ANTIMICROBIAL USE PRACTICES IN MBAGATHI HOSPITAL, NAIROBI-KENYA: A POINT PREVALENCE SURVEY

MUYU MWENDE GRATIA (BPharm)

U51/7177/2017

A thesis submitted in partial fulfillment for the requirements for the award of Master's Degree in Pharmacoepidemiology and Pharmacovigilance

Department of Pharmacology and Pharmacognosy

School of Pharmacy

University of Nairobi

JUNE 2020

UNIVERSITY OF NAIROBI DECLARATION OF ORIGINALITY

Name of Student:	Muyu Mwende Gratia
Reg. Number:	U51/7177/2017
College:	College of Health Sciences
School:	School of Pharmacy
Department:	Department of Pharmacology and Pharmacognosy
Course Name:	Master of Pharmacy, Pharmacoepidemiology and Pharmacovigilance
Title of the work:	Antimicrobial use patterns in Mbagathi Hospital, Nairobi-Kenya: A point prevalence survey

DECLARATION

1. I understand what Plagiarism is and I am aware of the University's policy in this regard.
2. I declare that this thesis is my original work and has not been submitted elsewhere for examination, the award of a degree or publication. Where other people's work or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.
3. I have not sought or used the services of any professional agencies to produce this work.
4. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work.
5. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University anti-Plagiarism Policy.

Signature _____ Date _____

Muyu Mwende Gratia (B. Pharm)

U51/7177/2017

APPROVAL BY SUPERVISORS

This is to certify that this thesis has been submitted for examination with our approval as University supervisors.

Dr. Eric M. Guantai, PhD
Department of Pharmacology and Pharmacognosy
School of Pharmacy, University of Nairobi

Signature:…….. Date…….

Prof. Faith A. Okalebo, PhD
Department of Pharmacology and Pharmacognosy
School of Pharmacy, University of Nairobi

Signature:…….. Date…….

DEDICATION

I dedicate this work to my family who have constantly encouraged me throughout the study period. My dear husband, George Moturi, for allowing me to read during family time.

ACKNOWLEDGEMENTS

First and foremost to God for giving me the knowledge, strength and zeal to pursue this course.

Secondly special thanks to Dr. Eric Guantai and Professor Faith Okalebo for the support, guidance, advise, mentorship and invaluable time offered towards completing this work.

Thirdly, Mbagathi Hospital Research Committee, headed by Dr Kimutai, who granted me permission to carry out research in the facility.

Lastly the research assistants who devoted their time to data collection.

TABLE OF CONTENTS

UNIVERSITY OF NAIROBI DECLARATION OF ORIGINALITY ii

APPROVAL BY SUPERVISORS iii

DEDICATION iv

ACKNOWLEDGEMENTS v

TABLE OF CONTENTS vi

LIST OF TABLES ix

LIST OF FIGURES x

LIST OF ABBREVIATIONS AND ACRONYMS xii

DEFINITIONS OF OPERATIONAL TERMS xiv

ABSTRACT xvi

Chapter 1 : INTRODUCTION 1

1.1 Background 1

1.2 Statement of the problem 2

1.3 Research Questions 3

1.4 Study Objectives 4

1.4.1 General objective 4

1.4.2 Specific objectives 4

1.5 Study Justification 4

Chapter 2 : LITERATURE REVIEW ..... …6

2.1 Types of antimicrobials 6

2.1.1.Antibacterials 6

2.1.2 Antifungals 7

2.1.3 Antivirals 8

2.1.4 Anti-parasitic agents 8

2.2 Types of Misuse of Antimicrobials 8

2.3 Factors that contribute to antimicrobial misuse 9

2.3.1 Poor quality antimicrobials 9

2.3.2 Poor regulatory framework 9

2.3.3 Health facility factors 10

2.3.4 Prescriber related factors 10

2.3.5 Patient related factors 10
2.3.6 Increasing consumption of antimicrobials in the agriculture and animal industry 10
2.4 Antimicrobial Resistance (AMR) 11
2.4.1 Prevalence of Antimicrobial Resistance 13
2.5 Clinical and Economic Impact of Antimicrobial Resistance 14
2.6 Strategies to mitigate Antimicrobial resistance 15
2.7 Protocols for studying antimicrobial use 16
2.8 Conceptual Framework on Types of Antimicrobial Misuse and their Causes 17

Chapter 3 : METHODS 19

3.1 Study design 19
3.2 Study site 19
3.3 Study Population 20
3.4 Eligibility criteria 20
3.4.1 Inclusion criteria 20
3.4.2 Exclusion criteria 20
3.5 Sampling 20
3.6 Data Collection instruments and procedures 21
3.7 Quality Assurance 22
3.8 Data Management 22

Chapter 4 : RESULTS 25

4.1 Participants Recruitment and Enrollment 25
4.2 Bed capacity and occupancy in the wards surveyed 25
4.3 Socio-demographic Characteristics of Study Participants. 26
4.4 Medical characteristics of study participants 26
4.5 Prior Antimicrobial Use by Participants of the Study 27
4.6 Antimicrobials prescribed during admission at Mbagathi Hospital 28
4.6.1 Types of antimicrobials prescribed 28
4.6.2 Distribution of number of antimicrobials prescribed per patient 29
4.6.3 Frequency of individual antimicrobials prescribed at Mbagathi Hospital 30
4.7 Duration, Frequency and Route of antimicrobial use 31
4.8 Indications for antimicrobial use 32
4.8.1 Indications in medical, maternity and surgical wards 32
4.8.2 Indications in the nursery and paediatric wards 33
4.9 Leading indications for antimicrobial use in Mbagathi Hospital 34

4.10 Prescribed Daily Doses and associated Defined Daily Doses in Patients above 18 Years 35
4.10.1 Association Between Prescribed Daily Doses and Gender 36
4.10.2 Comparison of Prescribed Daily Doses and Ward Type 37
4.11 Prophylactic use of the antimicrobials. 38
4.12 Culture and sensitivity testing 39
4.13 Compliance with WHO indicators and specific guidelines for antimicrobial prescribing at Mbagathi Hospital 39
4.14 Linear regression for risk factors for number of antimicrobials prescribed per patient 40
Chapter 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS 42
5.1 General Discussion 42
5.2 Strengths and Limitations of the Study 47
5.3 Conclusion 47
5.4 Recommendations 48
5.4.1 Recommendations for practice 48
5.4.2 Recommendations for policy 49
5.4.3 Recommendations for future research 49
REFERENCES 50
APPENDICES 57

LIST OF TABLES

Table 4.1: Bed capacity and occupancy in Mbagathi Hospital 26

Table 4.2. Social Demographic Characteristics of survey Participants 26

Table 4.3. Medical characterisics of study participants 27

Table 4.4. Prior Antimicrobial Use by the Participants in the Study 28

Table 4.5. Frequency of individual antimicrobials prescribed at Mbagathi Hospital 31

Table 4.6. Duration Frequency and Route of administration of antimicrobials 32

Table 4.7. Indications in medical, maternity and surgical wards 33

Table 4.8. Indications in nursery and paediatrics 34

Table 4.9. Prescribed and Defined Daily Doses in Patients above 18 Years 35

Table 4.10. Comparison of Prescribed Daily Doses by Gender 37

Table 4.11. Comparison of Prescribed Daily Doses and Ward Type 38

Table 4.12. Prophylactic use of the antimicrobials 38

Table 4.13. Compliance with WHO indicators for antimicrobial prescribing at Mbagathi Hospital 40

Table 4.14. Linear regression for risk factors for number of antimicrobials prescribed per patient 41

LIST OF FIGURES

Figure 2.1. Factors that contribute to antimicrobial misuse (22). 11

Figure 2.2. Conceptual Framework on Types of Antimicrobial Misuse and their Causes. 18

Figure 4.1. Consort diagram of participants in the study 25

Figure 4.2: Classes of antimicrobials prescribed 29

Figure 4.3: Frequency polygon of number of antimicrobials prescribed 30

Figure 4.4: Leading indications in Mbagathi Hospital 34

Figure 4.5: Proportion of patients that received doses above or below WHO defined daily doses 36

LIST OF APPENDICES

Appendix 1. Global Point Prevalence Survey (GLOBAL-PPS) Ward Form (55)..... 57

Appendix 2 . Antimicrobial Use Point Prevalence Survey - Patient Data collection form 60

Appendix 3. Diagnostic codes (what the clinician aims at treating) (55). 77

Appendix 4. Indication Codes for antimicrobials given (55)..... 81

Appendix 5. ATC codes for antimicrobials given (55)..... 83

Appendix 6. Letter of KNH-UON ERC approval..... 85

Appendix 7. Mbagathi Hospital Research Committee Approval Letter..... 877

Appendix 8. Co-efficients of determination for each of the bivariable models..... 88

LIST OF ABBREVIATIONS AND ACRONYMS

ADR	Adverse Drug Reactions
AMR	Antimicrobial Resistance
AMU	Antimicrobial Use
ASP	Antimicrobial Stewardship Programme
ATC	Anatomical Therapeutic Chemical Classification
AZT	Zidovudine
BJ	Bone and Joint Infections
ENT	Ear, Nose, Throat
CNS	Central Nervous System
CST	Culture and Sensitivity Test
CVS	Cardio Vascular System
DDD	Daily Defined Dose
DTG	Dolutegravir
ESBL	Extended Spectrum Beta lactamase
ESKAPE	*Enterococcus spp, S. aureus, K. pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp.*
GI	Gastrointestinal
GLOBAL PPS	Global Point Prevalence Survey
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immuno-Deficiency Virus
ICU	Intensive Care Unit
INN	International Non-Proprietary Name
KEML	Kenya Essential Medicines List

MDR TB	Multi Drug Resistant Tuberculosis
MP-GEN	Medical Prophylaxis in General
MRSA	Methicillin Resistant *Staphylococcus Aureus*
NVP	Nevirapine
NICU	Neonatal Intensive Care Unit
OBGY	Obstetric and Gynecological Infections
Proph BJ	Prophylaxis for Bone or Joint Infections
Proph OBGY	Prophylaxis for Obstetric or Gynecological Infections
PDD	Prescribed Daily Dose
PPS	Point Prevalence Survey
RHZE	Rifampicin Isoniazid Pyrazinamide Ethambutol
SST	Soft Tissue Infections
TB	Tuberculosis
TDF/3TC/EFV	Tenofovir Lamivudine Efavirenz
WHO	World Health Organization
XDR TB	Extensively drug resistant Tuberculosis

DEFINITIONS OF OPERATIONAL TERMS

Adverse drug reactions: harmful or unpleasant reactions, which result from an intervention related to the use of a medicinal product.

Antibiotic: A substance that can either be produced or derived from a microorganism. Antibiotics destroy or inhibit growth of microorganisms.

Antimicrobial: An agent that kills microorganisms or stops their growth. Antimicrobial medicines can be grouped according to the microorganisms they act primarily against. For example, antibiotics are used against bacteria and antifungals act against fungi. Antivirals work against viruses whereas anti-malarials are used for malaria parasites.

Antimicrobial resistance: This is resistance of a microorganism to an antimicrobial agent that was originally effective for treatment of infections caused by this microorganism. Bacteria, viruses, fungi and parasites adapt to antimicrobial drugs, resulting in drug inefficacy and persistent infections, with a subsequent increase in the risks of severe disease and transmission.

Antimicrobial stewardship: Well co-ordinated set of actions which are aimed at promoting responsible use of antimicrobials. They range from actions at the individual level as well as the national and global levels. This cuts across human health, animal health and the environment.

Daily defined dose: defined by World Health Organization as the assumed average maintainance dose per day for a drug used for its main indication in adults. It is a statistical measure of drug consumption that is used to standardize the comparison of drug usage between different drugs or between different health care environments.

Empiric therapy: therapy based on experience or clinical guesses in the absence of diagnostic confirmatory tests.

Irrational use of antimicrobials: Irrational use refers to prescribing that does not conform to prescribed standards of care. This is manifested by : under or over prescribing ,wrong prescribing, extravagant prescribing, and poly pharmacy.

Prescribed daily dose: The average daily amount of a drug that is actually prescribed. This can vary according to severity of illness or even amongst different countries.

Poly pharmacy: Occurs when patients use more medicines than required for their illness.

Rational use of antimicrobials: Refers to giving the right medicine, for the right recipient, at the right dose, within the right duration and at the right and lowest cost to them and their community.

ABSTRACT

Background: Antimicrobials are indispensable in the practice of medicine. Their misuse is one of the great forces behind the rapid growth of resistance. Antibiotics are the most frequently prescribed class of antimicrobials, locally and globally. However this use is very often irrational. This increases risk of serious untoward drug reactions, poor treatment outcomes, waste of resources as well as antimicrobial resistance. Antimicrobial resistance is a grave and growing public health threat today. Inappropriate and unnecessary use of antimicrobials is a big contributor to the growth of resistant pathogens. Advocating and promoting rational use of antimicrobial agents through antimicrobial stewardship programs is pivotal in curbing increasing growth of resistance. The World Health Organization recommends that each facility drafts its antimicrobial use policy.

Study objective: The main objective of this study was to establish patterns of antimicrobial use in Mbagathi Hospital, Nairobi County, Kenya.

Methods: A Point Prevalence Survey was conducted in all wards of Mbagathi Hospital, in Nairobi County. Universal sampling was employed, whereby all patients who met the inclusion criteria were included in the study. Participants were included in the study if they met the following criteria: Age ranged from 0 days to 100 years and were admitted before 8 am on the survey day. This is in line with the Global point prevalence survey protocol, 2018. Patient demographic and clinical data were extracted from the patient files, treatment sheets, laboratory culture and sensitivity reports. All raw data collected was entered into EPI info version 7 and a database created. Descriptive and linear regression data analysis was conducted.

Results: A total of 185 patient records were sampled of whom 146 (78.9%) received at least one antimicrobial. Overall, 363 antimicrobials were prescribed during current admission and on average each participant was prescribed for 2 antimicrobials. The most important risk factors for number of antimicrobials used were HIV status, prior hospitalization in the last 90 days, catheterization and nutritional status. Antibiotics formed the biggest proportion of antimicrobials prescribed in Mbagathi Hospital (n=294, 81%) followed by antivirals (n=48, 13%) and the least prescribed were antimalarials and antifungals at 3% each. Most commonly prescribed antimicrobial was ceftriaxone at 46% while the commonest indication for antimicrobial use was pneumonia with a prevalence of 33%. Culture and sensitivity tests were only ordered in 7 (3.8%) of the cases.

Conclusion: The prevalence of antimicrobial use was above the World Health Organization (WHO) reference value of 30% or less. Ceftriaxone was used to a great extent. Empiric prescribing of antimicrobials was mainly the practice as culture and sensitivity testing were not routinely done in

Mbagathi hospital. The hospital medicines and therapeutics committee should set up an antimicrobial stewardship committee to help in judicious antimicrobial use.

Chapter 1 : INTRODUCTION

1.1 Background

Majority of medicines are sub-optimally prescribed, dispensed or marketed especially in the developing world where drug regulatory mechanisms are in their infancy stages of development or not available, according to World Health Organization (WHO) (1). In lower income countries, pharmaceuticals contribute a high percentage of family and overall healthcare expense. Betterment in the way medicines are utilized is of great significance in increasing quality of life and reducing premature deaths. This helps to build public confidence as well as reinforce health system credibility. Scarce resources will also be optimally utilized and most of all help to curb the growing menace of antimicrobial resistance (AMR) (2).

Antimicrobial resistance occurs when microorganisms resist the effects of antimicrobial agents. Resistant microbes increase or endure even in high concentrations of an antimicrobial in relation to the sensitive counterpart of an identical species. Microbes such as bacteria, fungi, viruses, and parasites undergo change when exposed to antimicrobial drugs such as antibacterials, antimycotics, antimalarials, antivirals and anthelmintics. The medicines consequently become ineffective and infections continue to exist in the body, increasing the risk of dissemination to others. If these trends continue then simple infections will be no longer treatable (3).

AMR is a serious global concern and is considered one of the greatest dangers to human existence. According to World Health Organization (WHO) AMR Global Resistance Report on Surveillance, April 2014, AMR is a grave phenomenon in many parts of the world (4). The report, which focused on antibacterial resistance, noted that there were soaring rates of resistance among bacteria such as *Klebsiella pneumonia*, *Escherichia coli* and *Staphyloccocus aureus*, which cause upper respiratory tract, urinary tract and wound infections (3). These immense rates of resistance were observed across all WHO regions globally. Resistance has been associated with poor clinical end results in patients with pneumococcal meningitis and blood infections due to *Streptococcus pneumoniae* strains with diminished sensitivity to penicillin (3).

The rapidly increasing levels of AMR are strongly associated with using antibiotics inappropriately. Overusing and misusing antimicrobials increases AMR rates (5) , and hence there is crucial requirement to control as well as monitor the use of the existing antimicrobials (6). Multidimensional interventions rather than single initiatives have been found more effective to reduce overuse of antimicrobials. These include prohibiting over the counter sale of

antimicrobials, delayed antimicrobial prescribing strategies, develop and implement treatment guidelines, and institute Antimicrobial Stewardship Programmes (ASPs).

Antimicrobial Stewardship Programmes are broad quality enhancement activities to rationalize prescribing and reduce antimicrobial resistance. Some activities include regular clinical audits, use of valid rapid diagnostic tests, pragmatic studies on complications and clinical outcomes and improvement of communication proficiency with patients (1, 5). Such initiatives to improve rational use of antibiotics have been implemented across continents including some African countries like Botswana (7).

In Kenya , the antimicrobial use policy has objectives geared to improving awareness and understanding of antimicrobial resistance by effective communication, education and training. In addition, strengthening the knowledge and evidence base on antimicrobials through surveillance and research. Reduction of the incidence of infection through effective sanitation, hygiene and infection prevention and control is also targeted. Another objective aims to optimize the use of antimicrobials in human, animal and plant health. Increasing investment in new medicines, diagnostic tools, vaccines and other interventions (8).

1.2 Statement of the problem

Antimicrobials are today indispensable in all healthcare systems for the treatment and prevention of infections. Even major surgeries, cancer chemotherapy, organ transplantation cannot be performed without effective microbial infections treatment. The consequences of antimicrobial resistance are far-reaching. Unless real global coordinated actions including antimicrobial prevalence surveys are immediately taken, we might be faced with setbacks. Describing global, regional and local antimicrobial resistance helps to detect crucial areas where some action can be put into place within the shortest time possible (9).

The 2011 European Commission Action plan emphasized the importance of surveillance data in antimicrobial use and resistance and the role of antimicrobial stewardship (10).

It is estimated that in Europe and the United States, resistant infections are causing roughly 50,000 deaths annually (11). When other countries are included the figure escalates to many hundred thousands. Infections that are resistant to antimicrobials will become a number one cause of mortality by 2050, due to overuse of antimicrobials and AMR. This ultimately will significantly impact on the wealth of nations, potentially costing up to US$100 trillion/year by 2050 (7).

There is a compelling obligation to lower misuse of antimicrobials. Penicillins and cephalosporins account for around 60% of total global antibiotic consumption. Between 2000 and 2010 their usage increased by around 40% as did carbapenems, a reserve group of antibiotics. This increase in carbapenem use along with a 13% increase in the last resort agents, polymixins including colistin, and a doubling use of glycopeptides, like vancomycin, is attributed to the rising rates of antibiotic resistance and development of multi drug resistant organisms (12).

Overusing and misusing antimicrobials increases AMR rates (5). Antibiotic overuse and misuse results from unsuitable prescribing, widespread use in agriculture, lack of new antibiotics from the research world as well as very poor regulatory practices where prescribing antibiotics is not controlled at all (13).

A previous study on medicine use practices in Mbagathi hospital showed that up to 68% of the prescriptions issued at the outpatient department had an antibiotic prescribed and some contained more than one antibiotic (14). The previous study only involved out-patients. This study focused on in-patient antimicrobial use which had not been studied. This particular study was broader and looked broadly at antimicrobials as opposed to only antibiotics.

1.3 Research Questions

The study sought to answer the following questions:-

1. What is the prevalence of antimicrobial use among in-patients at Mbagathi Hospital?
2. What are the most common indications for antimicrobials in Mbagathi Hospital in-patients?
3. Are antimicrobials prescribed and used according to existing antimicrobial use guidelines?
4. What is the prevalence of use of culture and sensitivity tests to guide the choice of antimicrobials?

1.4 Study Objectives

1.4.1 General objective

To identify the patterns of antimicrobial use among patients admitted at Mbagathi Hospital in Nairobi County, Kenya.

1.4.2 Specific objectives

The specific objectives of the study were to:

1. Determine the prevalence of antimicrobial use among in-patients at Mbagathi Hospital
2. Describe the indications and extent of use of the different classes and groups of antimicrobials in the different wards.
3. Evaluate whether the antimicrobials were prescribed and used according to existing antimicrobial use guidelines
4. Examine the frequency and results of culture and sensitivity tests to guide the choice of antibiotics.

1.5 Study Justification

Information regarding consumption of antimicrobials from this Point Prevalence Survey (PPS) will be used to draw and implement antimicrobial guidelines at this facility (15). The findings of this study would highlight areas that the hospital is doing well as well as areas for improvement. This is expected to provide the basis for the formulation of an antimicrobial use policy for the facility that would reinforce the appropriate use of antimicrobials for the in-patients at Mbagathi Hospital. This will ultimately curb the emergence of antimicrobial resistance and preserve treatments for the future. This study also aimed to provide important information on trends and antimicrobial resistance (9).

Data is inadequate to inform policy on matters of antimicrobial use practices in hospitals in low income settings including Kenya. Very limited studies have evaluated the rationality of antimicrobial consumption among in-patients in the county hospitals in Kenya. Only two studies have been conducted in Kisii Level 5 and Jaramogi Odinga Oginga Teaching and Referral hospitals (20, 21). No studies have examined the appropriateness of antimicrobial use among in-patients at Mbagathi Hospital, a public Level 4 hospital in Nairobi that serves a large spectrum of

patients, mostly the urban poor. This study therefore aimed at determining patterns of antimicrobial use among in-patients in Mbagathi Hospital. The findings can be used to identify gaps in use and develop an antimicrobial stewardship policy.

The study is expected to help the facility Medicines and Therapeutics Committee to identify feasible targets to improve the standards of antimicrobial prescribing, thereby contributing to designing of hospital interventions to promote prudent antimicrobial use and ultimately combat antimicrobial resistance and improve patient outcomes.

Chapter 2 : LITERATURE REVIEW

2.1 Types of antimicrobials

An antimicrobial is a product that kills or slows down the spread of microorganisms. Anti microbials act against bacteria, viruses, protozoans, and fungi such as mold and mildew. Antimicrobials are classified into antibacterials, antifungals, antivirals and anti-parasitic agents (18).

2.1.1.Antibacterials

Pathogenic bacteria cause diseases and infections. Antibacterial agents are used to fight infectious diseases. These agents can be classified into 5 major groups based on the following characteristics (1).

Classification	Description	Examples
Type of action	Can be bacteriostatic or bactericidal. The former target the cell wall or membrane to destroy bacteria whereas the latter inhibit or slow down the growth of bacteria	Bacteriostatic-tetracyclines, macrolides Bactericidal –beta lactams
Their source	They can either be naturally obtained example from fungal sources or plants, semi-synthetic or fully synthetic.	Natural –Penicillins Semi synthetic-sulfur based antibiotics Synthetic-fluoroquinolones
Spectrum of activity	Here we have narrow or broad spectrum antibacterials. Narrow spectrum work against gram positive only or gram negative only but not both. Broad spectrum work on a wide range of antibacterials, both gram negative and positive bacteria	Narrow spectrum-macrolides Broad spectrum-aminoglycosides, second, third and fourth generation cephalosporins

Chemical structure	This arises from different skeletons to form different structrulal units.	Group A-beta lactams, beta lactamase inhibitor combinations Group B-Aminoglycosides, macrolides, quinolones, fluoroquinolones
Function	This classification is based on mode of action or how the antibacterial works. This results to four groups of antibacterials. Cell wall synthesis inhibitors, inhibitors of membrane function, protein synthesis inhibitors and nucleic acid synthesis inhibitors	Cell wall synthesis inhibitors-beta lactams, penicillins Cell membrane function inhibitors-polymyxins Protein synthesis inhibitors- tetracyclines, aminoglycosides, chloramphenicol Nucleic acid synthesis inhibitors-quinolones

2.1.2 Antifungals

Antifungals selectively eliminate fungal pathogens from hosts. There are different classes including polyene antifungals that interact with sterols in the in the cell membrane making the membrane leaky. Amphotericin B and nystatin are examples. Azoles like fluconazole which inhibit cytochrome p450 depended enzymes, which are needed in structure and function of fungal cell membrane. Allylamines and morpholine antifungals- blocks ergosterol biosynthesis at the level of squalene epoxidase. Include terbinafine. Antimetabolite antifungals like 5-fluorocytosine inhibit both DNA(De-oxyribo Nucleic Acid) and RNA (Ribo-Nucleic Acid) synthesis (19).

2.1.3 Antivirals

There are two classes here. Non retroviral antivirals include anti herpes virus agents-acyclovir, anti-influenza agents and anti hepatitis drugs. Anti-retroviral agents include nucleoside reverse transcriptase inhibitors, non-nuceoside reverse transcriptase inhibitors, protese inhibitors, entry inhibitors and integrase strand transfer inhibitors (20).

2.1.4 Anti-parasitic agents

This is a class of medications indicated for the management of parasitic diseases, such as those caused by helminths, amoeba, ectoparasites, parasitic fungi, and protozoa, among others. Some anti-parasics include antimalarials. Other agents include those used for trypanosomiasis, leishmaniasis, amebiasis, giardiasis and trichomoniasis (21).

2.2 Types of Misuse of Antimicrobials

Issues regarding inappropriate use of antimicrobials bear international importance. Despite the rapid growth of resistance to current antimicrobials, there is little or no investment into novel antimicrobials. It is postulated that one million fatalities globally will occur by 2025 due to multiple drug resistance (22).

Misuse occurs when antimicrobials for humans are given to animals and applying antibiotic sprays on plants in agriculture. In addition, when the incorrect antimicrobial is utilized at inappropriate doses and unsuitable durations of therapy constitutes misuse. Expansive utilization of items like soaps, detergents, toys, mattress pads stuffed with antibacterials like triclosan and triclocarban all account for misuse. Misuse of antimicrobials and antibacterials destroy the susceptible microbes but the immune ones are left unperturbed. According to the World Health Organization (WHO) 50% of prescriptions globally are illogical. This entails polypharmacy, inadequate prescribing, and unwarranted antibiotic combinations. The leading irrational uses include polypharmacy, suboptimal dosage of the antimicrobials, non-adherence to established clinical guidelines, unsuitable routes of administration and self-medication (23).

Antimicrobial misuse is on the rise, and forms the basis of the menace. Misuse includes underuse, unnecessary use, suboptimal use and inappropriate use. Underuse is caused by lack of access to healthcare services. Unnecessary use is where an antimicrobial is not indicated and there is no health benefit for the patient. Inappropriate or suboptimal use includes incorrect timing, antimicrobial

choice, dose and route, frequency of intake or period of treatment. An example of incorrect timing is delayed administration to a critically ill patient. Choosing an antimicrobial with an unnecessarily broad or too narrow a spectrum as well as drug-agent mismatch. The use of intravenous route when oral can be used is also misuse. When the dose is too high or too low compared to what is indicated for that patient or duration is too long or too short all constitute misuse (24).

Inappropriate use of antimicrobials often includes use of antibiotics for non-infectious conditions, unnecessary initiation or even continued use of broad spectrum antimicrobials. Suboptimal dosing and duration of therapy that is inappropriate also account to inappropriate use (25).

2.3 Factors that contribute to antimicrobial misuse

2.3.1 Poor quality antimicrobials

Poor quality antimicrobials to sub-inhibitory concentrations which consequently increase chances of resistant strains**.** The most common counterfeited antimicrobials include beta-lactams, chloroquine and artemisinin derivatives. Until 2009, 50% of substandard antibiotics were beta lactams, 12% quinolones, 11% macrolides, 7% cyclins, and 20% other antibiotics. Poor quality anti-tuberculosis agents have been reported in 28 different countries, mostly in Asia and Africa. In 2003, WHO reported that Cote d'Ivoire a triple antiretroviral contained only zidovudine. In 2004, antiretrovirals were found to containing antidepressants in Congo (14). In one study in Tanzania, counterfeit oseltamivir and interferon were reported. Antimalarials were found to be of low quality in 90% of the time in African studies. Azole antifungals were not spared either in the America, Ukraine, and West Africa, Sierra Leone and Nigeria (26).

2.3.2 Poor regulatory framework

This has led to antimicrobials being dispensed and sold over the counter without any diagnostic guidance. When it comes to regulatory affairs most countries fail to enforce policies on manufacturing and distribution of medicines due to poor funding and even lack of necessary skills and personnel. Variations and lack of skills in prescribers is also a big contributor to antimicrobial misuse. Dispensing on the other hand has been infiltrated by quacks that apart from making profits have no other patient safety knowledge. The patients themselves are not spared by this menace as they fail to adhere to their antimicrobials, buy medicines over the counter and do not take their courses to

completion. The Agriculture industry remains an enormous challenge when it comes to antimicrobial misuse. The food chain is responsible for transferring resistance from the animals and environment to humans (27).

2.3.3 Health facility factors

Health facility factors which lead to antimicrobial misuse include inadequate supply of certain antimicrobials leading to over-prescription of the available ones. Lack of diagnostic capability in the health facilities also lead to empiric prescribing leading to misuse. Other factors are health facility related. Poorly equipped facilities with no diagnostic facilities, lack of skilled staff, patient overloaded facilities (28).

2.3.4 Prescriber related factors

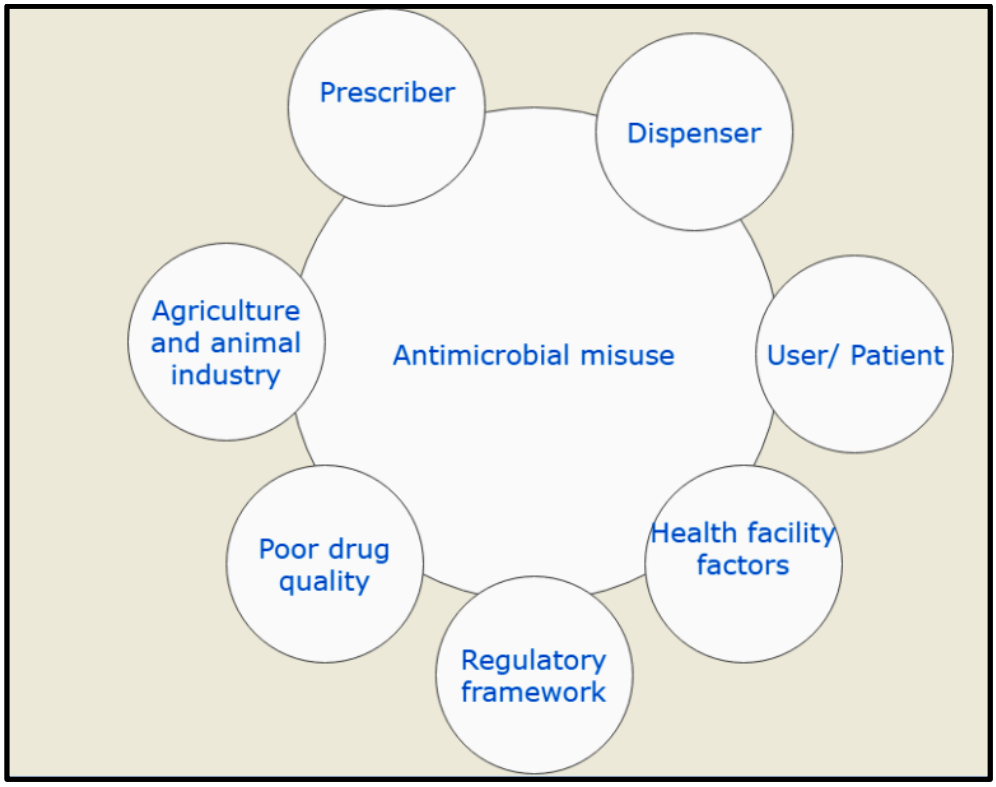
Lack of skills and knowledge about antimicrobials. Some prescribers due to lack of continuous medical education stick to old information and prescribe what is thought not to be evidence based. Some prescribers are drven by selfish gains like prescriptions for pay whereby medical representatives gift them to prescribe certain antimicrobials (28).

2.3.5 Patient related factors

Some lack resources whereby they cannot afford to pay for laboratory investigations therefore force prescribers to prescribe empirically. Furthermore still due to limited resources , some patients do not buy the complete dose for antimicrobials and end up using sub optimal doses. In this error of internet connectivity some patients go to hospitals with already the perceived prescription they should get therefore forcing prescribers to prescribe them (29).

2.3.6 Increasing consumption of antimicrobials in the agriculture and animal industry

Up to 40-80% of antimicrobials used on farm animals is highly questionable. Global antimicrobial use in agriculture is set to increase by 67% by 2030 due to the increasing demand of animal protein leading to intesive farming systems. In Kenya, studies done by the Global antibiotic resistance partnership(GARP) , report that, up to 70% of the antibiotics imported for use in the country are given to poultry, pigs and cattle for prophylaxis against infections (30).



Adopted with some changes from Goo *et al*, 2016.

Figure 2.1. Factors that contribute to antimicrobial misuse (22).

2.4 Antimicrobial Resistance (AMR)

Antimicrobial resistance arises when bacteria, parasites, viruses and fungi adjust to antimicrobial agents. This results to the drugs becoming ineffective hence the infections persist subsequently increasing risks of severe disease (31). Bacteria are able to identify and eject toxins from within the cell through efflux pumps before they even reach their targets. This is an important mechanism leading to AMR. These pumps can be selective or poly specific to many drugs (32).

Resistance can also develop naturally over time via genetic modifications. Emergence and spread of new mechanisms of resistance can be facilitated by inappropriate use of antimicrobials. In many countries antibiotics are dispensed without any professional guidance in both livestock and humans. Poor infection control, inadequate sanitary conditions and unsuitable food handling all lead to spread of AMR within populations (3).

Antimicrobial Resistance (AMR) is of great public health interest. Growing resistance is a threat in treatment of many infections. Using antibiotics judiciously is essential in slowing the development of antibacterial resistance and extending the lifetime of effective antibiotics. AMR occurs through

several mechanisms such as, modified antimicrobial target, efflux, impermeability or enzymatic degradation (33).

According to AMR Global Resistance Report on Surveillance 2014, there is high prevalence of resistance to third generation cephalosporins by *Esherichia coli* and *Klebsiella pneumonia.* This therefore means that severe infections by these bacteria have to rely on carbapenems which are reserved as the last resort for treating serious infections acquired in the community and hospital settings. Carbapenems are costly, and may be unavailable in poor settings. Of very worrying concern is that up to 54% of *K. pneumoniae* are resistant to carbapenems (3).

AMR directly threatens future patient safety. About 25 000 patients die every year in Europe alone due to infections resulting from resistant bacteria. The global estimate is approximately 700 000 deaths yearly. If the current AMR patterns are not changed, then ten million deaths annually are projected by 2050. Out of these only 0.7 million will happen in North America or Europe, with Africa and Asia topping the list (34). Methicillin Resistant *Staphyloccus aureus* (MRSA) kills more Americans yearly than HIV/AIDS, Parkinson's disease, pulmonary emphysema and manslaughter put together (3).

There are highly resistant organisms that cause urinary tract infections (UTIs) especially to common first line regimens like penicillins and sulfamethoxazole/trimethoprim. When a failing regimen is used to manage a UTI there is a danger of progression to kidney disease and high blood pressure. In the same way, with such resistance profiles, neonatal sepsis caused by *E. coli*, *K. pneumonia* and *S. aureus* will not be adequately eliminated with the preferred first line medicines such as penicillins, aminoglycosides and cephalosporins. This will escalate deaths of patients with severe infections. The increased levels of resistance to penicillins in *S. pneumonia* and *Haemophyllus influenza* are worrying since pneumonia is a main cause of mortality in children (35).

The world is unable to keep abreast with increasing AMR to current treatments. This sabotages the success of fundamental and new medicines in treating infections. Furthermore, the number of new classes of antibiotics has also dramatically declined over the past four decades. This means that the prospects of getting into a post antibiotic period are real, where ordinary infections will not be contained by accessible antibiotics (36). AMR must be treated as a global problem since it is not limited to national borders. Efforts are needed to change social norms and health system strengthening. AMR needs to be redefined broadly under agricultural, environmental and health security and not only concentrating on human health (36).

Antimicrobial resistance is not only a concern with antibiotics but affects all antimicrobials. It poses a danger in the successful prevention and care of a continuously growing variety of bacterial, viral, fungal and parasitic infections (9)**.** Widespread resistance among A(H1N1) and A(H3N2) viruses to adamantanes have rendered neuraminidase inhibitors as the primary antivirals for preventing and treating influenza (3). Resistance to the first-line management for *Plasmodium falciparum* malaria, artemisinin-based combination therapies, has been established in five countries in the Greater Mekong. Worse still , approximately 7% of patients beginning highly active antiretroviral therapy in middle income countries were drug-resistant (9). Azoles on the other hand have been effective in managing fungal infections but recently resistance in *Candida spp* has set in posing a great challenge (37).

2.4.1 Prevalence of Antimicrobial Resistance

Multi drug resistant Tuberculosis (MDR TB) is increasing. It is both challenging and costly to treat. Extensively drug resistant TB (XDR TB) has been reported in many countries according to WHO First Global Antibiotic Resistance Surveillance Report in 2014. It showed that five out of six WHO regions had more than 50% resistance to fluoroquinolones and third generation cephalosporins in *Escherichia coli* and methicillin resistance in *Staphylococcus aureus* in health care settings. Over 50% resistance to carbapenems and third generation cephalosporins was observed in *Klebsiella pneumonia*. In Africa and South East Asia, 45% of fatalities were associated with multi drug resistant bacteria. Up to 77% deaths in Africa are associated with *Klebsiella pneumonia* resistant to third generation cephalosporins. The rates of MRSA in hospital settings are high. In South Africa it is at 52% and in Nigeria 29.6%. Methicillin Resistant *Staphylococcus aureus* prevalences in Cameroon, Ethiopia , Morocco and Kenya are 72%, 42.8%, 14.4% and 27.7% respectively (33).

Antimicrobial resistance is a big menace in Sub Saharan Africa, in line with other world trends, *E. coli* resistance to third-generation cephalosporins presents a disturbing scenario, especially in urinary tract infections (UTIs). Fluoroquinolone resistance among *E. coli* also appeared to be increasing in UTIs to 28%, as well as amongst community-acquired febrile illness/bacteremia to 8% (38).

Many middle income countries do not have robust surveillance systems. In Rwanda, Kigali University Teaching Hospital, 31.4% and 58.7% of *Escherichia coli* and *Klebsiella* isolates, respectively, were not responding to at least one of the third generation, last resort cephalosporins. Eight percent of *E. coli* isolates were non responsive to imipenem and 82% and 6% of *Staphylococcus aureus* isolates were resistant to oxacillin and vancomycin respectively. Antimicrobial resistance is soaring in Rwanda and presents a grave challenge in treatment of basic infections (39).

There is increased resistance to earlier approved quinolones and extended-spectrum cephalosporins. The surveillance for AMR in Kenya was carried out to establish the prevalence and variety of AMR of gonococcal isolates from Sex Workers Outreach Program (SWOP) Clinic. Forty one isolates in 2012, 119 isolates in 2013, 24 isolates in 2014 and 54 isolates in 2015 showed up to 100% susceptibility to cefixime, ceftriaxone and spectinomycin, with a mean susceptibility of 82%, 37.7%, 19.5%, 1.6% and 0% for azithromycin, erythromycin, ciprofloxacin, penicillin and tetracycline respectively. Resistance against ciprofloxacin rose from 56% in 2012, 58.8% in 2013, 66.7% in 2014 and 68.5% in 2015 (40). Ciprofloxacin a widely prescribed quinolone is no longer dependable for management of gonorrhea. Worsening gonococcal drug resistance will affect effective treatment and demean disease control attempts (40).

An evaluation of antimicrobial resistance in East Africa showed soaring levels of AMR to first line antimicrobial agents including 50-100% resistance to ampicillin and cotrimoxazole. Non response to gentamicin was at 20-47% in gram negative isolates. Up to 100% and 50-100% of gram positive isolates were resistant to gentamicin and ceftriaxone respectively (41).

In a study conducted in Pumwani Maternity Antenatal Clinic, Kenya, on treatment of urinary tract infections (UTIs) in pregnancy, more than 49% of all gram-negative organisms were resistant to third generation cephalosporins, sulfamethoxazole-trimethoprim, fluoroquinolones, cefoxitin, amoxicillin-clavulanic acid and nitrofurantoin. Gram-positive strains were susceptible to nitrofurantoin, amoxicillin-clavulanic acid, linezolid and ofloxacin. The frequency of multi-drug resistance in the study isolates was at 96%. This suggests a serious resistance trend among UTI strains. Expectant mothers therefore need screening by urine culture testing and therapy should be informed by antimicrobial susceptibility laboratory results (42).

2.5 Clinical and Economic Impact of Antimicrobial Resistance

Antimicrobial resistance is associated with increased overall health care costs, both direct and indirect. It is also associated with increased hospital stay, mortality and morbidity in both developed and middle income countries. It is approximated that by 2050, AMR will be responsible for up to 10 million deaths. Its estimated 100 trillion USD will go to waste if substantial efforts are not made to avert this danger (33). A study published by the World Bank in March 2017 roughly estimated that AMR would exert a lag on global GDP of between 1.1 and 3.8 percentage points by the year 2050 (8).

Soaring antimicrobial resistance would also bring about shocking secondary consequences on aspects childbirth safety, including caesarean sections, with resulting increases in maternal and infant

mortality. Previous health scares such as severe acute respiratory syndrome (SARS), have revealed that travel and trade really have a tangible effect on the economy. If there is no successful treatment for malaria, people from non-malaria countries may not be ready to visit malaria endemic zones. This poses great trouble for most economies, especially those depending on tourism, foreign direct investment or global trade (44).

Resistant bacteria particularly *Enterococcus spp, S. aureus, K. pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter spp*. jointly referred as ESKAPE have been classified by WHO as important antibiotic resistant bacteria. They are used as target organisms in research, discovery and designing of novel antibiotics. These ESKAPE bacteria and their resistant counterparts are passed over in health care facilities in high and middle income countries. Multi drug resistant ESKAPE bacteria have also been identified in ICUs (29).

Cancer treatments often suppress patients' immune systems. This makes these patients more vulnerable to infections. Without efficacious antimicrobials for prevention and treatment of infections, chemotherapy would turn out to be a very risky affair (46). Caesarean sections contribute almost 2% to world GDP. The broad cancer chemotherapeutics add more than 0.75% while organ grafts add approximately 0.1%. These milestones in modern medicine risk being sabotaged if effective antibiotics are not available in the future. Together they add almost 4% to the world's GDP, worth over 120 trillion USD by 2050. The effects of AMR could lead to lose of more than 7% of GDP by 2050 or a total of 210 trillion USD over the next 35 years. These are not problems of high income countries only but also have dire and undesirable effects on developing countries expected to achieve universal health coverage over the future decades. Procedures such as bowel surgery and bone marrow transplants, might be undertaken less often or not even at all (47).

2.6 Strategies to mitigate Antimicrobial resistance

There is pressing need to get answers in fighting antimicrobial resistance. Legislation, political agendas, educational initiatives and development of treatments have been suggested amongst other strategies in combating antimicrobial resistance. Monitoring, continuous watch of practice and policy provide answers in human and agricultural sectors. There is need for a multidimensional approach if health care outcomes are to be scaled up (48).

Antimicrobial stewardship programs, (ASPs) , revolves around selecting the best antimicrobial, at its optimum dose and sufficient period of therapy that results in the best clinical outcome for the treatment or prophylaxis against an infection, with the least harm to the user and posing minimum

impact on future resistance (49). They are also geared on bettering clinical end results and safety, at minimal related costs and ultimately lower treatment related costs. The end goal is usually the reduction of antimicrobial resistance. Antimicrobial stewardship programs rely on education together with front end interventions like restriction of some selected antimicrobials. Development of guidelines and formularies and education of prescribers constitute good ASP practices. Others include accurate organism identification, selection of optimal dose and correct duration of treatment. These include reviewing or streamlining treatment on the basis of antimicrobial sensitivity testing. Reducing antibiotic use in agriculture is also important (50).

The populace needs to be educated on antimicrobial overuse and how to mitigate it and the use of analytic tools for monitoring development and spread of AMR. Vaccinations promote herd immunity and their use is also a strategy of minimizing antimicrobial use and ultimately resistance (51).

The growing AMR challenge can also be addressed by immunization and vaccination programmes. These can reduce prevalence of AMR pathogens as has been achieved with *Haemophilus influenza* and *pneumococcal* vaccines. Research has been on top gear to come up with HIV, malaria and universal influenza vaccines (47).

Antimicrobial surveillance together with ASP ensures quality use of antimicrobials. It means using as little as possible and as much as necessary to ensure welfare and high levels of health (11).

2.7 Protocols for studying antimicrobial use

Several protocols have been developed to study antimicrobial use. The Global Point Prevalence survey, is one of these (52). European Centre for Disease Prevention and Control (ESAC) has developed a protocol to guide point prevalence surveys. Data on antimicrobial consumption is collected at product level (53).

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (GLOBAL-PPS) regulates surveillance of antimicrobial prescribing and resistance in hospitalized adults, children and neonates worldwide. The GLOBAL-PPS creates awareness across the world regarding the use and antimicrobial resistance. It is instrumental in planning and supporting international and local stewardship interventions in various resource and geographical settings. The first Global-PPS was conducted in 2015 and included 335 hospitals in 53 countries in six continental regions, using a standardized and validated method (54).

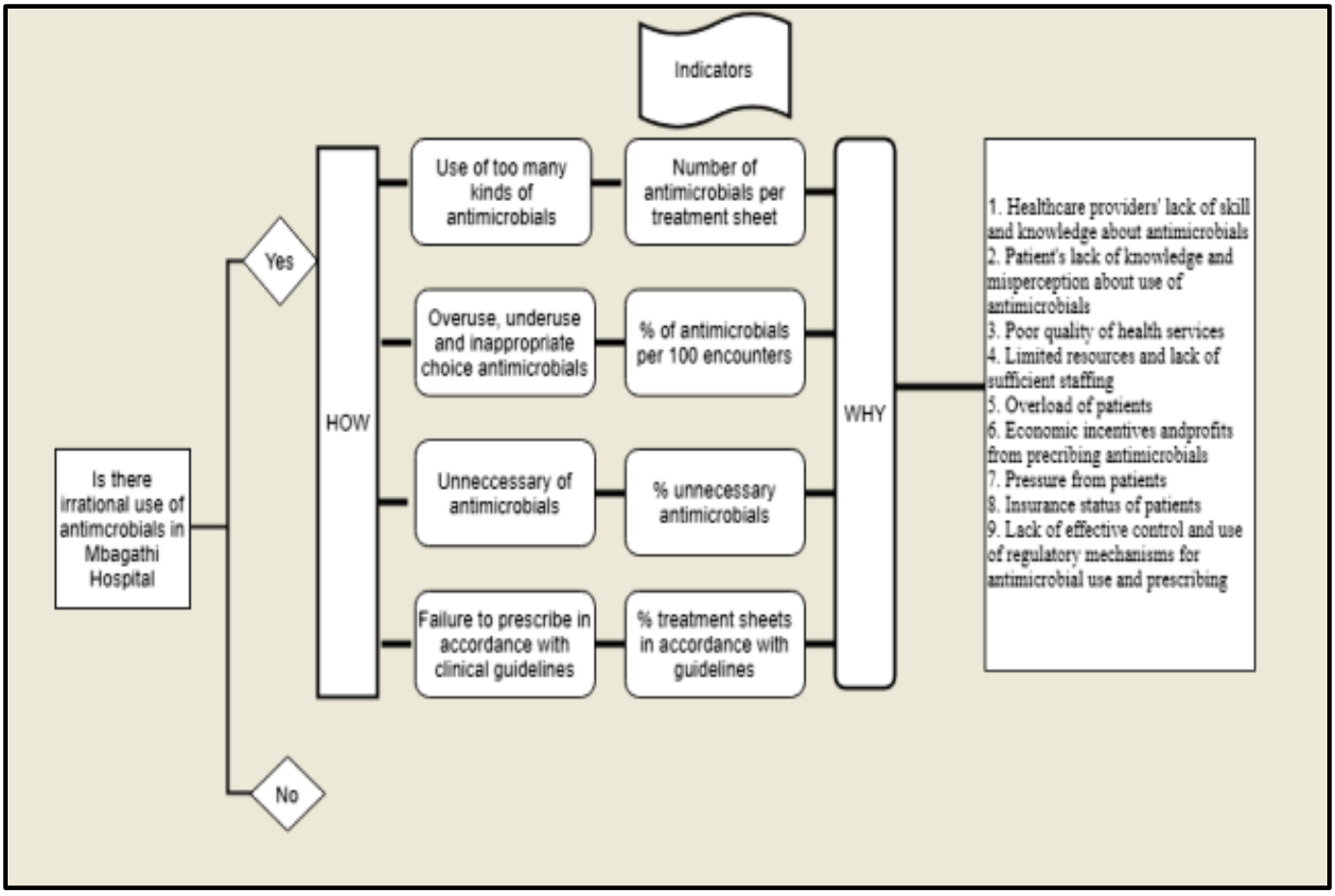
Some prevalence surveys that have been performed include; A point prevalence survey of healthcare-associated infections (HAIs) and antimicrobial consumption organized by European Centre for Disease Prevention and Control (ECDC-PPS). Global Point Prevalence Survey of antimicrobial use (Global-PPS). These studies were done in succession in Belgian acute care hospitals in 2017 (55). First was antimicrobial consumption in acute care hospitals: A national point prevalence survey on healthcare-associated infections and antimicrobial consumption in Switzerland, 2017 (56), then the Global Point Prevalence Survey (G-PPS) of antimicrobial use and antimicrobial resistance among hospitalized children in Georgia (57).

Medicine use surveys in partnership with Management sciences for Health. The activities herein include pharmacovigilance, rational medicine use, good dispensing practices and also medicines and therapeutics information (58).

Strengthening Pharmaceutical Systems organization (SPS), has also come up with ways of investigating antimicrobial consumption in hospitals (59). Surveillance of antimicrobial use identifies both rational and irrational use. This informs treatment and management decisions and also evaluates impact of resistance.

2.8 Conceptual Framework on Types of Antimicrobial Misuse and their Causes

The contribution of various facets and attendant reasons for irrational use of antimicrobials is illustrated in the conceptual framework shown in Figure 2.2 (60).



(Adopted with some adjustments from Mao W *et al* ;2015).

Figure 2.2. Conceptual Framework on Types of Antimicrobial Misuse and their Causes

Some indicators of irrational antimicrobial use are average number of drugs per prescription set at an optimum level between 1.6-1.8. Percent of drugs prescribed by generic name should be at 100%. Encounters with an antibiotic should range between 20.0 to 26.8%. An injection should be prescribed 13.4 to 24.1 % of the time. Up to 100% of total drugs prescribed should be from the essential medicine list (61)

Chapter 3 : METHODS

3.1 Study design

The study was a descriptive cross sectional Point Prevalence Survey (PPS) of antimicrobial use at Mbagathi Hospital. A point prevalence survey is a cross sectional study. It estimates the prevalence of a parameter at a specific point in time. Point Prevalence Surveys are the commonest population based epidemiological studies (54). Prevalence surveys can also be used to investigate relationships between risk factors and disease. A PPS offers a standardized tool which can be used to choose indicators for quality improvement in health care settings. Furthermore PPSs are less time consuming, less costly and easy to conduct.

A point prevalence survey is a practical surveillance tool for providing information about antibiotic use and assessing effects of antibiotic stewardship interventions. This study borrowed it's methodology from, and ultimately contributed to, the Global PPS of Antimicrobial Consumption and Resistance (GLOBAL-PPS, http://www.global-pps.com/).

3.2 Study site

The study was conducted at Mbagathi Hospital. It is situated in Golf Course location, Dagoretti District of Nairobi County. It was originally known as Infectious Diseases Hospital. It was built in the 1950s to offer health care services mainly for infectious diseases which required isolation such as TB, measles, meningitis and leprosy. In 1995 it was carved from Kenyatta National Hospital and transformed into an autonomous district hospital for Nairobi.

Mbagathi hospital is the largest public health facility under Nairobi county. It is a 200 bed capacity facility with several wards. These include a medical TB ward, general medicine, surgical, paediatric, post natal wards and a newborn unit. The bed occupancy rate is usually over 75% most of the time. Mbagathi Hospital serves mainly the urban poor and the informal settlements in south, west and North of Nairobi County, Kenya. Up to 1 000 patients are admitted in Mbagathi Hospital monthly. The outpatient department serves an average of 700 patients daily and admits an average 20 patients daily.

3.3 Study Population

The study population was all inpatients admitted to the wards of Mbagathi Hospital during the survey. The survey was carried out in the internal medicine, paediatric, surgical (both male and female), post natal wards and the new born unit. The study was conducted between March and April, 2019.

3.4 Eligibility criteria

3.4.1 Inclusion criteria

Participants were included in the study if they met the following criteria:

1. Age ranged from 0 days to 100 years.
2. Were of either sex.
3. Were admitted before 8 am on the survey day.

3.4.2 Exclusion criteria

Participants were excluded if they,

1. Were admitted for same-day procedures such as dialysis and day surgeries.
2. Had files missing from the ward for more than 24 hours on the day of the specific ward's survey.
3. Their treatment sheets were missing from their files.
4. Had files with incomplete data.

3.5 Sampling

Universal sampling was done therefore a minimum sample size was not computed. All patients admitted before 8 am on the day of the survey were sampled. According to the Global Point Prevalence Protocol of 2018, in hospitals with <500 bed capacity, all patients who meet the inclusion criteria should be included in the study (62).

Data was collected in a single day for each ward. Major ward rounds are done on Mondays and Thursdays. These two days were avoided for surveillance except for paediatric ward, new born unit and maternity where ward rounds are conducted daily. Data was mainly collected on Tuesdays, Wednesdays and Fridays. The total time frame for data collection for all wards was three weeks. Survey of surgical wards was carried out on weekdays that allowed retrospective data collection on surgical prophylaxis. These wards were not surveyed on a weekday immediately after a weekend or holiday.

3.6 Data Collection instruments and procedures

The Global Point Prevalence Survey (G-PPS) data collection forms (Appendices 1, 2, 3 and 4) were adapted (63). A Ward Data Collection Form (Appendix 1) was used to record information on the name of the ward and type of patients admitted therein. The Patient Data Collection Form (Appendix 2) was used to record the patient's bio-data, medicines prescribed, duration and all accompanying information on any antimicrobials prescribed.

This study involved extraction of data from the patient files, treatment sheets and laboratory culture and sensitivity reports. Antimicrobial interventions after 8 am on the survey day were not included in the survey (63).

Data on patients' age, weight and gender were collected. The antimicrobial agent used, dose per administration, number of doses per day, and route of administration were recorded. The anatomical site of infection or target for prophylaxis (according to provided reasons for treatment) as well as the admitting ward, admitting diagnosis and indication for therapy (community acquired versus hospital acquired infection or prophylaxis) were also determined. Availability of microbiological or biomarker data in determining choice of antimicrobial was very key in this study and laboratory reports were sought to establish this.

Bed occupancy was determined by dividing the total number of patients by the total number of beds in the hospital. Data on compliance to guidelines, documentation of reasons warranting antimicrobial use and stop/review date of prescriptions was also collected. Data on the route of administration, the type and class of antimicrobial used for an indication and whether there were antimicrobials prescribed with no indication were collected using the patient data collection tool (Appendix 2).

The antimicrobial agents were listed by generic name and classified according to the WHO ATC (Anatomic Therapeutic Chemical Classification). This is illustrated in appendix 5. In the ATC classification system, the drugs are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. Drugs are classified into five different levels. The first level is the organ class, the second level main therapeutic class, third level pharmacological action, fourth level chemical class and the last level is the chemical compound itself. It is a hierarchical level classification and provides a convenient way of presenting drug use consumption statistics (64).

Based on the ATC classification system, data was collected for the following antimicrobial agents: Antibacterials (J01), antimycotics (D01BA) and antifungals (J02) for systemic use, antibiotics used

as drugs for treatment of tuberculosis (J04A), intestinal anti infectives (A07AA), antiprotozoals used as antibacterial agents, nitroimidazole derivatives (P01AB) and antimalarials (P01B). Antimicrobials for topical use were excluded from the survey.

Information on the diagnosis as well as indication for antimicrobial use was classified and coded according to the classes/ codes presented in Appendix 3 and Appendix 4. These classes and codes have been adapted from GLOBAL PPS data collection tools (63).

Adherence to guidelines was inferred by comparing the collected data to what is stipulated in the guidelines: WHO (World Health Organization) drug use indicators (65), Basic Paediatric Protocols (66), Clinical Management and Referral Guidelines Volume 111 (67), National guidelines for the Diagnosis ,Treatment and Prevention of Malaria in Kenya (68).

3.7 Quality Assurance

Data collection tools, the ward data collection tool (Appendix 1) and the patient data collection tool (Appendix 2) was pre-tested before the study commenced. Research assistants constituted two registered pharmacists and one registered medical officer working at Mbagathi Hospital at the time of the study. They were trained on how to fill the data tools and also taken through the Global Point Prevalence Protocol of 2018 of conducting a point prevalence survey. They were also taken through the various national antimicrobial guidelines mentioned in sub section 3.10.

3.8 Data Management

Patient information was coded and no real names or patient identifiers were used. Data was counterchecked after entering into the research instruments and missing information sought. Data collection instruments were kept under key and lock and the computer files password protected. Data was entered within 24 hours of data collection. Regular backup of the database was done to guarantee data integrity.

All raw data was entered into Epi info version 7 software and a database created. The data was then exported to STATA version 14.2 software for analysis.

3.9 Study Variables

The primary outcomes of interest were the occurrence of antimicrobial use and its prevalence, the various classes of antimicrobial agents prescribed, the indications for antimicrobial use, posology of antimicrobials prescribed and whether antibiotic prescribing was informed by culture and sensitivity

results. For multilinear regression analysis the outcome variable was number of antimicrobials used. The predictor variables were age category, ward type, catheterization status, prior hospitalization in the last 90 days, HIV status, intubation status , gender, nutritional status and referral from another facility.

3.10 Data Analysis

Data was extracted from the patient's files and analyzed using STATA version 14.2 (StataCorp, USA). Descriptive statistics such as prevalence, frequencies, means and standard deviations were used to summarize the antimicrobial use patterns. The socio-demographic variables, indications of irrational use and prescribing patterns were compared across wards. Given that these variables were a mix of categorical and continuous variables, different inferential methods were used. The distribution of categorical variables were compared across wards using the Fischers exact and Pearsons chi-squared tests. Variables that were normally distributed were compared using one way analysis of variance. Continuous variables that were not normally distributed were compared using Kruskal Wallis test. Total number of patients admitted formed the denominator variable for the calculation of the overall prevalence of antimicrobial use. Summative WHO indicators of antimicrobial use were computed and compared with the ideal levels.

Bivariable linear regression analysis was done to identify risk factors for prescribing multiple antimicrobials which is a major problem. The outcome variable was number of antimicrobials prescribed. The predictor variables were, ward type, catheterization status, age category, intubation status, gender, HIV status, nutritional status, previous hospitalization or referral from another facility were the potential co-variates considered. Multivariable regression was done to adjust for confounders. Model building was done using a forward stepwise approach. The level of significance was set at 0.05.

3.11 Ethical Considerations

Approval to carry out this study was sought from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UoN-ERC) in February 2019 (Ref.no.KNH-

ERC/RR/48, Appendix 6). To implement the study, permission was sought from the Mbagathi Hospital research committee in March 2019, (NO. MDH/RS/1/VOL.1) Appendix 7.

Utmost care to ensure maximum privacy and confidentiality of the information obtained during the study was exercised. Patient codes were used instead of patient identifier information. The data instruments were stored in a password-protected database only accessible to the principal researcher. The data collection instrument and any other materials that were used during the study were kept under lock and key. The requirement for consent from the patients was waived since only medical records were used.

Chapter 4 : RESULTS

4.1 Participants Recruitment and Enrollment

Data was collected over three weeks. A total of 205 patients were screened for eligibility of which 185 met the criteria. Twenty patients were excluded for reasons presented in Figure 4.1. Nine patients had already been discharged on the day of the survey, another five patient files were in theatre or not available while six others had been admitted after 8 a.m. on the day of survey.

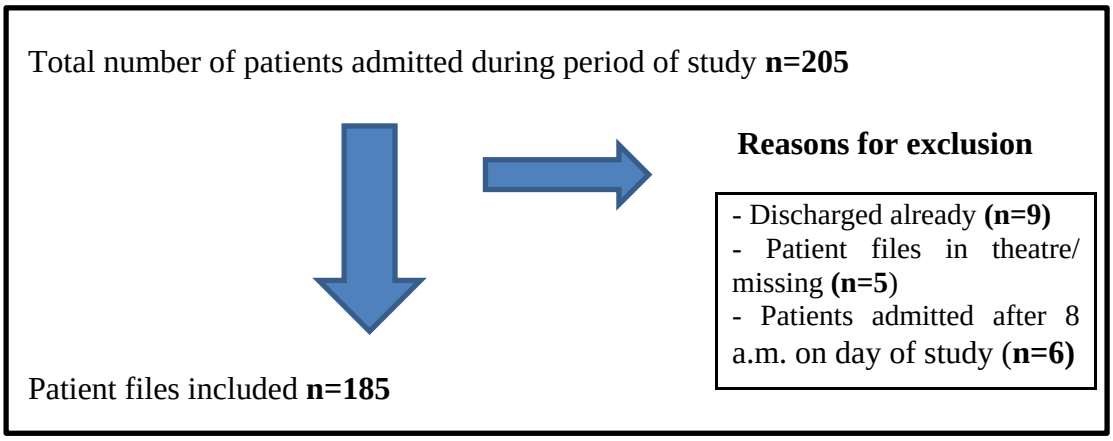


Figure 4.1. Consort diagram of participants in the study

4.2 Bed capacity and occupancy in the wards surveyed

The total number of patients admitted in the hospital at the time of the survey was 205. The total number of beds were 169 with medical ward having the most number (n=84, 49.7%). Percentage bed occupancy per ward was given by number of patients in a ward divided by the number of beds in the respective ward. The overall bed occupancy was 121%. Nursery had the highest bed occupancy at 450% followed by maternity with 263.2%. Medical ward had the lowest occupancy at 63.1%. This is summarized in Table 4.1.

Table 4.1: Bed capacity and occupancy in Mbagathi Hospital

Ward	Number of beds	Number of patients admitted in ward	Bed occupancy per ward (%)
Maternity	19	50	263.2
Medical	84	53	63.1
Nursery	6	27	450
Paediatrics	40	50	125
Surgery	20	25	125
Totals	**169**	**205**	**121.3**

4.3 Socio-demographic Characteristics of Study Participants.

Table 4.2 is a summary of the baseline characteristics of the 185 participants who met the inclusion criteria. Majority of the participants were above 18 years (n=108, 58%) and the fewest were children between 1 and 17 years (n=19, 10.3%). More than half of the participants were female (n=110, 59%). A large proportion of patients came from medical ward (n=51, 28%) followed by paediatrics (n=48, 26%). The least number of patients were from the surgical wards (n=21, 11%).

Table 4.2. Social Demographic Characteristics of survey Participants

Characteristic		n (%)
Age in years	Adult (≥ 18 Years)	108 (58.4)
	Child (≥ 1 and ≤ 17 Years)	28 (15.1)
	Infant (≥ 1 and ≤ 11 Months)	19 (10.3)
	Neonate (≤ 28 Days)	30 (16.2)
Gender	Female	110 (59.5)
	Male	75(40.5)
Ward type	Maternity	40 (21.6)
	Medical	51 (27.6)
	Nursery	25 (13.5)
	Paediatrics	48 (26.0)
	Surgery	21 (11.4)

4.4 Medical characteristics of study participants

There were significant correlations between the ward type and most of the medical characteristics observed. Out of the 185 patients sampled, 79 (42.7%) had been referred from other facilities and the bulk 33 (64.7%) were in the medical ward . A total of 145 patients were catheterized at some point

during their hospital stay. This constituted 78% of total patients surveyed. Almost half of the patients n=91 (49%) were malnourished and 38 (74.5%) were in the medical ward. Thirty four (18.4%) were HIV positive of which 29 (56.9%) were admitted in the medical ward. Most of the patients on TB treatment were also from medical ward 27 (52.9%). This is summarized in Table 4.3.

Table 4.3. Medical characterisics of study participants

Variable	Maternity	Medical	Nursery	Paediatric	Surgery	p-value
Referred from another facility	3 (7.5)	33 (64.7)	3 (12)	26 (54.2)	14 (66.7)	**<0.001**
Catheterized	15 (37.5)	46 (90.2)	23 (92.0)	46 (95.8)	15 (71.43)	**<0.001**
Intubated	0 (0.0)	4 (7.8)	2 (8.0)	3 (6.3)	2 (9.5)	0.473
Malaria test done	1 (2.5)	13 (25.5)	0 (0.0)	38 (79.2)	0 (0.0)	**<0.001**
Malnourished	2 (5.0)	38 (74.5)	18 (72.0)	28 (58.3)	5 (23.8)	**<0.001**
HIV +ve	2 (5.0)	29 (56.9)	0 (0.0)	2 (4.17)	1 (4.8)	**<0.001**
On TB treatment	0 (0.0)	27 (52.9)	0 (0.0)	3 (6.25)	1 (4.76)	**<0.001**

4.5 Prior Antimicrobial Use by Participants of the Study

Table 4.4 summarises the number of participants who had used an antimicrobial in the last 90 days preceding current admission. Nearly 1 out of 4 patients had used an antimicrobial before admission. Prior use was particularly high amongst paediatric patients. In this sub-population, slightly over 80% had been treated with an antimicrobial before admission. Amoxicillin was the commonly used antimicrobial. Only 2 patients reported to have used ceftriaxone in the last 90 days. It was noted that unlike other wards, the paediatric ward was consistent in the recording of prior use of antimicrobials. There were no records of antimicrobial use amongst patients admitted in maternity ward.

Table 4.4. Prior Antimicrobial Use by the Participants in the Study

	Maternity	Medical	Nursery	Paediatric	Surgery	p-value
Prevalence of prior use	0(0%)	5(11.1%)	2(4.4%)	37(82.2%)	1(2.2)	<**0.001**
Common antimicrobial used prior to admission						
Amoxicillin	0(0)	0(0)	2(8.3)	22(91.7)	0(0)	<**0.001**
Co-trimoxazole	0(0)	5(35.7)	0(0)	9(64.3)	0(0)	0.157
Benzathine penicillin	0(0)	(0)	0(0)	0(0)	1(100.0)	<**0.001**
RHZE	0(0)	(0)	0(0)	4(100.0)	0(0)	<**0.001**
Ceftriaxone	0(0)	(0)	0(0)	2(100.0)	0(0)	<**0.001**

4.6 Antimicrobials prescribed during admission at Mbagathi Hospital

Of the 185 patient records sampled, 146 prescriptions had one or more antimicrobial translating to a prevalence of antimicrobial use of 78.9%. A total of 363 antimicrobials were prescribed during admission. There were statistically significant differences in the patterns of prior antimicrobial use. Paediatric ward had the highest prevalence of use.

4.6.1 Types of antimicrobials prescribed

Antibiotics formed the biggest proportion of antimicrobials prescribed during admission in Mbagathi Hospital, n=294(81%). Antivirals n=48(13%) followed and the least prescribed were antimalarials and antifungals at 3% each. This is displayed in Figure 4.2.

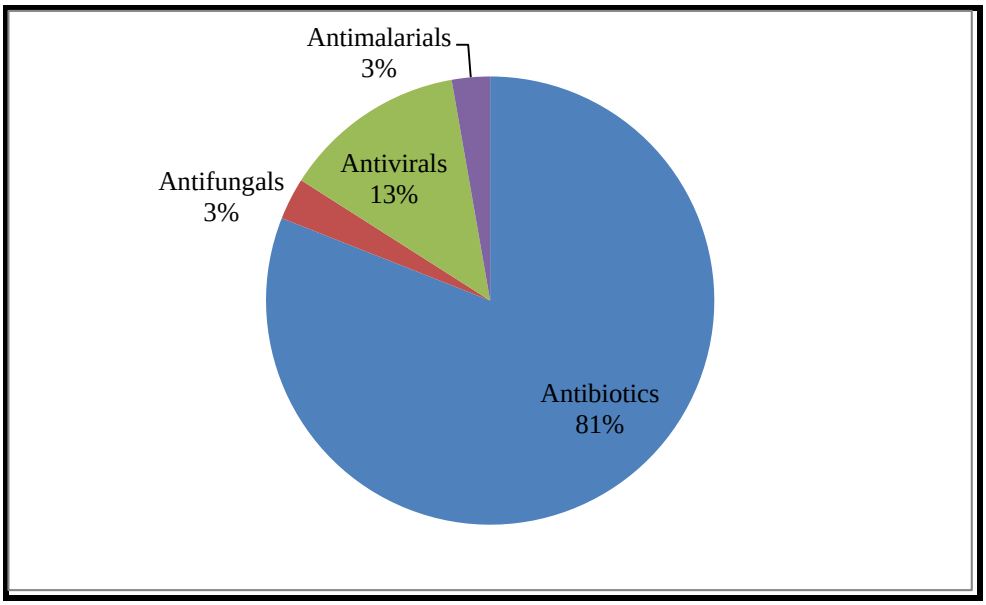


Figure 4.2: Classes of antimicrobials prescribed

4.6.2 Distribution of number of antimicrobials prescribed per patient

The number of antimicrobials prescribed per patient ranged from 1 to 8. On average 2 antimicrobials were prescribed per patient, though extremes of up to 6 and 8 antimicrobials prescribed to a single patient were noted. Figure 4.3 shows the overall frequency distribution of the number of antimicrobials per patient. Six patients from medical ward and one from paediatric ward had six antimicrobials each. These patients had many co-morbities among them pneumonia, retroviral disease and opportunistic infections. One patient from medical ward was on 8 antimicrobials. This patient was also intubated and quite sick and had been put on wide empirical antimicrobial cover.

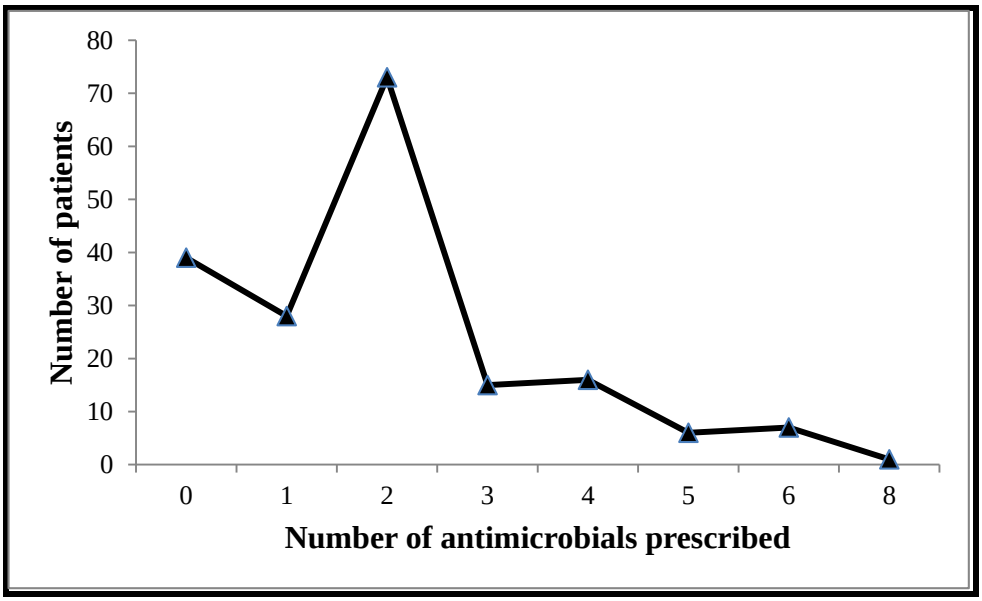


Figure 4.3: Frequency polygon of number of antimicrobials prescribed

4.6.3 Frequency of individual antimicrobials prescribed at Mbagathi Hospital

The most commonly prescribed antimicrobial was ceftriaxone at 23.7% (n=86) followed by gentamicin (10.2%), metronidazole (9.4%), RHZE (9.1%) and co-trimoxazole (8.5%). The top five antimicrobials were all antibiotics. Some low frequency antimicrobials included dolutegravir, amphotericin-B, norfloxacin and vancomycin. This is illustrated in Table 4.5

Table 4.5. Frequency of individual antimicrobials prescribed at Mbagathi Hospital

Antimicrobial	n (%)	Antimicrobial	n (%)
Ceftriaxone	86 (23.7)	Clindamycin	3 (0.8)
Gentamicin	37 (10.2)	NVP*	3 (0.8)
IV Metronidazole	34 (9.4)	Oral Metronidazole	3 (0.8)
RHZE*	33 (9.1)	Benzathine penicillin	2 (0.6)
Co-trimoxazole	31 (8.5)	Clarithromycin	2 (0.6)
TDF/3TC/EFV*	31 (8.5)	Cefuroxime	2 (0.6)
Benzyl penicillin	28 (7.7)	Meropenem	2 (0.6)
Acyclovir	10 (2.8)	Nystatin	2 (0.6)
Ceftazidime	8 (2.2)	DTG*	1 (0.3)
Fluconazole	8 (2.2)	TDF/3TC*	1 (0.3)
Amikacin	7 (1.9)	Amphoterin B	1 (0.3)
AL*	6 (1.7)	AZT*	1 (0.3)
Flucloxacillin	6 (1.7)	ABC/3TC/AZT*	1 (0.3)
Erythromycin	5 (1.4)	Norfloxacin	1 (0.3)
Artesunate	4 (1.1)	Vancomycin	1 (0.3)
Amoxicillin	3 (0.8)		

RHZE*- Rifampicin Isoniazid Pyrazinamide Ethambutol, TDF/3TC/EFV*-Tenofovir Lamivudine Efavirenz, AL* Artemether Lumefantrine, NVP* Nevirapine, DTG* Dolutegravir, TDF/3TC* Tenofovir Lamivudine, AZT* Zidovudine, ABC/3TC/AZT* Abacavir Lamivudine Zidovudine.

4.7 Duration, Frequency and Route of antimicrobial use

Most of the antimicrobials were prescribed once a day (46%), followed by twice daily at 29% as shown in Table 4.6. The most common route of administration was intravenous at 59%. Oral route accounted for 41% of prescribed antimicrobials.

Most of the antimicrobials were prescribed over a period of 4-7 days (26.4%). Several antimicrobials accounting for 53.2%, had no duration of use on the treatment sheet. This meant that the nurses administered them daily until discharge. A stop review date was available for 60.9% (221) of the antimicrobials prescribed but 39.1% (142) had no documentation on when to stop or review treatment. Almost half of the patients admitted (45.5%) missed at least one dose during their hospitalization with some missing up to 30 doses. This is illustrated in Table 4.6.

Table 4.6. Duration Frequency and Route of administration of antimicrobials

Variable	Parameter	n(%)
Frequency	Weekly	2(0.5)
	Five times a day	9(2.5)
	Four times a day(QID)	20(5.5)
	Thrice a day(TID)	54(14.8)
	Twice a day (BID)	106(29.0)
	Once a day(OD)	166(45.5)
	Not indicated	8(2.2)
Route	Intravenous	214(58.5)
	Intramuscular	2(0.5)
	Oral	147(40.2)
	Not indicated	3(0.8)
Duration of use indicated	Yes	170(46.8)
	No	193(53.2)
Duration of use (days)	1-3 days	35(9.6)
	4-7 days	96(26.4)
	8-10 days	28(7.7)
	More than 10 days	11(3.0)
	Not indicated	193(53.2)
Is there a stop review for the antimicrobial?	Not indicated	142(39.1)
Missed doses during course of therapy	Yes	165(45.5)

4.8 Indications for antimicrobial use

The leading indication of antimicrobial use in maternity ward was prophylaxis for obstetric gynecology surgical infections. In medical wards it was pneumonia, while in the surgical ward it was soft tissue infections.

4.8.1 Indications in medical, maternity and surgical wards

In medical ward approximately one in four of the antimicrobials prescribed was an antiretroviral. Pneumonia was the second highest indication (18.4%) for antimicrobial use in the medical ward. In the maternity ward slightly over 80% of the time antimicrobials were used for prophylaxis for obstetric gynecology surgical cases as shown in Table 4.7.

Table 4.7. Indications in medical, maternity and surgical wards

Medical	**Indication**	n (%)	**Maternity**	**Indication**	n (%)
	Antiretroviral therapy	35(23.0)		Proph OBGY	29(82.9)
	Pneumonia	28(18.4)		OBGY	3(8.6)
	Tuberculosis	27(17.8)		Antiretroviral Therapy	2(5.7)
	General medical prophylaxis	25(16.4)		Pneumonia	1(2.9)
	Gastrointestinal infections	8(5.3)	**Surgical**	Skin and soft tissue infections	11(30.6)
	Central Nervous System infections	7(4.6)		Prophylaxis for bone and joint infections	7(19.4)
	Unknown	6(3.9)		Bone and Joint infections	6(16.7)
	PROPH CNS	3(2.0)		Sepsis	4(11.1)
	Sepsis	3(2.0)		Proph OBGY	3(8.3)
	Bacteremia	2(1.3)		Proph CVS	1(2.8)
	Cysturia	2(1.3)		Unknown	1(2.8)
	Malaria	2(1.3)		Anti Retroviral Therapy	1(2.8)
	Upper respiratory tract infections	2(1.3)		Ear Nose Throat infections	1(2.8)
	Lung infection	1(0.7)		Tuberculosis	1(2.8)
	Proph RESP	1(0.7)			

Key: PROPH OBGY-Prophylaxis for obstetric gynecology surgical cases. OBGY-therapy for obstetric gynecology cases. PROPH CNS-prophylaxis for central nervous system conditions, Proph RESP-Prophylaxis for respiratory infections, Proph CVS-prophylaxis for cardio-vascular infections.

4.8.2 Indications in the nursery and paediatric wards

In the nursery, neonatal jaundice and sepsis were the most prevalent indications of antimicrobial use. There were more co-morbidities in the paediatric ward as compared to the nursery. Pneumonia was the main indication in paediatrics as shown on Table 4.8.

Table 4.8. Indications in nursery and paediatrics

Indication	Nursery	Paediatrics
Pneumonia	-	49(50)
Neonatal jaundice and sepsis	27(64.4)	6(6.1)
Malaria	-	8(8.2)
Gastrointestinal infections	-	8(8.2)
Respiratory distress	7(16.7)	-
Cental nervous system infections	-	6(6.1)
Bacteremia	-	6(6.1)
Upper respiratory tract infections	1(2.4)	6(6.1)
Medical prophylaxis for neonatal infections	4(9.5)	-
General medical prophylaxis	-	3(3.1)
Anti retroviral therapy	3(7.1)	3(3.1)
Tuberculosis	-	3(3.1)
Skin and soft tissue infections	-	1(1.0)

4.9 Leading indications for antimicrobial use in Mbagathi Hospital

Pneumonia was the most common indication for antimicrobial use across the wards (n=78) followed by, prophylaxis for obstetric gynecology surgical cases (n=32). Tuberculosis was third, (n=31), general medical prophylaxis fourth n=28, and sepsis n=21. This is illustrated in Figure 4.4.

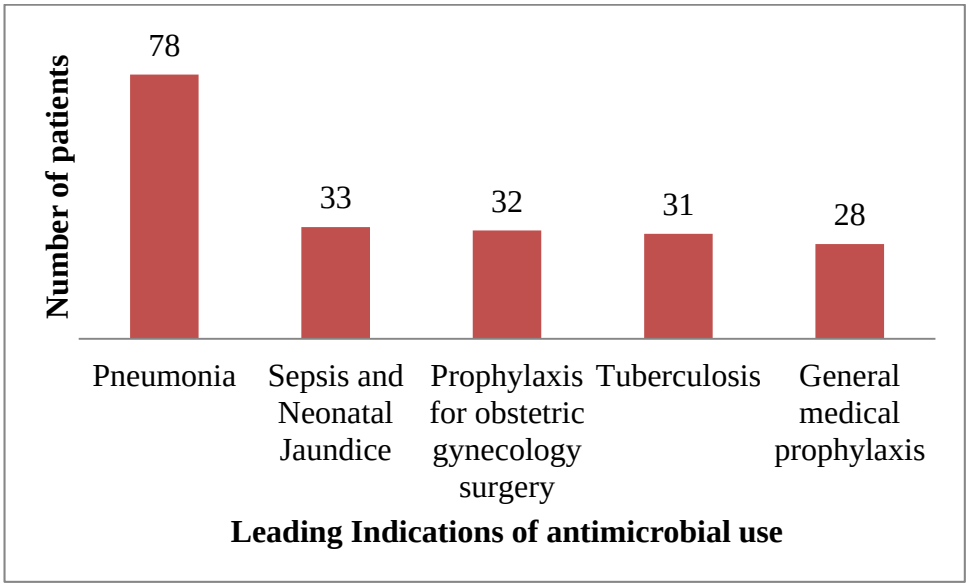


Figure 4.4: Leading indications in Mbagathi Hospital

4.10 Prescribed Daily Doses and associated Defined Daily Doses in Patients above 18 Years

Most of the antimicrobials were prescribed within the World Health Organization (WHO) recommended Daily Defined Doses (DDDs). The exceptions were acyclovir whereby only 2 (18%) got the recommended DDDs and the rest 82% were prescribed lower doses. Only 2 (28%) got the recommended defined daily dose of fluconazole while 71% got higher doses. The recommended DDD for RHZE is 4 tablets but only 31% got this. The remaining 69% got lower doses. This is presented in Table 4.9

Table 4.9. Prescribed and Defined Daily Doses in Patients above 18 Years

Antimicrobial	PDD[a] in mg/ tabs	DDD[b]	n (%)	Daily Cumulative DDDs
Ceftriaxone	1000	0.5	5 (8.5)	68.5
(DDD=2g)	2000	1	42 (71.2)	
	4000	2	12 (20.3)	
Metronidazole	1000	0.67	1 (3.1)	31.47
(DDD=1.5g)	1200	0.8	1 (3.1)	
	1500	1	30 (93.8)	
Acyclovir (DDD=4g)	400	0.1	1 (9.1)	5.4
	800	0.2	1 (9.1)	
	1000	0.25	2 (18.2)	
	2000	0.5	5 (45.5)	
	4000	1	2 (18.2)	
Fluconazole	200	1	2 (28.6)	18
(DDD=0.2g)	400	2	3 (42.9)	
	800	4	1 (14.3)	
	1200	6	1 (14.3)	
Flucloxacillin	1500	0.75	1 (16.7)	5.75
(DDD=2g)	2000	1	5 (83.3)	
Erythromycin	2000	1	2 (100.0)	2
(DDD=2g)				
Cotrimoxazole	960	1	24 (92.3)	30
(DDD=960mg)	1920	2	1 (3.85)	
	3840	4	1 (3.85)	
RHZE	1tab	0.25	1 (3.5)	23.25
(DDD=4 Tabs)	2 tabs	0.5	1 (3.5)	
	3 tabs	0.75	18 (62.1)	
	4 tabs	1	9 (31.0)	

RHZE-Rifampicin Isoniazid Pyrazinamide Ethambutol, [b]-Defined Daily Doses, [a]-Prescribed Daily Doses

The total daily prescribed doses have been compared to the World Health Organization's defined daily doses in figure 4.5.

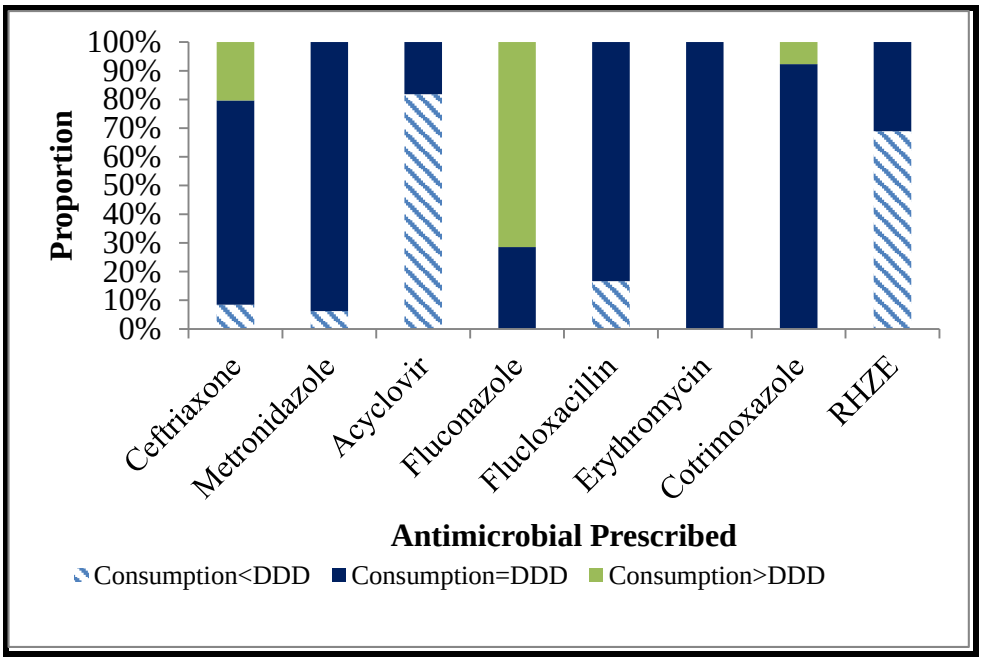


Figure 4.5: Proportion of patients that received doses above or below WHO defined daily doses

4.10.1 Association Between Prescribed Daily Doses and Gender

There was a statistically significant difference in prescribed daily doses of ceftriaxone across males and females whereby females received more quantities (p=0.016). Among the twelve patients who received a prescribed daily dose of 4000mg of ceftriaxone, 11(91.7%) were female and only 1(8.3%) was male. Forty two patients got the recommended daily dose of 2000 mg per day, females being more at n=28 while males were 14. This is summarized in Table 4.10.

Table 4.10. Comparison of Prescribed Daily Doses by Gender

Antimicrobial	PDDs	Female	Male	p-value
Ceftriaxone	1000	1 (2.5)	4 (21.1)	**0.016**
	2000	28 (70.0)	14 (73.7)	
	4000	11 (27.5)	1 (5.3)	
Metronidazole	1000	1 (3.7)	0 (0)	1.000
	1200	1 (3.7)	0 (0)	
	1500	25 (92.6)	5 (100)	
Acyclovir	400	1 (12.5)	0 (0)	0.636
	800	0 (0.0)	1 (33.3)	
	1000	2 (25.0)	0 (0.0)	
	2000	4 (50.0)	1 (33.3)	
	4000	1 (12.5)	1 (33.3)	
Fluconazole	200	0 (0)	2 (100)	0.095
	400	3 (60)	0 (0)	
	800	1 (20.0)	0 (0)	
	1200	1 (20.0)	0 (0)	
RHZE	1	0 (0)	1 (7.1)	0.232
	2	1 (6.7)	0 (0)	
	3	11 (73.3)	7 (50.0)	
	4	3 (20.0)	6 (42.9)	

4.10.2 Comparison of Prescribed Daily Doses and Ward Type

Prescribed daily doses were not affected by the type of the ward patient was admitted to as illustrated in Table 4.11. There was possible association between PDDs of flucloxacillin and ward type but the number of patients was too small to demonstrate it.

Table 4.11. Comparison of Prescribed Daily Doses and Ward Type

Antimicrobial	PDDs	Maternity	Medical	Surgery	p-value
Ceftriaxone	1000	1 (7.1)	4 (11.1)	0(0.0)	0.740
	2000	11 (78.6)	23 (63.9)	8 (88.9)	
	4000	2 (14.3)	9 (25.0)	1 (11.1)	
Metronidazole	1000	0 (0)	0 (0)	1 (14.3)	0.486
	1200	1 (6.7)	0 (0)	0 (0)	
	1500	14 (93.3)	10 (100)	6 (85.7)	
Flucloxacillin	1500	0 (0)	1 (100)	0 (0)	0.167
	2000	0 (0)	0 (0)	5 (100.0)	
RHZE	1	0 (0)	1 (3.6)	0 (0)	0.379
	2	0 (0)	1 (3.6)	0 (0)	
	3	0 (0)	18 (64.3)	0 (0)	
	4	0 (0)	8 (28.6)	1 (100.0)	

RHZE (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol) PDD-Prescribed Daily Dose

4.11 Prophylactic use of the antimicrobials.

Of the total 185 sampled study participants, 146 had an antimicrobial prescribed. Out of 146 patients on antimicrobials, 86 (59%) were for prophylaxis, of which medical prophylaxis constituted 51.2% while surgical prophylaxis formed 48.8%. This is presented in Table 4.12.

All the prophylaxis administered either surgically or medically was given for more than one day. Antimicrobials used for prophylaxis constituted ceftriaxone, co-trimoxaxole, flucloxacillin, fluconazole and metronidazole. The most commonly used antimicrobial for surgical prophylaxis was ceftriaxone and co-trimoxazole was used widely for medical prophylaxis.

Table 4.12. Prophylactic use of the antimicrobials

	Maternity	Medical	Nursery	Paediatrics	Nursery	p-value
Antimicrobial used for prophylaxis	30 (34.9)	32 (37.2)	7 (8.1)	4 (4.7)	13 (15.1)	**<0.001**
Medical prophylaxis	1 (2.3)	32 (72.7)	7 (15.9)	4 (9.1)	0 (0.0)	**<0.001**
Surgical prophylaxis	29 (69.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (31.0)	**<0.001**

4.12 Culture and sensitivity testing

There were only 7 culture and sensitivity requests (3.8%). The highest number of requests n=4(57.1%) came from nursery. Medical and maternity wards did not have any requests. Out of the seven requests, results were available for only 4 requests. The other three were still being processed.

4.13 Compliance with WHO indicators and specific guidelines for antimicrobial prescribing at Mbagathi Hospital

Nearly 80% of patients studied were on one or more antimicrobials. The reference WHO value is 30% hence antimicrobial use was quite high in this study. The average number of antimicrobials prescribed was approximately 2 which is within the reference range of 1.3 to 2.2. Proportion of medicines prescribed by generic name was 80%. The ideal should be 100%. Almost 50% of patients missed one or more doses during their course of treatment. Over 50% of prescribed antimicrobials did not have duration of use specified.

None of the patients received surgical prophylaxis as per the guidelines in our study. Guidelines stipulate no more than 24 hours antimicrobial prophylaxis for caesarian sections but all the patients received prophylaxis for a minimum of 72 hours. The paediatric protocols suggest all patients with pneumonia be treated with dispersible amoxicillin but none of the paediatric patients was on this formulation. They had all been started on ceftriaxone. For malaria management 10% were put on second line treatment without a positive malaria test which is a leading cause of antimalarial drug resistance. These indicators are summarized in Table 4.13.

Table 4.13. Compliance with WHO indicators for antimicrobial prescribing at Mbagathi Hospital

Measure	Indicator	Mbagathi Hospital score	WHO optimal values
Extent of antimicrobial use	Percentage of prescriptions with an antimicrobial	78.9%	<30%
Polypharmacy	Average number of antimicrobials per encounter	1.96	1.3-2.2
Compliance to generic prescribing	Percentage of antimicrobials prescribed by generic name	80%	100%
Guideline compliance	Proportion of patients who received surgical prophylaxis as per guideline	0.0%	>70%
	Proportion of patients with pneumonia who received antibiotic treatment as recommended in the treatment guidelines	40%	>70%
	Proportion of patients who received second line antimalarials after a positive malaria test	90%	100%
	Percentage of drugs prescribed from the essential drugs list	100%	100%
Irrational use of surgical prophylaxis	Percentage of encounters with Surgical prophylaxis exceeding 24 hours	100%	-
Prescribing errors	Frequency not indicated on prescription	2.2%	Errors should be avoided 100% of the time
	Route not indicated	0.8%	
	Duration of use lacking	53.2%	
	No stop review for antimicrobial	39.1%	
	Missed doses during course of treatment	45.5%	

4.14 Linear regression for risk factors for number of antimicrobials prescribed per patient

Bivariable linear regression was carried out by regressing the number of antimicrobials prescribed against each of the covariates. A parsimonious model of the most important predictors of number of antimicrobials prescribed was also conducted. The co-efficients of determination for each of the bivariable models are summarized in appendix 8. The co-efficients showed that the most important

determinants of the number of antimicrobials prescribed were HIV status, nutritional status, presence of catheterization and previous hospitalization. These variables were retained in the most parsimonious model. The most powerful predictor for number of antimicrobials prescribed was HIV status with adjusted β co-efficient of 2.187. This meant that, on average, HIV positive patients had an addition 2 antimicrobials prescribed. On average, catheterization increased the number of prescribed antimicrobials by 1. This is as shown in Table 4.14

Table 4.14. Linear regression for risk factors for number of antimicrobials prescribed per patient

Variable	Crude β coefficient		Adjusted β coefficient	
	β (95% CI)	p-value	β (95% CI)	p-value
HIV status	2.867 (2.436 - 3.297)	**<0.001**	2.187 (1.617 - 2.759)	**<0.001**
Catheterization	2.089 (1.740 - 2.438)	**<0.001**	1.317(1.055 - 1.580)	**<0.001**
Previous hospitalization in the last 90 days	1.307 (.848 - 1.766)	**<0.001**	0.516 (.183 - .850)	**0.003**
Nutritional status	1.510 (1.101 - 1.920)	**<0.001**	0.264(-.0314 - .560)	**0.080**
Referred from another facility	1.193 (.747 - 1.639)	**<0.001**	-	-
Age group	-0.124 (-.294 - .0460)	0.152	-	-
Ward type	0.642 (-.087 - .215)	0.402	-	-
Intubation	0.137 (-.862 - 1.135)	0.787	-	-
Sex	-0.026 (-.480 .428)	0.91	-	-

Chapter 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 General Discussion

This prevalence survey found that 79.8% of patients admitted in Mbagathi hospital received one or more antimicrobials. This is comparable with a previous study done in Kenyatta Referral Hospital in Kenya where 67.7% of patients surveyed were on antimicrobials (17). Similar outcomes were observed in a study done in Ethiopia where 86% participants prescribed with one or more antimicrobials (69). However hospitals in Ghana and South Africa had lower antimicrobial use prevalences of 51.4% and 31% respectively (70). World Health Organization (WHO), optimal value is 30% or less. The deviation from the WHO norm could be due to many co-morbidities including retroviral disease, tuberculosis and several opportunistic infections. Empiric therapy was adminstered to cover all these infections and any other that had not been diagnosed. Secondly, most low and middle income countries have a higher prevalence of infectious disease.

On average each participant was prescribed two (2) antimicrobials which was within the WHO permissible levels. The optimum number of antimicrobials as per WHO guidelines is 1.3-2.2. In a study of antimicrobial assessment at a tertiary hospital in north-western Nigeria, 22% of prescriptions contained more than one antimicrobial (71). Similar findings were observed in Gujarat, India with an average of 1.8 antimicrobials per patient (72).

In this study the most important risk factor for number of antimicrobials prescribed was HIV status. The others were previous hospitalization, catheterization and nutritional status. In a point prevalence survey in Botswana some risk factors associated with number of antimicrobials used included age-group, prior admission, referral from another facility, being malnourished, having tuberculosis and HIV infection (73).

Prior antimicrobial use in our study was noted in 45(24.3%) of participants. The bulk of these patients were in paediatric ward and this was attributed to thorough history taking of prior use. It could also be attributed to increased prevalence of parents self medicating their children. This proportion could have been actually higher if all wards routinely sought this information from patients.The commonest antimicrobial among the adults was co-trimoxazole while amoxillin was commonest among the children. Similar results were observed in an outpatient study conducted in Kiambu County, Kenya, the most prescribed antibiotic was amoxicillin 46(36%). This corroborates with other studies in Accra Ghana and United Arab Emirates which both had amoxicillin use prevalence of 46% (29). In a point prevalence study in Botswana (18.85) patients had prior exposure in the last 90 days, cefotaxime at

28.4% and amoxicillin 26.1% (73). This is in tandem with our study whereby amoxicillin was widely used pre-admission. Self medication especially with amoxicillin has led to extensive antimicrobial resistance. In a study done in Kakamega town, Kenya, amoxicillin had the highest resistance at 72% (74).

A total of 363 antimicrobials were prescribed during hospitalization at Mbagathi Hospital. Antibiotics formed the biggest proportion of antimicrobials prescribed in Mbagathi Hospital n=294(81%). Antivirals n=48(13%) followed and the least prescribed were antimalarials and antifungals at 3% each. The bulk of prescribed antivirals were antiretroviral drugs. Similar results were obtained in another study conducted among 53 countries, 41,213 antimicrobials were prescribed. Antibacterials constituted 36,792 (89.3%), both antimalarials and antifungals were 1,724(4.2%) (75). Results from the first global point prevalence study showed that out of 48,565 antimicrobials prescribed, 43,513 (89.6%) were antibacterials, 2,062 antifungals for systemic use (76). These findings are consistent with our study and in all the studies antibiotics were the leading antimicrobials prescribed.

In our study, third generation cephalosporin ceftriaxone topped the list of prescribed antimicrobials 86(23.7%) followed by gentamicin 37(10.2%) and metronidazole 34(9.4%). These values are consistent with reports in the literature. In a study conducted at Kenyatta referral Hospital, Kenya, ceftriaxone was the commonest antimicrobial prescribed (55%). This was followed by metronidazole (41.8%) and broad spectrum penicillins (41.8%) (17). Comparable findings were seen in a retrospective observational analysis of antimicrobials (20) where ceftriaxone was the commonest prescribed antimicrobial at (32.5%) of the time. Amikacin was second at 25.0% and metronidazole third at 22%. In the contrast in an Ethiopian study, the most prescribed antimicrobial was penicillin G crystalline at (20)%, followed by gentamicin at (19%) and third ampicillin(16%) (77). Cephalosporins particularly third generation are very popular. They have wide spectrum of activity, minimal toxicity, are easy to administer and readily available as well. In an antimicrobial use review by Verspoten *et al*; (75), vancomycin and carbapenems were highly utilized in both North and Latin American hospitals unlike our study where they were minimally used. Reasons could be high prevalence of methicillin resistant *Staphylococcus aureus* (MRSA) in Latin American Hospitals (75). The high cost of these antibacterials is also an inhibition to their use especially in low and middle income countries like Kenya. Most studies on antimicrobial have found a high prevalence of ceftriaxone use . A study conducted in India had 48.5% prevalence and in Tehran 34% (78). In a study conducted in a Kenyan referral hospital ceftriaxone was the most common prescribed antibiotic (39.7%) followed by benzyl penicillin (29.0%) and metronidazole (25.1%) (16). overuse may be attributed to non-adherence to guidelines as well as a weak medicines and therapeutics committee to

reinforce good prescribing practices. The implications of overuse of ceftriaxone are dire. With the dwindling pipeline of new antibiotics and growing risk of resistance to ceftriaxone mortality rates from simple infections is expected to increase. Empowering the hospitals medicines and therapeutics committee as well as establishing an antimicrobial stewardship programme (ASP) might help to curb this menace. Other point prevalence surveys are suggested in future to compare and evaluate impact of established ASP.

Our study did not find any association of use of ceftriaxone with age but there was some association with gender (p-value 0.016). This was consistent with a study in Thailand which found out that there was a higher incidence of ceftriaxone use in females compared to males (78). However a US based study had 86.2% males on ceftriaxone as opposed to only 13.8% females (79). This may have resulted from the larger proportion of females in the Mbagathi study 59.5% versus 40.5%. Most of ceftriaxone was consumed for surgical prophylaxis for obstetric gynecology surgical cases and all the patients here are female. This could also have been due to unavailability of alternative less broad spectrum antimicrobials. Restricting ceftriaxone use and antimicrobial stewardship programs would be of benefit in adding life to antimicrobials. Future studies should be conducted to establish if there are any differences in ceftriaxone consumption across the genders.

Parenteral route was the commonest accounting for 216 (58.5%) while oral route took 147 (40.2%). Some 3 (0.8%) prescriptions had no route indicated. Our study had no transition from parenteral to oral formulations which is a critical requirement of judicial antimicrobial use. In one Ugandan study, 81% of patients on antimicrobials during their hospital stay got at least one parenteral formulation of their antimicrobial(s) (70). In Ghana antimicrobials were majorly administered parenterally (54%) than orally at 46% (80). In Gujarat, India however things were different and most common route of administration was oral at 73% (20). Early switch during treatment from intravenous to oral antimicrobials has many benefits, including reductions in catheter-related complications, health-care costs, and duration of hospital stays, and is recognized as a key facet for stewardship processes in hospitals. Switching to oral medication also enables faster discharge from hospital further lowering hospital costs associated with long hospital stay (70).

Several antimicrobials accounting for 22.6% did not have accompanying duration of use in the treatment sheet. In a study conducted in Uganda, the prescriber omitted duration in 7%–8% of prescriptions (70). A stop review date was available for 60% (221) of the antimicrobials but 40% (142) had no indication on when to stop or review treatment. This means that the nurses will administer them daily until discharge. This is serious misuse and leads to high costs and resistance.

A big proportion of patients 45.5% missed at least one dose during their hospitalization with some missing up to 30 doses. Missing doses aggravates resistance since efficacy is already compromised. This is comparable to a study done among hospitalized patients in Uganda where 44% (243/558) missed at least one dose of their antimicrobial treatment (70). In Botswana, 1923 doses from 437 prescriptions failed to be administered, with a mean of 1.96 doses (73). Missed doses may have been occasioned some system related problems including stock-outs, understaffing especially since most were parenteral and a nurse is needed for administration and poor communication between the health care providers and the patients.

In our study the most common indication was pneumonia (n=76) followed by neonatal sepsis and neonatal jaundice n=33, prophylaxis for obstetric gynecology surgeries third (n=32), tuberculosis (n=31) and general medical prophylaxis n=28. Similar findings in Ethiopia were reported indicating pneumonia and sepsis as top indications where ceftriaxone was indicated (81). Similarly in an internet based study among 53 countries pneumonia was the commonest overall indication n=5722(19.2%) of patients treated (75). However in a survey at Kenyatta referral hospital, Kenya, the most prevalent indication was medical prophylaxis (29%) (17). Contrary to our study, in a point prevalence survey in Ethiopia, the biggest indications were associated with obstetrics and gynecology in 94(13.22%) participants (73).

Out of 146 antimicrobial episodes observed, 86(59%) were for prophylaxis. Medical prophylaxis constituted 44(51.2%) while surgical prophylaxis was at 42(48.8%). The most widely used antimicrobial for surgical prophylaxis was ceftriaxone and co-trimoxazole for medical prophylaxis. This is comparable with another study in Barcelona whereby sulfamethoxazole –trimethoprim was most prevalent in medical prophylaxis accounting for 63·4% (59 of 93 patients). In Northern Europe surgical prophylaxis constituted 17·8% and cefazolin was commonly used accounting for 1801 (27·5%). In Eastern Europe ceftriaxone was used 49(39.5%) times and 28% (559) for Southern Europe. In Africa ceftriaxone was used 78 [27·7%] of the times (75).

Surgical prophylaxis was administered for>24 hours in 100% of the surgical cases in this study. In an antimicrobial use survey, surgical prophylaxis lasting>24 hours was very rampant ranging from 40.6% in Oceania to 86.3% in eastern Europe (82). In an Australian study, surgical antimicrobial prophylaxis rates greater than the benchmark of 24 hours was high (36%) (83). In a point prevalence survey among 4 Nigerian hospitals only 4.1% surgical prophylaxis was in tandem with institutional guidelines (84). According to one African study prophylaxis for more than 24 hours for most surgical indications does not prevent development of postoperative infections compared with surgical

prophylaxis for 24 hours or less, but increases the risk of antimicrobial resistance, elevated odds of acute kidney injury coupled with *Clostridium difficile* infestation (75). Inappropriate surgical prophylaxis entails use of broad spectrum agents, like in our study use of ceftriaxone, and prolonged duration> 24 hours. Duplicate doses are only advocated if blood loss is more than 2 liters during the procedure, hypotension occurs or if surgery goes on for more than thrice the half-life of antimicrobial administered. All these can lead to resistance and increased costs. There is also an emphasis from reports that the most of irrational antibiotic prescriptions in surgical units are due to inappropriate prophylaxis (69).

In our study generic prescribing was done 80% of the times. The rest 20% were prescribed in their brand names. All medicines prescribed were from the essential medicine list. WHO optimal values for generic prescribing is 100% as well as 100% for prescribing from the essential medicine list. Almost similar findings were observed in an Ethiopian study where 97% of the drugs were prescribed using their generic name while 92% were from the Ethiopian Essential Medicine List (85). In a study in four governmental hospitals at United Arab Emirates (UAE) 100% was prescribed from the essential medicine list for all hospitals surveyed as per WHO recommendations. In India 90.3% were from the essential list while in Nepal only 42.3% was from essential medicine list (86). In a Tanzanian study, East Africa, 96.7% were prescribed from essential medicine list while generic prescribing was at 95.7% (87). Sub-optimal generic prescribing was noted in North west Nigeria where only 57% antimicrobials were prescribed using their generic names (71). Some prescribers use brand names due to pressure from medical representatives. Economic gains are usually the motivation at the expense of the patient. Brand prescribing is expensive therefore bad practice. Some clinicians may be unaware of the dangers associated with it for example It can also lead to adverse drug events where look alike or sound alike medicines are confused. Strict regulation and oversight should be done by the medicines and therapeutics committee to ensure prescribing by generic name. Prescribing audits should also be encouraged time to time.

The proportion of patients with pneumonia who received antibiotic treatment as recommended in the treatment guidelines was only 40%. None of the paediatric patients got dispersible amoxicillin which is the recommended first line treatment for pneumonia in this population. In a systematic review in Indian children aged below 5 years, oral antibiotics may be used in children with tachypnea and chest indrawing but who do not have signs of severe pneumonia (88). Most patients with pneumonia were started intravenous therapy. When a patient reaches clinical stability switch to orals should be considered. Less severe pneumonia is treated for 5 days while 7 days is permissible for more severe cases. Biomarkers are then utilized to guide on duration of antibiotic use (82). Many clinicians avoid

oral antibiotics because of greater faith in intravenous administration. Secondly most paediatric patients had already been on amoxil prior to admission. Regulatory framework needs to really look into over the counter sale of antimicrobials without definitive diagnosis. Studies on the proportion of antimicrobials sold without prescriptions should be done and such outlets deregistered.

Out of the sampled 185 records there were only 7 culture and sensitivity requests (3.8%). Similarly, in a point prevalence survey in Botswana, culture and sensitivity was rarely requested and mostly in specialized hospitals (73). In Ghana only 14 out of 382 patients on antibiotics (4%) had a biomarker test done (80). This compares poorly to a study done in The Gambia where approximately 50% participants managed with antibiotics had at least one biomarker test requested. Empirical antibiotic use was very common and clinical judgement was very rampant especially among neonatal admissions. Laboratory utilization for microbiology is very limited at Mbagathi Hospital. This may be due to unavailability of the services, delays in processing results, clinical suspicions of septicemia warranting immediate antimicrobial use. Molecular methods of testing can be adopted which may be cheaper and cost effective to the patients.

5.2 Strengths and Limitations of the Study

The use of a standardized protocol is a big strength for this study. This allows for comparability nationally and internationally. Since it was a retrospective study it had several limitations. The small number of patients hence caution is to be observed while generalizing the results. The study was done over three weeks therefore a different pattern could also have been noted had the study period been prolonged over other months or seasons.

This study did not measure severity of illness hence it was not feasible to relate drug use patterns with severity of patients sicknessnesses. The quality of the records was also poor and lots of observations had to be done since the study design did not allow for interviews. Nevertheless it is a feasible design for surveillance in limited resource settings since this data is beneficial and pin-points prevailing antimicrobial prescribing practices in Mbagathi Hospital.

5.3 Conclusion

This prevalence point study found several areas of concern regarding antimicrobial use. Increased rates of antimicrobial use both prior to hospitalization as well as during admission were observed. Of

note was the high prevalence (78.9%) of antimicrobial use. This was almost three times higher compared to WHO optimal value of 30%. Ceftriaxone was extensively prescribed in this study.

The commonest indication for antimicrobial use in our study was pneumonia. Other top indications included neonatal sepsis, tuberculosis and prophylaxis for obstetric gynecology surgery.

Adherence to guidelines was a great concern especially in surgical prophylaxis where all the patients received doses lasting more than 24 hours as opposed to the recommended WHO permissible less than 24 hours. Only 40% of the patients receiving pneumonia treatment adhered to the standard treatment guidelines and paediatric protocols on pneumonia treatment.

Culture and sensitivity was rarely requested. Only seven patients out of the sampled 185 patients had a culture and sensitivity requested. Patient management was largely empiric.

5.4 Recommendations

5.4.1 Recommendations for practice

All hospitals and health facilities should have antimicrobial stewardship committees to assist in judicious antimicrobial use. The hospital pharmacist in-charge should set up such a committee which should have representation from all members of the hospital medicines and therapeutics team. More data is needed on the cost and outcomes of antimicrobial stewardship programmes (ASPs) for decision makers to make a strong case for venturing in ASPs since there are other competing preferences to invest in. Such data in middle and low income countries is unavailable (89)

The antimicrobial stewardship committee should make it a policy in the hospital to conduct culture and sensitivity testing before commencing antimicrobial therapy. The hospital should facilitate development of appropriate guidelines recommending targeted therapy guided by culture and sensitivity results.

Hospital medicine and therapeutics committee chair should assign continuous medical education sessions touching on proper prescribing habits. This include prescribers sensitization to indicate antimicrobial treatment frequency, duration and stop review. Dangers of missed doses should be emphasized. Attention could also be directed on facilitating intravenous to oral switch of antimicrobials as well as focus on improving adherence to surgical prophylaxis guidelines. This should form the orientation package for all interns and newly employed health care workers.

5.4.2 Recommendations for policy

Government needs to empower the drug regulatory authority to carry out its mandate and enforce illegal practice of buying antimicrobials without a prescription.

Continuous medical education by the national and county medicines and therapeutics committee to educate and supervise prescribers on rational use of antimicrobials .

Special attention could be directed at reducing overall use of ceftriaxone in the hospital when possible and this should be taken up by the hospital medicine and therapeutics committees.

Pharmacist Interventions on antimicrobial prescriptions may be effective in enhancing appropriate use of antimicrobials, reducing their toxicity, reducing the use of special-vigilance drugs and reducing overall antimicrobial cost. Hospital management teams should ensure that all ward rounds have a pharmacist in the team all the time (77).

This data forms a very good indication of antimicrobial use in public facilities in Nairobi county and policy makers could use it for formulating policies and guidelines to improve antimicrobial use.

5.4.3 Recommendations for future research

Arising from this study the following are suggestions for future research.

1. Our study could not identify antimicrobial resistance patterns because of the few number of culture and sensitivity tests ordered. A study should therefore be conducted to determine resistance patterns so as to develop an antibiogram for the facility.
2. We found that culture and sensitivity testing was not routinely done. This could be avoided by adoption of molecular techniques of identification of positive organisms and their antimicrobial susceptibility . A cost effectiveness study comparing molecular diagnostics with the current culture and sensitivity practices is also highly recommended.
3. A follow up study to quantify extent of economic burden due to antimicrobial resistance is also recommended.

REFERENCES

1. Selcuk A, Yap KZ, Wong CL, Yang JX, Yong PC, Chan SY, et al. A Point Prevalence Study of Antimicrobial Use and Practice Among Nursing Homes in Singapore. Drugs Aging. 2019 Jun;36(6):559–70.

2. Ofori-Asenso R, Brhlikova P, Pollock AM. Prescribing indicators at primary health care centers within the WHO African region: a systematic analysis (1995–2015). BMC Public Health. 2016 Aug 22;16(1):724.

3. World Health Organization, editor. Antimicrobial resistance: global report on surveillance. Geneva, Switzerland: World Health Organization; 2014. 232 p.

4. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathog Glob Health. 2015 Oct 3;109(7):309–18.

5. Schellack N, Meyer JC, Kruger D, Bennie M, Kurdi A, Godman B. A countrywide point prevalence study in South Africa – using technology to determine use and appropriateness. In: 4th Training Workshop and Symposium MURIA Group [Internet]. 2018 [cited 2018 Jul 20]. Available from: https://strathprints.strath.ac.uk/64474/

6. Gharbi M, Doerholt K, Vergnano S, Bielicki JA, Paulus S, Menson E, et al. Using a simple point-prevalence survey to define appropriate antibiotic prescribing in hospitalised children across the UK. BMJ Open. 2016 Nov 1;6(11):e012675.

7. Massele A, Tiroyakgosi C, Matome M, Desta A, Muller A, Paramadhas BDA, et al. Research activities to improve the utilization of antibiotics in Africa. Expert Rev Pharmacoecon Outcomes Res. 2017 Jan 2;17(1):1–4.

8. Kenya-AMR-Containment-Policy-_Final_April.pdf [Internet]. [cited 2020 Mar 21]. Available from: http://www.health.go.ke/wp-content/uploads/2017/04/Kenya-AMR-Containment-Policy-_Final_April.pdf

9. Laxminarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradit N, et al. Antibiotic resistance—the need for global solutions. Lancet Infect Dis. 2013 Dec 1;13(12):1057–98.

10. Versporten A, Bielicki J, Drapier N, Sharland M, Goossens H, Calle GM, et al. The Worldwide Antibiotic Resistance and Prescribing in European Children (ARPEC) point prevalence survey: developing hospital-quality indicators of antibiotic prescribing for children. J Antimicrob Chemother. 2016 Apr 1;71(4):1106–17.

11. Lawes T, Lopez-Lozano J-M, Nebot CA, Macartney G, Subbarao-Sharma R, Dare CR, et al. Effects of national antibiotic stewardship and infection control strategies on hospital-associated and community-associated meticillin-resistant Staphylococcus aureus infections across a region of Scotland: a non-linear time-series study. Lancet Infect Dis. 2015 Dec;15(12):1438–49.

12. Davey P, Brown E, Charani E, Fenelon L, Gould IM, Holmes A, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev. 2013 Apr 30;(4):CD003543.

13. Ventola CL. The Antibiotic Resistance Crisis. Pharm Ther. 2015 Apr;40(4):277–83.

14. Muyu G, Mbakaya C, Makokha A. Out-Patient Prescribing Practices at Mbagathi District Hospital-Nairobi County. East Afr Med J. 2013;9.

15. Gandra S, Singh SK, Jinka DR, Kanithi R, Chikkappa AK, Sharma A, et al. Point Prevalence Surveys of Antimicrobial Use among Hospitalized Children in Six Hospitals in India in 2016. Antibiotics. 2017 Sep 13;6(3):19.

16. Momanyi L, Opanga S, Nyamu D, Oluka M, Kurdi A, Godman B. Antibiotic prescribing patterns at a leading referral hospital in Kenya : a point prevalence survey. 2019 [cited 2019 May 20]; Available from: https://core.ac.uk/reader/195294679

17. Okoth C, Opanga S, Okalebo F, Oluka M, Kurdi AB, Godman B. Point prevalence survey of antibiotic use and resistance at a referral hospital in Kenya: findings and implications. Hosp Pract. 2018 May 27;46(3):128–36.

18. Antimicrobials Fact Sheet [Internet]. [cited 2020 Mar 21]. Available from: http://npic.orst.edu/factsheets/antimicrobials.html

19. WHO Global Strategy for Containment of Antimicrobial Resistance. :105.

20. Analysis Of Antimicrobial Usage Pattern: A Retrospective Observational Study | International Journal Of Pharmaceutical Sciences And Research [Internet]. [cited 2019 Jun 20]. Available from: http://ijpsr.com/bft-article/analysis-of-antimicrobial-usage-pattern-a-retrospective-observational-study/?view=fulltext

21. Chaw PS, Schlinkmann KM, Raupach-Rosin H, Karch A, Pletz MW, Huebner J, et al. Antibiotic use on paediatric inpatients in a teaching hospital in the Gambia, a retrospective study. Antimicrob Resist Infect Control. 2018 Jul 16;7(1):82.

22. Pont LG, Morgan TK, Williamson M, Haaijer FM, van Driel ML. Validity of prescribing indicators for assessing quality of antibiotic use in Australian general practice. Int J Pharm Pract. 2017 Feb;25(1):66–74.

23. Bairy LK, Nayak V, A A, Kunder SK. Advances in pharmacovigilance initiatives surrounding antimicrobial resistance-Indian perspective. Expert Opin Drug Saf. 2016 Aug 2;15(8):1055–62.

24. Kuper KM. Learning Objectives 1. Discuss the benefi ts of antibiotic streamlining.

25. Goo RAS, Chu CH, Yoneda MK, Ma CS. The Daniel K. Inouye College of Pharmacy Scripts. Hawaii J Med Public Health. 2016 Jul;75(7):208–11.

26. Kelesidis T, Falagas ME. Substandard/Counterfeit Antimicrobial Drugs. Clin Microbiol Rev. 2015 Apr;28(2):443–64.

27. Ayukekbong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: causes and control strategies. Antimicrob Resist Infect Control. 2017 May 15;6(1):47.

28. Leopold SJ, van Leth F, Tarekegn H, Schultsz C. Antimicrobial drug resistance among clinically relevant bacterial isolates in sub-Saharan Africa: a systematic review. J Antimicrob Chemother. 2014 Sep 1;69(9):2337–53.

29. Ngigi CK. Self Medication With Antibiotics Prior To Seeking Treatment Among Adult Patients Attending Outpatient Department At Gatundu Sub-County Hospital, Kiambu County, Kenya. :83.

30. Misuse of antibiotics in farm animals needs to stop | World Animal Protection [Internet]. [cited 2020 Mar 28]. Available from: https://www.worldanimalprotection.or.ke/blogs/misuse-antibiotics-farm-animals-needs-stop

31. Hay SI, Rao PC, Dolecek C, Day NPJ, Stergachis A, Lopez AD, et al. Measuring and mapping the global burden of antimicrobial resistance. BMC Med. 2018 Jun 4;16:78.

32. Chitsaz M, Brown MH. The role played by drug efflux pumps in bacterial multidrug resistance. Essays Biochem. 2017 Mar 3;61(1):127–39.

33. Founou RC, Founou LL, Essack SY. Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. PLOS ONE. 2017 Dec 21;12(12):e0189621.

34. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf. 2014 Dec;5(6):229–41.

35. Tadesse BT, Ashley EA, Ongarello S, Havumaki J, Wijegoonewardena M, González IJ, et al. Antimicrobial resistance in Africa: a systematic review. BMC Infect Dis. 2017 Sep 11;17(1):616.

36. Jasovský D, Littmann J, Zorzet A, Cars O. Antimicrobial resistance—a threat to the world's sustainable development. Ups J Med Sci. 2016 Jul 2;121(3):159–64.

37. Whaley SG, Berkow EL, Rybak JM, Nishimoto AT, Barker KS, Rogers PD. Azole Antifungal Resistance in Candida albicans and Emerging Non-albicans Candida Species. Front Microbiol [Internet]. 2017 [cited 2018 Oct 15];7. Available from: https://www.frontiersin.org/articles/10.3389/fmicb.2016.02173/full

38. Workneh M, Katz MJ, Lamorde M, Cosgrove SE, Manabe YC. Antimicrobial Resistance of Sterile Site Infections in Sub-Saharan Africa: A Systematic Review. Open Forum Infect Dis [Internet]. 2017 Oct 1 [cited 2018 Jul 28];4(4). Available from: https://academic.oup.com/ofid/article/4/4/ofx209/4356807

39. Ntirenganya C, Manzi O, Muvunyi CM, Ogbuagu O. High Prevalence of Antimicrobial Resistance Among Common Bacterial Isolates in a Tertiary Healthcare Facility in Rwanda. Am J Trop Med Hyg. 2015 Apr 1;92(4):865–70.

40. Omolo MJ, Pole L, Mwangi I, Kimani J, Anzala O, Oloo J, et al. P2.30 Survey of antimicrobial resistance in clinical neisseria gonorrhoeae isolated over a period of four years in nairobi – kenya. Sex Transm Infect. 2017 Jul 1;93(Suppl 2):A81–2.

41. Ampaire L, Muhindo A, Orikiriza P, Mwanga-Amumpaire J, Bebell L, Boum Y. A review of antimicrobial resistance in East Africa. Afr J Lab Med. 2016 Sep 15;5(1):6.

42. Onyango HA, Ngugi C, Maina J, Kiiru J. Urinary Tract Infection among Pregnant Women at Pumwani Maternity Hospital, Nairobi, Kenya: Bacterial Etiologic Agents, Antimicrobial Susceptibility Profiles and Associated Risk Factors. Adv Microbiol. 2018 Mar 21;08:175.

43. Laxminarayan R, Matsoso P, Pant S, Brower C, Røttingen J-A, Klugman K, et al. Access to effective antimicrobials: a worldwide challenge. The Lancet. 2016 Jan;387(10014):168–75.

44. Ahmed SA, Bariş E, Go DS, Lofgren H, Osorio-Rodarte I, Thierfelder K. Assessing the Global Economic and Poverty Effects of Antimicrobial Resistance [Internet]. The World Bank; 2017 [cited 2018 Aug 4]. (Policy Research Working Papers). Available from: http://elibrary.worldbank.org/doi/book/10.1596/1813-9450-8133

45. Founou RC, Founou LL, Essack SY. Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. PLoS ONE [Internet]. 2017 Dec 21 [cited 2018 Jul 22];12(12). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5739407/

46. Gafter-Gvili A, Fraser A, Paul M, Vidal L, Lawrie TA, van de Wetering MD, et al. Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy. Cochrane Database Syst Rev. 2012 Jan 18;1:CD004386.

47. Kraker MEA de, Stewardson AJ, Harbarth S. Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050? PLOS Med. 2016 Nov 29;13(11):e1002184.

48. Frieri M, Kumar K, Boutin A. Antibiotic resistance. J Infect Public Health. 2017 Jul 1;10(4):369–78.

49. Stenehjem E, Hyun DY, Septimus E, Yu KC, Meyer M, Raj D, et al. Antibiotic Stewardship in Small Hospitals: Barriers and Potential Solutions. Clin Infect Dis. 2017 Aug 15;65(4):691–6.

50. Lee C-R, Cho IH, Jeong BC, Lee SH. Strategies to Minimize Antibiotic Resistance. Int J Environ Res Public Health. 2013 Sep;10(9):4274–305.

51. Spika J, Rud E. Immunization as a tool to combat antimicrobial resistance. Can Commun Dis Rep. 2015 Nov 19;41(Suppl 5):7–10.

52. Versporten A, Drapier N, Zarb P, Caniaux I, Gros M-F, Miller M, et al. The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): A Worldwide Antimicrobial Web-Based Point Prevalence Survey. Open Forum Infect Dis [Internet]. 2015 Dec 1 [cited 2018 Oct 24];2(suppl_1). Available from: https://academic.oup.com/ofid/article/2/suppl_1/147/2634706

53. Berendonk TU, Manaia CM, Merlin C, Fatta-Kassinos D, Cytryn E, Walsh F, et al. Tackling antibiotic resistance: the environmental framework. Nat Rev Microbiol. 2015 Mar 30;13:310.

54. Sticchi C, Alberti M, Artioli S, Assensi M, Baldelli I, Battistini A, et al. Regional point prevalence study of healthcare-associated infections and antimicrobial use in acute care hospitals in Liguria, Italy. J Hosp Infect. 2018 May 1;99(1):8–16.

55. Vandael E, Latour K, Goossens H, Magerman K, Drapier N, Catry B, et al. Point prevalence survey of antimicrobial use and healthcare-associated infections in Belgian acute care hospitals: results of the Global-PPS and ECDC-PPS 2017. Antimicrob Resist Infect Control. 2020 Jan 13;9(1):13.

56. Zingg W, Metsini A, Gardiol C, Balmelli C, Behnke M, Troillet N, et al. Antimicrobial use in acute care hospitals: national point prevalence survey on healthcare-associated infections and antimicrobial use, Switzerland, 2017. Eurosurveillance. 2019 Aug 15;24(33):1900015.

57. Korinteli IG, Mchedlishvili I, Javakhadze M, Versporten A, Goossens H, Phagava H, et al. The Global Point Prevalence Survey (Pps) Of Antimicrobial Use And Antimicrobial Resistance Among Hospitalized Children In Georgia. Georgian Med News. 2019;72–5.

58. mds3-ch28-investigatinguse-mar2012.pdf [Internet]. [cited 2020 Apr 8]. Available from: https://www.msh.org/sites/msh.org/files/mds3-ch28-investigatinguse-mar2012.pdf

59. Mendelson M, Røttingen J-A, Gopinathan U, Hamer DH, Wertheim H, Basnyat B, et al. Maximising access to achieve appropriate human antimicrobial use in low-income and middle-income countries. The Lancet. 2016 Jan;387(10014):188–98.

60. Mao W, Vu H, Xie Z, Chen W, Tang S. Systematic Review on Irrational Use of Medicines in China and Vietnam. PLOS ONE. 2015 Mar 20;10(3):e0117710.

61. Atif M, Azeem M, Sarwar MR, Shahid S, Javaid S, Ikram H, et al. WHO/INRUD prescribing indicators and prescribing trends of antibiotics in the Accident and Emergency Department of Bahawal Victoria Hospital, Pakistan. SpringerPlus [Internet]. 2016 Nov 8 [cited 2018 Nov 14];5(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5099312/

62. Global-PPS-2019-protocol.pdf [Internet]. [cited 2019 Jan 25]. Available from: http://www.global-pps.com/wp-content/uploads/2019/01/Global-PPS-2019-protocol.pdf

63. Versporten A, Zarb P, Caniaux I, Gros M-F, Drapier N, Miller M, et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. Lancet Glob Health. 2018 Jun;6(6):e619–29.

64. WHO | The Anatomical Therapeutic Chemical Classification System with Defined Daily Doses (ATC/DDD) [Internet]. WHO. [cited 2018 Aug 19]. Available from: http://www.who.int/classifications/atcddd/en/

65. How to Investigate Drug Use in Health Facilities: Selected Drug Use Indicators - EDM Research Series No. 007 [Internet]. [cited 2019 Jul 4]. Available from: https://apps.who.int/medicinedocs/en/d/Js2289e/

66. c0d3675787d651dedbf4a0edfc9a2898.pdf [Internet]. [cited 2019 Jul 4]. Available from: https://www.psk.or.ke/public/uploads/file/c0d3675787d651dedbf4a0edfc9a2898.pdf

67. s21000en.pdf [Internet]. [cited 2019 Jul 4]. Available from: http://apps.who.int/medicinedocs/documents/s21000en/s21000en.pdf

68. Kenya_Malaria_Tx_Guideline_2010.pdf [Internet]. [cited 2019 Jul 4]. Available from: https://www.thecompassforsbc.org/sites/default/files/project_examples/Kenya_Malaria_Tx_Guideline_2010.pdf

69. Bozkurt F, Kaya S, Tekin R, Gulsun S, Deveci O, Dayan S, et al. Analysis of antimicrobial consumption and cost in a teaching hospital. J Infect Public Health. 2014 Mar 1;7(2):161–9.

70. Kiguba R, Karamagi C, Bird SM. Extensive antibiotic prescription rate among hospitalized patients in Uganda: but with frequent missed-dose days. J Antimicrob Chemother. 2016 Jun 1;71(6):1697–706.

71. Abdu-Aguye SN, Haruna A, Shehu A, Labaran KS. An assessment of antimicrobial prescribing at a tertiary hospital in north-western Nigeria. Afr J Pharmacol Ther [Internet]. 2016 Dec 22 [cited 2019 Jun 17];5(4). Available from: http://journals.uonbi.ac.ke/ajpt/article/view/1541

72. A Study Of Antimicrobial Prescription Pattern In The Ear, Nose And Throat Infections At A Tertiary Care Teaching Hospital, Rajkot | International Journal Of Pharmaceutical Sciences And Research [Internet]. [cited 2019 Jul 12]. Available from: http://ijpsr.com/bft-article/a-study-of-antimicrobial-prescription-pattern-in-the-ear-nose-and-throat-infections-at-a-tertiary-care-teaching-hospital-rajkot/?view=fulltext

73. Paramadhas BDA, Tiroyakgosi C, Mpinda-Joseph P, Morokotso M, Matome M, Sinkala F, et al. Point prevalence study of antimicrobial use among hospitals across Botswana; findings and implications. Expert Rev Anti Infect Ther. 2019 Jul 3;17(7):535–46.

74. Felipe S de M, Juciene de JB da S, Ana LMA, Isabella de MM da S. Using light emitting diodes at 450 nm for in vitro treatment of water intended for human consumption. Afr J Microbiol Res. 2018 Aug 7;12(29):681–7.

75. Versporten A, Zarb P, Caniaux I, Gros M-F, Drapier N, Miller M, et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey. Lancet Glob Health. 2018 Jun 1;6(6):e619–29.

76. Yusuf E, Versporten A, Goossens H. Is there any difference in quality of prescribing between antibacterials and antifungals? Results from the first global point prevalence study (Global PPS) of antimicrobial consumption and resistance from 53 countries. J Antimicrob Chemother. 2017 Oct 1;72(10):2906–9.

77. Kebede HK, Gesesew HA, Woldehaimanot TE, Goro KK. Antimicrobial use in paediatric patients in a teaching hospital in Ethiopia. PLOS ONE. 2017 Mar 6;12(3):e0173290.

78. Berhe YH, Amaha ND, Ghebrenegus AS. Evaluation of ceftriaxone use in the medical ward of Halibet National Referral and teaching hospital in 2017 in Asmara, Eritrea: a cross sectional retrospective study. BMC Infect Dis. 2019 May 24;19(1):465.

79. Durham SH, Wingler MJ, Eiland LS. Appropriate Use of Ceftriaxone in the Emergency Department of a Veteran's Health Care System. J Pharm Technol JPT Off Publ Assoc Pharm Tech. 2017 Dec;33(6):215–8.

80. Bediako-Bowan AAA, Owusu E, Labi A-K, Obeng-Nkrumah N, Sunkwa-Mills G, Bjerrum S, et al. Antibiotic use in surgical units of selected hospitals in Ghana: a multi-centre point prevalence survey. BMC Public Health. 2019 Jun 21;19(1):797.

81. Shimels T, Bilal AI, Mulugeta A. Evaluation of Ceftriaxone utilization in internal medicine wards of general hospitals in Addis Ababa, Ethiopia: a comparative retrospective study. J Pharm Policy Pract. 2015 Nov 9;8(1):26.

82. Prina E, Ranzani OT, Torres A. Community-acquired pneumonia. The Lancet. 2015 Sep 12;386(9998):1097–108.

83. Turnidge JD, Thursky K, Chen CS, McNeil VR, Wilkinson IJ. Antimicrobial use in Australian hospitals: how much and how appropriate? Med J Aust. 2016;205(S10):S16–20.

84. Oduyebo OO, Olayinka AT, Iregbu KC, Versporten A, Goossens H, Nwajiobi-Princewill PI, et al. A point prevalence survey of antimicrobial prescribing in four Nigerian Tertiary Hospitals. Ann Trop Pathol. 2017 Jan 1;8(1):42.

85. Bilal AI, Osman ED, Mulugeta A. Assessment of medicines use pattern using World Health Organization's Prescribing, Patient Care and Health facility indicators in selected health facilities in eastern Ethiopia. BMC Health Serv Res. 2016 Apr 23;16(1):144.

86. Mahmood A, Elnour AA, Ali AAA, Hassan NAGM, Shehab A, Bhagavathula AS. Evaluation of rational use of medicines (RUM) in four government hospitals in UAE. Saudi Pharm J. 2016 Mar 1;24(2):189–96.

87. Irunde H, Minzi O, Moshiro C. Assessment of Rational Medicines Prescribing in Healthcare Facilities in Four Regions of Tanzania. J Pharm Pract Community Med. 2017 Oct 15;3(4):225–31.

88. Lodha R, Randev S, Kabra SK. Oral antibiotics for community–acquired pneumonia with chest-indrawing in children aged below five years: A Systematic Review. Indian Pediatr. 2016 Jun 1;53(6):489–95.

89. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review. Antimicrob Resist Infect Control. 2019 Feb 12;8(1):35.

90. Mas-Morey P, Ballesteros-Fernández A, Sanmartin-Mestre E, Valle M. Impact of clinical pharmacist intervention on antimicrobial use in a small 164-bed hospital. Eur J Hosp Pharm. 2018 Mar 1;25(e1):e46–51.

APPENDICES

Appendix 1. Global Point Prevalence Survey (GLOBAL-PPS) Ward Form (62)

Global Point Prevalence Survey

Please fill in one form for each ward included in the PPS

Date of survey (dd/mm/year)	_____/_____/_____	
Person completing form (Auditor code)		
Hospital name		
Ward Name		
Department Type: Place a tick against the type of department	**Paediatric departments:** **PMW** (Paediatric Medical Ward) **HO-PMW** (Haematology-Oncology PMW) **T-PMW** (Transplant (BMT/Solid) PMW) **PSW** (Paediatric Surgical Ward) **PICU** (Paediatric Intensive Care Unit)	**Adult departments:** **AMW** (Adult Medical Ward) **HO-AMW** (Haematology-Oncology AMW) **T-AMW** (Transplant (BMT/solid) AMW) **P-AMW** (Pneumology AMW) **ASW** (Adult Surgical Ward)

	Neonatal departments: **NMW** (Neonatal Medical Ward) **NICU** (Neonatal Intensive Care Unit)		**AICU** ([Adult] Intensive Care Unit)
Mixed Department	**Yes** **No**		
Activity: Tick as appropriate. In case of mixed departments, tick all the encountered activities/specialties	**Medicine**	**Surgery**	**Intensive Care**
Total number of admitted patients on the ward present at 8.00 am on day of PPS split up by activity. For mixed departments, fill the total number of patients corresponding to each of the encountered activities.			
Total number of beds on the ward present at 8:00 am on day of PPS split up by activity.			

For mixed departments fill in the total number of beds corresponding to each of the encountered activities.			

Include only patients admitted before 8am on the day of study

Appendix 2 . Antimicrobial Use Point Prevalence Survey - Patient Data collection form

Participant Code

_____

Research Assistant code _____

Date of data collection

_____

Name of the Hospital Mbagathi District Hospital (MDH)

Name of the ward group: surgery, medical, paediatrics, maternity, nursery

Ward Name

Inpatient file number (IP)/ code

_____

Admission date

_____

Age Group Adult (≥ 18 Years)
Child (≥ 1 and ≤ 17 Years)
Infant (≥ 1 and ≤ 11 Months)
Neonate (≤ 28 Days)

(For adults, state in Years (e.g. 34))

_____

(For children, state in Years (e.g. 14))

_____

(For infants, state in Months (e.g. 9))

_____

(For neonates, state in days (e.g. 16))

Sex Male Female

Any hospitalization in the last 90 days, excluding current hospitalization

Yes No Not documented

Was participant transferred from another hospital for this admission?

Yes No Not documented

Any catheterization on participant during this admission? Yes No

Urinary ,

Peripheral (IV Cannula)

Central

Peritoneal

Haemodialysis

Unspecified

Other

Not documented

Other, Specify_____

Any intubation on participant during current admission? Yes No

Endotracheal

Gastro duodenal

Tracheostomy

Nasogastric/ Feeding

Suction

Unspecified

Not documented

Other, Specify _____

Has the participant undergone any surgery during this admission? Yes No

If yes, which type (most recent surgery)?	Invasive Minimally Invasive Procedure Non-Invasive
Was a malaria test done?	Yes , No
What was the result?	Positive , Negative
Is the participant malnourished/wasted?	Yes No Undocumented
HIV Status	Positive Negative Undocumented
Is the participant on HAART?	Yes No Undocumented
Is the participant on TB treatment?	Yes No

Is antimicrobial use prior to current admission documented (within past 90 days)?

Yes No

How many antimicrobials were used before current admission (within 90 days)? 1, 2, 3, 4, 5

Antimicrobial 1

ATC Code for Antimicrobial 1 (*See Appendix 5*)

Duration of use indicated Yes No

Duration (Number of days on any antimicrobial)

Antimicrobial 2

ATC Code for Antimicrobial 2 (*See Appendix 5*)

Duration of use indicated Yes No

Duration (Number of days on any antimicrobial)

Antimicrobial 3

ATC Code for Antimicrobial 3 (*See Appendix 5*)

Duration of use indicated Yes No

Duration (Number of days on any antimicrobial)

How many antimicrobials have been used and already stopped during current admission 1, 2, 3, 4, 5

ATC Code for Antimicrobial 1 (*See Appendix 5*)

Duration of use indicated Yes no

Duration (Number of days on the antimicrobial)

ATC Code for Antimicrobial 2 (*See Appendix 5*)

Duration of use indicated Yes no

Duration (Number of days on the antimicrobial)

ATC Code for Antimicrobial 3 (*See Appendix 5*)

Duration of use indicated Yes no

Duration (Number of days on the antimicrobial)

SECTION 2

To be completed only for participant currently on Antimicrobial therapy other than for TB (Do not proceed further if the participant is treated only for TB)

Indications for which antimicrobials were given

Number of indications
1
2
3
4
5

Indication Code 1 (*See Appendix 4*)

Type of indication
Community Acquired Infection
Hospital Acquired Infection
Not documented
Other, specify _____

Indication Code 2 (*See Appendix 4*)

Type of indication

Community Acquired Infection

Hospital Acquired Infection

Not documented

Other, specify _____

Indication Code 3 (*See Appendix 4*

Type of indication

Community Acquired Infection

Hospital Acquired Infection

Not documented

Other, specify _____

Indication Code 4 (*See Appendix 4*)

Type of indication

Community Acquired Infection

Hospital Acquired Infection

Not documented

Other, specify _____

Indication Code 5 (*See Appendix 4*

Type of indication

Community Acquired Infection

Hospital Acquired Infection

Not documented

Other, specify _____

Number of antimicrobials given

Number of antimicrobials participant is on

1

2

3

4

5

Antimicrobial 1

ATC code for Antimicrobial: 1 (*See Appendix 5*)

Start date

_____

Dose per administration _____

Unit of measure

- g
- mg
- IU
- MU
- Not documented
- Other, specify _____

Route of administration
- Oral (PO)
- Intravenous (IV)
- Intramuscular (IM)
- Other, specify _____

Frequency of administration
- STAT dose
- Once a day (OD)
- Twice a day (BID)
- Thrice a day (TID)
- Four times a day (QID)
- Every 4 hours (Q4H)
- Other, specify _____

Is a stop/review date for the antimicrobial documented? Yes No

Is the antimicrobial being used for Prophylaxis? Yes No Not documented

Was it Medical or Surgical prophylaxis? Medical Prophylaxis Surgical Prophylaxis

Prophylaxis duration One single dose

Multiple doses within 24 hours

More than 1 day

For which indication/diagnosis is the antimicrobial being given?

Indication 1

Indication 2

Indication 3

Indication 4

Indication 5

Not documented

(These are the indications selected earlier)

Was the antimicrobial prescribed using the INN (generic name)? Yes No

Is the antimicrobial on the Kenya Essential Medicines List (KEML)? Yes No

No. of missed doses since antimicrobial started _____

(Count from the date of initiation to current date how many doses were missed and state it as simple count. If 6 doses missed capture as 6; if none state 0.)

Antimicrobial 2

ATC code for Antimicrobial 2: (*See Appendix 5*)

Start date

_____

Dose per administration

_____

Unit of measure g

mg

IU

MU

Not documented

Other, specify _____

Route of administration Oral (PO)

Intravenous (IV)

Intramuscular (IM)

Other, specify _____

Frequency of administration STAT dose

Once a day (OD)

Twice a day (BID)

Thrice a day (TID)

Four times a day (QID)

Every 4 hours (Q4H)

Other, specify _____

Is a stop/review date for the antimicrobial documented? Yes No

Is the antimicrobial being used for Prophylaxis? Yes No Not documented

Was it Medical or Surgical prophylaxis? Medical Prophylaxis Surgical Prophylaxis

Prophylaxis duration One single dose

Multiple doses within 24 hours

More than 1 day

For which indication/diagnosis is the antimicrobial being given?

Indication 1
Indication 2
Indication 3
Indication 4
Indication 5
Not documented
(These are the indications selected earlier)

Was the antimicrobial prescribed using the INN (generic name)? Yes No

Is the antimicrobial on the Kenya Essential Medicines List (KEML)? Yes No

No. of missed doses since antimicrobial started

_____

Antimicrobial 3

ATC code for Antimicrobial 3: (*See Appendix 5*)

Start date

_____

Dose per administration

_____

Unit of measure g

mg
IU
MU
Not documented
Other, specify _____

Route of administration Oral (PO)

Intravenous (IV)

Intramuscular (IM)

Other, specify _____

Frequency of administration

STAT dose

Once a day (OD)

Twice a day (BID)

Thrice a day (TID)

Four times a day (QID)

Every 4 hours (Q4H)

Other, specify _____

Is a stop/review date for the antimicrobial documented? Yes No

Is the antimicrobial being used for Prophylaxis? Yes No Not documented

Was it Medical or Surgical prophylaxis? Medical Prophylaxis Surgical Prophylaxis

Prophylaxis duration

One single dose

Multiple doses within 24 hours

More than 1 day

For which indication is the antimicrobial being given?

Indication 1

Indication 2

Indication 3

Indication 4

Indication 5

Not documented

(These are the indications selected earlier)

Was the antimicrobial prescribed using the INN (generic name)? Yes No

Is the antimicrobial on the Kenya Essential Medicines List (KEML)? Yes No

No. of missed doses since antimicrobial started

_____

Antimicrobial 4

ATC code for Antimicrobial 4 (*See Appendix 5*)

Start date

_____

Dose per administration

_____

Unit of measure g

mg

IU

MU

Not documented

Other, specify _____

Route of administration Oral (PO)

Intravenous (IV)

Intramuscular (IM)

Other, specify _____

Frequency of administration STAT dose

Once a day (OD)

Twice a day (BID)

Thrice a day (TID)

Four times a day (QID)

Every 4 hours (Q4H)

Other, specify _____

Is a stop/review date for the antimicrobial documented? Yes No

Is the antimicrobial being used for Prophylaxis? Yes No Not documented

Was it Medical or Surgical prophylaxis? Medical Prophylaxis Surgical Prophylaxis

Prophylaxis duration One single dose

Multiple doses within 24 hours

More than 1 day

For which indication/diagnosis is the antimicrobial being given?

Indication 1

Indication 2

Indication 3

Indication 4

Indication 5

Not documented

(These are the indications selected earlier)

Was the antimicrobial prescribed using the INN (generic name)? Yes No

Is the antimicrobial on the Kenya Essential Medicines List (KEML)? Yes No

No. of missed doses since antimicrobial started

_____

Antimicrobial 5

ATC code for Antimicrobial 5: (*See Appendix 5*)

Start date

_____

Dose per administration

_____

Unit of measure

g

mg

IU

MU

Not documented

Other, specify _____

Route of administration

Oral (PO)

Intravenous (IV)

Intramuscular (IM)

Other, specify _____

Frequency of administration

STAT dose

Once a day (OD)

Twice a day (BID)

Thrice a day (TID)

Four times a day (QID)

Every 4 hours (Q4H)

Other, specify _____

Is a stop/review date for the antimicrobial documented? Yes No

Is the antimicrobial being used for Prophylaxis? Yes No Not documented

Was it Medical or Surgical prophylaxis? Medical Prophylaxis Surgical Prophylaxis

Prophylaxis duration One single dose
Multiple doses within 24 hours
More than 1 day

For which indication/diagnosis is the antimicrobial being given?
Indication 1
Indication 2
Indication 3
Indication 4
Indication 5
Not documented
(These are the indications selected earlier)

Was the antimicrobial prescribed using the INN (generic name)? Yes No

Is the antimicrobial on the Kenya Essential Medicines List (KEML)? Yes No

No. of missed doses since antimicrobial started
_____

Culture Tests

Culture and Sensitivity (CST) ordered Yes No

How many culture tests were done during the current admission? 1 2 3

Culture Test 1

Which specimen was used Blood
Pus swab
Urine

Stool

Tracheal aspirate

Tissue

Cerebrospinal fluid

High vaginal swab(HVS)

Pleural fluid

Peritoneal fluid

Joint aspirate

Other, specify _____

Culture results available Yes No

Culture Test 2

Which specimen was used Blood

Pus swab

Urine

Stool

Tracheal aspirate

Tissue

Cerebrospinal fluid

High Vaginal Swab (HVS)

Pleural fluid

Peritoneal fluid

Joint aspirate

Other, specify _____

Culture results available Yes No

Culture Test 3

Which specimen was used Blood

Pus swab

Urine

Stool

Tracheal aspirate

Tissue

Cerebrospinal fluid

High Vaginal Swab (HVS)

Pleural fluid

Peritoneal fluid

Joint aspirate

Other, specify _____

Culture results available Yes No

Appendix 3. Diagnostic codes (what the clinician aims at treating) (62)**.**

Site	Codes	Examples
CNS	**Proph CNS**	Prophylaxis for CNS (neurosurgery, meningococcal)
	CNS	Infections of the **C**entral **N**ervous **S**ystem
EYE	**Proph EYE**	Prophylaxis for Eye operations
	EYE	Therapy for Eye infections e.g., Endophthalmitis
ENT	**Proph ENT**	Prophylaxis for **E**ar, **N**ose, **T**hroat (**Surgical or Medical prophylaxis=SP/MP**)
	ENT	Therapy for **E**ar, **N**ose, **T**hroat infections including mouth, sinuses, larynx
RESP	**Proph RESP**	Pulmonary surgery, prophylaxis for **Resp**iratory pathogens
	LUNG	Lung abscess including aspergilloma
	URTI	**U**pper **R**espiratory **T**ract viral **I**nfections including influenza but not ENT
	Bron	Acute **Bron**chitis or exacerbations of chronic bronchitis
	Pneu	**Pneu**monia or LRTI (lower respiratory tract infections)
	TB	Pulmonary TB (Tuberculosis)

CVS	**Proph CVS**	**C**ardiac or **V**ascular Surgery, endocarditis prophylaxis
	CVS	**C**ardio**v**ascular **S**ystem infections: endocarditis, endovascular prosthesis or device e.g. pacemaker, vascular graft
GI	**Proph GI**	Surgery of the **G**astro-**I**ntestinal tract, liver or biliary tree, GI prophylaxis in neutropaenic patients or hepatic failure
	GI	GI infections (salmonellosis, *Campylobacter*, parasitic, *C.difficile*, etc.)
	IA	**I**ntra-**A**bdominal sepsis including hepatobiliary, intra-abdominal abscess *etc*.
SSTBJ	**Proph BJ**	Prophylaxis for plastic or orthopaedic surgery (**B**one or **J**oint)
	SST	**S**kin and **S**oft Tissue: Cellulitis, wound including surgical site infection, deep soft tissue not involving bone e.g., infected pressure or diabetic ulcer, abscess
	BJ	**B**one/**J**oint Infections: Septic arthritis (including prosthetic joint), osteomyelitis
UTI	**Proph UTI**	Prophylaxis for urological surgery **(SP)** or recurrent **U**rinary **T**ract **I**nfection **(MP)**
	Cys	Lower UTI
	Pye	Upper UTI including catheter related urinary tract infection, pyelonephritis

GUOB	**Proph OBGY**	Prophylaxis for **Ob**stetric or **Gy**necological surgery
	OBGY	**Ob**stetric/**Gy**naecological infections, **S**exual **T**ransmitted **D**iseases (**STD**) in women
	GUM	**G**enito-**U**rinary **M**ales + Prostatitis, epididymo-orchitis, STD in men
No	**BAC**	Bacteremia with no clear anatomic site and no shock
defined	**SEPSIS**	Sepsis, sepsis syndrome or septic shock with no clear anatomic site
Site	**Malaria**	
(NDS)	**PUO**	**P**yrexia of **U**nknown **O**rigin - Fever syndrome with no identified source or site of infection
	PUO-HO	Fever syndrome in the non-neutropaenic **H**aematology–**O**ncology patient with no identified source of pathogen
	FN	**F**ever in the **N**eutropaenic patient
	LYMPH	Infection of the **lymph**atics as the primary source of infection e.g.suppurative

		lymphadenitis
	Other	Antibiotic prescribed with documentation for which there is no above diagnosis group
	MP-GEN	Drug is used as **M**edical **P**rophylaxis in **gen**eral, without targeting a specific site, e.g. antifungal prophylaxis during immunosuppression
	UNK	Completely **Unk**nown Indication
	PROK	Antimicrobial (e.g. erythromycin) prescribed for **Prok**inetic use
Neonatal	**MP-MAT**	Drug is used as **M**edical **P**rophylaxis for **MAT**ERNAL risk factors e.g. maternal prolonged rupture of membranes
	NEO-MP	Drug is used as **M**edical **P**rophylaxis for **NE**WBORN risk factors e.g. VLBW (Very Low Birth Weight) and IUGR (Intrauterine Growth Restriction)

Appendix 4. Indication Codes for antimicrobials given (62)

- **CNS** - refers to infections of the central nervous system(e.g. Meningitis, brain abscess)
- **EYE** - refers to eye infections, e.g. endophthalmitis
- **ENT** - refers Infections of ear, nose, throat, larynx and mouth (Upper respiratory tract excluding bronchus)
- **BRON** - Acute bronchitis or exacerbations of chronic bronchitis
- **PNEU** - Pneumonia (other than TB; if TB see below for different code)
- **CVS** - Cardiovascular infections: (e.g. endocarditis, vascular graft.)
- **GI** - Gastrointestinal infections (e.g. salmonellosis, antibiotic-associated diarrhoea)
- **IA** - Intra-abdominal sepsis (between diaphragm and pelvic floor) including hepatobiliary and peritoneal cavity infections
- **SST** - Soft tissue infections (e.g. cellulitis, wound, and deep soft tissue) not involving bone
- **BJ** - Bone and Joint Infections (e.g. septic arthritis, prosthetic joint infections, osteomyelitis...)
- **CYS** - Symptomatic lower urinary tract infection (urethra and bladder) e.g. cystitis
- **PYE** - Symptomatic upper urinary tract infection (ureter and kidney)e.g. pyelonephritis
- **ASB** - Asymptomatic bacteriuria (Presence of bacteria in urine without symptoms)
- **OBGY** - Obstetric or gynaecological infections (e.g. STDs in women, abortion related sepsis, post-partum sepsis etc...)
- **GUM** - Prostatitis, epididymo-orchitis, and STD in men
- **BAC** - Laboratory-confirmed bacteraemia (Positive blood culture with isolated bacteria)
- **CSEP** - Clinical sepsis (suspected bloodstream infection without lab confirmation/results are not available, no blood cultures collected or negative blood culture), excluding febrile neutropenia
- **FN** - Febrile neutropenia or other form of manifestation of infection in immunocompromised host, e.g. HIV, chemotherapy, etc., with no clear anatomical site

- **SIRS -** Systemic Inflammatory Response Syndrome with no clear anatomical site of infection.
- **UND** - Completely undefined; site with no systemic inflammation
- **NA** - Not applicable; for antimicrobial use other than treatment

Appendix 5. ATC codes for antimicrobials given (62)

Antimicrobial	**Code**	**Antimicrobial**	**Code**
Amikacin	J01GB06	Amoxicillin	J01CA04
Amoxicillin and enzyme inhibitor	J01CR02	Ampicillin, combinations	J01CA51
Artesunate	P01BE03	Artemether and Lumefantrine	P01BF01
Artesunate and Mefloquine	P01BF02	Artesunate and Amodiaquine	P01BF02
Albendazole	P02CA03	Mebendazole	P02CA01
Quinine	P01BC01	Azithromycin	J01FA10
Benzathinebenzylpenicillin	J01CE08	Benzyl penicillin	J01CE01
Cefaclor	J01DC04	Cefadroxil	J01DB05
Cefalexin	J01DB01	Cefepime	J01DE01
Cefixime	J01DD08	Cefazolin	J01DB04
Cefotaxime	J01DD01	Cefpodoxime	J01DD13
Ceftazidime	J01DD02	Ceftriaxone	J01DD04
Cefuroxime	J01DC02	Chloramphenicol	J01BA01
Ciprofloxacin	J01MA02	Clarithromycin	J01FA09
Cefoxitin	J01DC01	Cefprozil	J01DC10
Clindamycin	J01FF01	Cloxacillin	J01CF02
Doxycycline	J01AA02	Erythromycin	J01FA01
Flucloxacillin	J01CF05	Gentamicin	J01GB03
Griseofulvin	D01BA01	Imipenem and enzyme inhibitor	J01DH51
Kanamycin	A07AA08	Kanamycin	J01GB04

Levofloxacin	J01MA12	Linezolid	J01XX08
Meropenem	J01DH02	Metronidazole (oral, rectal)	P01AB01
Metronidazole (parenteral)	J01XD01	Minocycline	J01AA08
Moxifloxacin	J01MA14	Nalidixic acid	J01MB02
Nitrofurantoin	J01XE01	Norfloxacin	J01MA06
Nystatin	A07AA02	Ofloxacin	J01MA01
Ornidazole (oral)	P01AB03	Penicillins,combinations with other antibacterials	J01RA01
Rifampicin	J04AB02	Secnidazole	P01AB07
Secnidazole	P01AB07	Sulfadiazine	J01EC02
Sulfadiazine and trimethoprim	J01EE02	Sulfamethoxazole	J01EC01
Sulfamethoxazole and trimethoprim	J01EE01	Sulfonamides, combinations with other antibacterials (excl. trimethoprim)	J01RA02
Tigecycline	J01AA12	Tinidazole (oral, rectal)	P01AB02
Vancomycin (parenteral)	J01XA01		

Appendix 6. Letter of KNH-UON ERC approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/80

5th March, 2019

KENYATTA NATIONAL HOSPITAL APPROVED 05 MAR 2019 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Muyu Gratia
Reg. No.U51/7177/2017
Dept.of Pharmacology and Pharmacognosy
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Gratia

RESEARCH PROPOSAL: ANTIMICROBIAL USE PATTERNS IN MBAGATHI HOSPITAL – A POINT PREVALENCE SURVEY (P793/11/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 5th March 2019 – 4th March 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Pharmacy, UoN
The Chair, Dept. of Pharmacology and Pharmacognosy, UON
Supervisors: Dr.Eric M. Guantai, Prof.Faith A. Okalebo

Protect to discover

Appendix 7. Mbagathi Hospital Research Committee Approval Letter

NAIROBI CITY COUNTY

Tel: 2724712, 2725791, 0721 311 808
Email: mbagathihosp@gmail.com

Mbagathi Hospital
P.O. Box 20725- 00202
Nairobi

COUNTY HEALTH SERVICES

Ref: MDH/RS/1/VOL.1

15th March 2019

Dr. Gratia Muyu
University of Nairobi

RE: RESEARCH AUTHORIZATION

This is in reference to your application for authority to carry out a research on *"Antimicrobial use patterns in Mbagathi Hospital: A point prevalence survey"*

I am pleased to inform you that your request to undertake the research in the hospital has been granted.

On completion of the research you are expected to submit one hard copy and one soft copy of the research report / thesis to this office.

MBAGATHI HOSPITAL
15 MAR 2019
Tel: 0721 311 803
P.O. BOX 20725 - 00202, NAIROBI

Dr. Marion Ong'ayo
For: Chairman – Research Committee
Mbagathi Hospital

Appendix 8. Co-efficients of determination for each of the bivariable models

Variable	Crude β co-efficient (95% CI)	P-value	R-Squared
Ward type	0.642 (-.0867 - .215)	0.402	0.0030
Age group	-0.124 (-.294 - .046)	0.152	0.0080
Sex	-0.026 (-.480 - .428)	0.91	0.0001
Previous hospitalization	1.307 (.846 - 1.766)	<**0.001**	0.1624
Referred from another facility	1.193 (.747 - 1.639)	<**0.001**	0.1386
Catheterization	2.089(1.739 - 2.438)	<**0.001**	0.2943
Intubation	0.137(-.862- 1.135)	0.787	0.0004
HIV status	2.867(2.436 - 3.297)	<**0.001**	0.5002
Nutritional status	1.510 (1.101 1.920)	<**0.001**	0.2277