This could be attributed to the higher level of use of UCGs. This shows that guidelines are still useful in promoting rational use of antibacterial agents. This agrees with the findings obtained by Kafuko JM et al, 2004 and G. Werner and S. Bronzwaer (2001) study.

The low rates of knowledge about an EML and low prevalence of use of laboratory testing (9.1% in KIU-TH and 2% in Kitagata) indicate that little has been done by hospitals to promote rational use. Therefore, WHO's concern about little being done to promote rational use of drugs seems to be a real threat.

"Indicators such as use of generic name can be used to identify problems in general prescribing and quality of care at these facilities. Results from the use of these indicators can help identify the motives for irrational use and other problems in the use of medicines. (International Medicines Situation-WHO, 2004). In this current study no substantial relation between use of generic name and rational use could be established. However, use of generic name was found to be related to drug knowledge as seen in Fig 4.2.3 and 4.3.

From Fig 4.4.2 it can be seen that most of the prescriber were not aware of the presence of a therapeutics or formulary committee in either hospital. Yet both hospitals have an existing formulary of therapeutics board or committee. This indicates that these committees are nonfuctional.

CONCLUSION

This data, although limited in scope, support the crucial role of the infectious disease consultant as well as more use of laboratory tests when antibiotic therapy is selected or adapted empirically, which is evidently the situation in the vast majority of the cases. If the selected spectrum of treatment is too narrow or inappropriate (hence irrational) complications may ensure, or the patient's condition may worsen. If treatment is too broad-spectrum, improving patients usually remain on the chosen regimen; if they do not respond, this may well lead to change to even broader spectrum agents or addition of other agents (polypharmacy). Both situations, with heavy use of broad-spectrum agents, will lead to emergence of multi-drug-resistant organisms, as well as significant expenses.

The importance of standard treatment guidelines cannot be undermined. The rates of rational use were found to be good, probably to overall popularity of STGs such as UCGs. The hypothesis was nullified as a result of this study. Hence, amoxicillin, cotrimoxazole and metronidazole are generally used rationally. However there is need for improvement because if any irrational use is left unchecked, resistance and other expenses will keep increasing.

The overall rate of rational use of common antibacterial agents such as amoxicillin, cotrimoxazole and metronidazole in KIU-TH and Kitagata hospitals in Bushenyi district still leaves a lot to be desired. KIU-TH had higher rates of rational use of antibiotics compared to Kitagata district hospital, which has very low numbers of prescribers in relation to patients.

Drug knowledge was found to have no positive effect on rational use of antibacterials. In addition, the low percentages of awareness about existence of therapeutics/formulary committees, knowledge about an EML and the use of laboratory testing, point to the fact that little has been done by these hospitals to curb irrational use of antibacterials. Therefore, more should be done by the respective hospitals' administrations.

RECOMMENDATIONS

- The presence of standard treatment guidelines (such as UCGs), their widespread publication, ongoing education of hospital staff regarding their use, are all necessary components in the effort to control spiraling expenditure in the treatment of bacterial infections, and the emergence of multi-drug-resistant organisms.
- Infectious disease consultation should be mandatory prior to prescription of these antibacterial agents.
- Laboratory testing should take a front row seat in not only diagnosis but drug choice decisions.
- Routinely carry out antibiotic utilization evaluations by using the recommended standard unit of measurement of antibiotic consumption for hospitals defined daily dose (DDD) per 100 bed-days', as promoted by the World Health Organization (WHO)
- Establish functional Therapeutics and Formulary committee which are hospital specific.

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APPENDICES

Appendix 1 WORK PLAN AND BUDGET

The estimated time frame is from April 2010 to January 2011

WORK PLAN

ACTIVITY	FROM	TO
SEARCH OF LITERATURE	March 2010	April 2010
PROPOSAL WRITING	May 2010	September 2010
COLLECTION OF DATA	October 2010	December 2010
INTERPRETATION OF DATA	January 3rd 2011	January 31st 2011
REPORT WRITING	February 1st 2011	February 28th 2011
HANDING IN OF REPORT	March 2011	

BUDGET AND EXPENDITURE

ITEM	AMOUNT (Uganda shillings-UShs)
Reams of paper	20,000/=
Pens	2000/=
Data collection	180,000/=
Supervisor	50,000/=
Transport	60,000/=
Accommodation and Food	100,000/=
Printing	100,000/=
Photocopy and binding	150,000/=
Miscellaneous	100,000/=
Total	762,000/=

Appendix 2 QUESTIONNAIRE

Questionnaire to Assess rational use of selected antibacterial drugs; amoxicillin, cotrimoxazole and metronidazole; in KIU-TH and Kitagata district hospital in Bushenyi district as part of a research study.

How are you? I am Musinguzi Mercy a student of pharmacy at KIU doing a research in the above mentioned area. Your participation in voluntarily answering this questionnaire will be highly appreciated. Your identity is not required. Tick the only one option of your choice

1. What is qualification are you?
   a) Physician
   b) Clinical officer
   c) Pharmacist
   d) Other
2. What is the average number of medicines prescribed per patient encounter?
   a) 1
   b) 2
   c) 3
   d) 4
3. Do you prescribe by generic name?
   Yes No
4. If yes, how often do you prescribe by generic name?
   a) All the time
   b) Most of the time
   c) Seldom
   d) When you remember
5. How often do you prescribe the above mentioned antibiotics?
   a) All patients encountered
   b) When a diagnosis deems it necessary
   c) When they are available
   d) When a patient asks for it
6. When do you prescribe the following drugs in injection form?(tick under the drug your answer of choice)

	Amoxycillin	cotrimoxazole	Metronidazole
When a patient asks for it			
When it is available			
When the National Clinical guidelines stipulate			
When you feel like			

7. Do you know what an essential medicines list is? If yes, please briefly explain.

.....

8. Do you think these medicines are from the essential medicines list or formulary?(tick under the drug your answer of choice)

	Amoxicillin	Cotrimoxazole	Metronidazole
Yes			
No			
I don't know			

9. Do you use or have an essential medicines list or formulary with you all the time?

   Yes No

10. Do you use the Uganda clinical guidelines when prescribing?

    Yes No

11. What are the common indications and their doses for which you prescribe these drugs?

Drug	Amoxicillin	Cotrimoxazole	Metronidazole
Indication, dose and drug form			

12. Do you receive prescription corrections concerning the above mentioned drugs from the dispensers?

    Yes No

13. Do you base all of your prescriptions including the said drugs on a confirmed laboratory diagnosis?

    a) Yes
    b) No
    c) Sometimes
    d) Never

14. Do you consider the cost of medication while prescribing antibiotics? Explain

    .....

    .....

15. Does this hospital have a Medicines and Therapeutic Committee of a Formulary?

    Yes No

16. What are the major causes of treatment failure for the following drugs?

Drug	Amoxicillin	cotrimoxazole	Metronidazole
Causes of treatment failure			

Appendix 3 **MORGANS' TABLE**

Required Sample Size†

Population Size	Confidence = 95% Margin of Error				Confidence = 99% Margin of Error			
	5.0%	3.5%	2.5%	1.0%	5.0%	3.5%	2.5%	1.0%
10	10	10	10	10	10	10	10	10
20	19	20	20	20	19	20	20	20
30	28	29	29	30	29	29	30	30
50	44	47	48	50	47	48	49	50
75	63	69	72	74	67	71	73	75
100	80	89	94	99	87	93	96	99
150	108	126	137	148	122	135	142	149
200	132	160	177	196	154	174	186	198
250	152	190	215	244	182	211	229	246
300	169	217	251	291	207	246	270	295
400	196	265	318	384	250	309	348	391
500	217	306	377	475	285	365	421	485
600	234	340	432	565	315	416	490	579
700	248	370	481	653	341	462	554	672
800	260	396	526	739	363	503	615	763
1,000	278	440	606	906	399	575	727	943
1,200	291	474	674	1067	427	636	827	1119
1,500	306	515	759	1297	460	712	959	1376
2,000	322	563	869	1655	498	808	1141	1785
2,500	333	597	952	1984	524	879	1286	2173
3,500	346	641	1068	2565	558	977	1510	2890
5,000	357	678	1176	3288	586	1066	1734	3842
7,500	365	710	1275	4211	610	1147	1960	5165
10,000	370	727	1332	4899	622	1193	2098	6239
25,000	378	760	1448	6939	646	1285	2399	9972
50,000	381	772	1491	8056	655	1318	2520	12455
75,000	382	776	1506	8514	658	1330	2563	13583
100,000	383	778	1513	8762	659	1336	2585	14227
250,000	384	782	1527	9248	662	1347	2626	15555
500,000	384	783	1532	9423	663	1350	2640	16055
1,000,000	384	783	1534	9512	663	1352	2647	16317
2,500,000	384	784	1536	9567	663	1353	2651	16478
10,000,000	384	784	1536	9594	663	1354	2653	16560
100,000,000	384	784	1537	9603	663	1354	2654	16584
300,000,000	384	784	1537	9603	663	1354	2654	16586

Appendix 4 MAP OF BUSHENYI DISTRICT