COLLEGE OF MEDICINE

Assessing Antibiotic Prescribing Patterns and Utilization of Microbiological Tests Results for Common Bacterial Infections in Under Five Inpatients at Ntchisi District Hospital, Malawi

By

Davie Kondowe

(BSc in Biomedical Sciences)

A thesis submitted in partial fulfillment of the requirements for the Degree of

Master of Science in Health Sciences- Anti-Microbial Stewardship

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DECLARATION

I, Davie Kondowe, hereby declare that this proposal is my own original work. Reference to, quotation from and discussion of the work of any other person has been correctly acknowledged within this proposal. It is being submitted to College of Medicine for my Master's Sciences Degree in Health Sciences (Antimicrobial Stewardship). It has never been submitted before anywhere for any purpose, by anyone.

Signature: 

Date: 30 April 2021

CERTIFICATE OF APPROVAL

The dissertation of Davie Kondowe is approved by the Dissertation Examination Committee:

_____

Associate Professor Genesis Chorwe

(Chairman, Post Graduate Committee)

_____

Dr Felix Khuluza

(Primary Supervisor)

_____

Miss Dina Kamowa

(Secondary Supervisor)

_____

Dr Tony Nyirenda

(Head of Pathology Department)

DEDICATION

This study is dedicated to:

My late father Charles Kondowe

My mother Lucia Kondowe

My wife Pamela Kondowe

My children Charles, Cynthia, Carlos and Chancy

I am indebted to you all for your support.

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ABSTRACT

Antibiotics have remained useful to humans and animals in the treatment of serious infectious diseases for decades now. Unfortunately, irrational antibiotic use has resulted in the emergency of antimicrobial resistance. The aim of this study was to assess antibiotic prescribing patterns and utilization of microbiological test results in common bacterial infections, and enhance existing interventions for the improvement of rational antibiotic use. This was a hospital based study, designed as prospective cross-sectional, which was conducted at Ntchisi district hospital, Malawi. The study used a structured questionnaire which involved prospectively reviewing and recording information from files of under-five patients admitted in peaditric ward. Convenience sampling method was used to enroll participants in the study. The study enrolled 373 participants who were prescribed antibiotics. The outcomes of the study were to assess antibiotic prescribing patterns in under five inpatients, evaluate utilization of microbiological test results of common bacterial infection in under five patients and find out the correlation or association between antibiotic prescribing pattern and utilization of microbiological test results in under five inpatients. According to Malawi Standard Treatment Guidelines, among the 373 recruited participant 76.68 % were appropriately prescribed antibiotics and 23.32 % were inappropriately prescribed antibiotics (p=<0.001). The most prescribed antibiotics were a combination of Benzyl penicillin and gentamycin 276(74.0%), followed by ceftriaxone 87(23.2%) and metronidazole 10(2.7%) (p=<0.001), 318(85.25%) had antibiotic prescription without a request for microbiological test and only 55(14.75%) had antibiotic prescription with a requested microbiological test (p=<0.001). Among the 55(14.75%) cerebral spinal fluid (CSF) samples sent to the

laboratory, 46/55 CSF samples were analyzed and all the samples had negative result. Culture and sensitivity was not performed because of lack of laboratory resources. There was no utilization of these microbiological test results to maintain, change or discontinue treatment by the prescribers. It was observed that antibiotic prescriptions were made empirically. The study found that the correlation between antibiotic prescribing pattern and utilization of microbiological test results was not statistically significant (p=0.288).

Keywords

Antibiotic prescribing, antimicrobial resistance, microbiological test

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ABBREVIATIONS AND ACRONYMS

AMR	Antimicrobial Resistance
BBiomedSc	Bachelor of Science in Biomedical Sciences
CDC	Center for Disease Control
COM	College of Medicine
COMREC	College of Medicine Research and Ethics Committee
DDD	Define Daily Dose
DHMT	District Health Management Team
GAP	Global Action Plan
MSc-HS	Master of Science in Health Sciences
MSTG	Malawi Standard Treatment Guidelines
PID	Participant Identity
SPSS	Statistical Package for Social Sciences
UNC	University of North Carolina
URPC	University Research and Publication Committee

GLOSSARY OF CONCEPTS AND TERMS

Antibiotic: Medicines that are used to treat bacterial infections in people and animals

Antimicrobial: It's any substance of natural, semisynthetic or synthetic origin that kills or inhibits the growth of microorganism but causes little or no damage to the host.

Antimicrobial resistance: it's a situation that occurs when microorganism such as bacteria, viruses, fungi and parasites change in ways that render the medications used to cure the infections they cause infective.

Clinical or empirical Diagnosis: diagnosis made based on experience and observation rather than on systematic logic.

Microbiology: The study all living organisms that are too small to be visible with naked eye.

Microbiological test or analysis: the use of biological, biochemical or chemical methods for the detection, identification or enumeration of microorganism

Laboratory diagnosis: a diagnosis arrived at after study of secretions, excretions, or tissue through chemical, microscopic or bacteriological means or biopsy

Physician: A person qualified to practice medicine

Prescription: instructions from the medical practitioners that authorizes a patient to be given medicines or treatment

CHAPTER ONE: BACKGROUND

Since Alexander Fleming made his historic breakthrough in the discovery of penicillin decades ago, antibiotics have remained useful to human and animal health in the treatment of serious infectious diseases. Unfortunately, now there is a threat, as widespread use, misuse or inappropriate prescribing has resulted in the emergency of drug-resistant bacteria (1). One of the contributing factors to antimicrobial resistance is irrational antibiotic use (2),for example making clinical diagnoses of bacterial infections without confirmatory microbiological tests. Studies have reported the positive relationship between antibiotic utilization and the level of antibiotic resistance (1).This study was conducted to assess antibiotic prescribing patterns and utilization of microbiological test results to enhance existing interventions for the improvement of rational use of antibiotics thereby help mitigate the problem of antibiotic resistance.

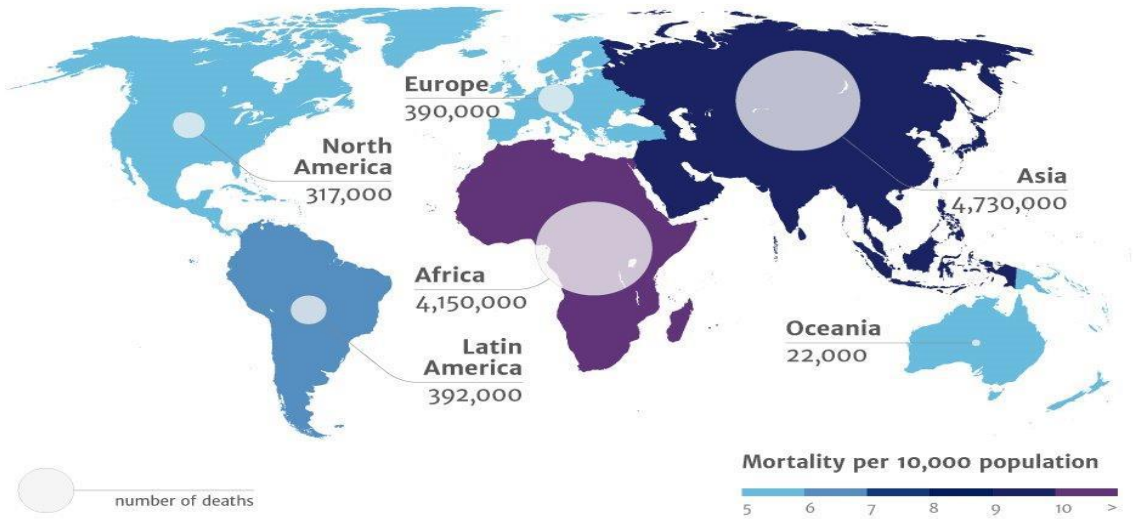
It is estimated that globally every year 700, 000 deaths of people occur which are attributed to drug-resistant bacterial infections (3). According to the 2013 report by Center for Disease Control and Prevention (CDC), in the United States alone, each year about 2 million people got serious bacterial infections which are resistant to one or two antibiotics that were previously meant to treat them and about 23000 people die as a direct result of antibiotic-resistant infections (4).

Antimicrobial resistance has become a public health threat (5) that needs collective efforts. For instance, a study in 2015 reported that the total global antibiotic consumption

was estimated at 42.3 billion defined daily doses (DDDs) (15.8 DDDs per 1,000 inhabitants per day) and in Low and Middle-Income Countries it accounted for 31.6 billion DDDs (6). Furthermore, it projected that the total global antibiotic use would increase by 15% between 2015 and 2030 (6).

According to the report by Neil Jimo (7) on a Review on Antimicrobial Resistance, it was projected that by 2050 the burden of deaths from antimicrobial resistance could increase to 10 million each year and based on that, it would mean one person would die every three seconds. Figure 1: below is the global picture of the burden of antimicrobial resistance by 2050 adopted from the Review on Antimicrobial Resistance (8). Based on future projections, if antibiotic usage is not well managed, mortality in the African countries could be over of four million lives per year. This projected loss of lives is quite huge and thus a need to combat antibiotic usage to reduce antimicrobial resistance.

Figure 1: World map showing the burden of antimicrobial resistance



Death attributable to AMR by 2050: Tackling a crisis for health and wealth nations

Source: Review on Antibiotic Resistance 2014, Chaired by Jim O'Neill

https://amr-review.org/sites/default/files/AMR Review Paper - Tackling a crisis for the health and

In sub-Saharan Africa, the prevalence of infectious diseases is very high and the disease burden results in great demand for antimicrobial use. For instance, the high burden of communicable diseases results in the overuse of antimicrobials and subsequent resistance as shown in the WHO's Global Report on surveillance of antimicrobial resistance (AMR), as well as a systematic review of AMR among clinically relevant bacterial isolates in sub- Saharan Africa (9).

Malawi, a country in southern Africa with current population of 17,563,749(10), one of the least-developed countries in the world (11), is not spared from antimicrobial resistance. A study performed by Makoka *et al.* at Kamuzu Central Hospital, Malawi, in

2012 observed widespread resistance to almost all antibiotics that were empirically used (12). For instance, 80% of the isolates were resistant to commonly used antibiotics (12). Similarly, the "Antimicrobial resistance Global Report on Surveillance" by WHO, showed high resistant rates in bacterial pathogens that cause common hospital, community. and food-chain related infections (9).

The increasing prevalence of antibiotic-resistant bacterial infections seen in clinical practice stems from antibiotic use both within human health and veterinary medicine (13). For instance, in human medicine, the contributing factor is misuse and overuse of antibiotics whereas in veterinary medicine the contributing factor is use of antibiotic in livestock feed to promote faster growth (13–15). Additionally, some factors that contribute to the problem of antimicrobial resistance include the availability of antimicrobial drugs without prescriptions, inappropriate physicians prescriptions and inappropriate practice of antimicrobial resistance prevention and control among health workers (16).

Health care workers play a vital role in preserving power of antimicrobial medicines (5). If they lack up to date information about AMR, they cannot be able to identify infection, instead will yield to patient pressure to empirically prescribe antibiotics which may result in inappropriate prescribing and dispensing (5). In line with this, in 2015 the World Health Assembly endorsed a Global Action Plan (GAP) to tackle antimicrobial resistance, including antibiotic resistance and the most urgent drug resistance trend, of which Malawi is a signatory (5). In 2017, Malawi developed and adopted the

antimicrobial resistance strategy plan to provide guiding principles for implementation of antimicrobial stewardship.

According to CDC the four core actions to prevent antibiotic resistance include: preventing infections and spread of resistance, tracking of antibiotic resistant infections, improving antibiotic prescribing and stewardship and finally developing new drugs and diagnostic tests (4).

A deeper understanding of these core actions would enable the policy makers, prescribers and frontiers of antimicrobial stewardship to enforce existing interventions or think of new innovative ways of reducing drug resistance. For example, enforcing existing Malawi Standard Treatment Guidelines (MSTG) and Integrated Management of Childhood Illness (IMCI) would help improve appropriate antibiotic use and therefore reduce antimicrobial resistance (17,18).

It was against this background, that the study was conducted to assess antibiotic prescribing pattern and utilization of microbiological test results of common bacterial infections in under five inpatients at Ntchisi District Hospital, Malawi.

1.1 Rationale or justification of the study

Malawi is one of several underdeveloped countries in the world which have high prevalence of infectious diseases of which, children are more vulnerable. Strides have been made by the government of Malawi to improve laboratories of central or tertiary

hospitals, however, most district hospitals lack fully equipped medical laboratories that can help in quick diagnosis of infectious diseases. For example, through observation and experience, at Ntchisi District Hospital where the study was conducted, some important laboratory tests like culture and sensitivity were not performed regularly because the hospital lacked laboratory supplies, had malfunctioned laboratory equipment and shortage of laboratory personnel. As remedy to this problem most of the infectious diseases are diagnosed based on empirical diagnosis. The antibiotics are prescribed based on Malawi Standard Treatment Guidelines and Integrated Management of Childhood Illness guidelines without confirmatory microbiological test results.

It was also observed in the peaditric ward that, in cases where laboratory test result were available, the clinicians usually didn't use laboratory test results to evaluate the necessity to stop or continue giving the prescribed antibiotic to their patients. Although empirical diagnosis help in saving lives, it mushrooms serious problem of antibiotic resistance as prescribers inappropriately prescribe antibiotics even to non-bacterial infections because of uncertainty about the diagnosis they make.

It is true, that interventions are in place that look at proper use of antibiotics in hospitals across Malawi, for instance each hospital has Drug Therapeutic Committee and Infection Prevention & Control Committee. Despite efforts made by these committees, the antibiotics are still being used inappropriately and drug resistance is pacing at faster rate. This study was significant because it wanted to ascertain the antibiotic prescribing pattern and utilization of microbiological test results of common bacterial infections and enforce

already existing interventions, in order to help improve rational antibiotic use and reduce antibiotic resistance.

1.2 Study objectives

1.2.1 Broad objective

To assess antibiotic prescribing pattern and utilization of microbiological test results of common bacterial infections in under five inpatients at Ntchisi district hospital, Malawi.

1.2.2 Specific objectives

a. To assess the antibiotic prescribing pattern in under five in-patients at Ntchisi district hospital.

b. To evaluate the utilization of microbiological tests results of common bacterial infections in under five inpatients at Ntchisi district hospital.

c. To find out the correlation between antibiotic prescribing patterns and utilization of microbiological test results

CHAPTER TWO: LITERATURE REVIEW

2.1 Chapter overview

This chapter gives an account of the review of literature on antibiotic prescribing patterns and utilization of microbiological test results in under five inpatients based on the following study objectives:

a. Assessing antibiotic prescribing pattern in under five inpatients.
b. Evaluating utilization of microbiological tests results of common bacterial infections in under five inpatients.
c. To find out the correlation between antibiotic prescribing patterns and utilization of microbiological test results.

Antibiotic prescribing is one of the important clinical decisions that prescribers make to treat their patients, which is choosing the right antibiotic for the correct diagnosis made on the patient. However, for the prescriber, to arrive at the correct diagnosis, they need microbiological tests to confirm the absence or presence of disease-causing organisms. In low-resourced country like Malawi, the unavailability of reliable laboratory services such as culture and sensitivity pose a great challenge to prescribers, as a result, they rely on empirical a clinical diagnosis, which is making clinical diagnosis based on signs and symptoms or clinical presentation. The outcome of this is that most patients are either inappropriately or irrationally prescribed antibiotics which in turn facilitate antimicrobial resistance. This chapter looks at literature related to this study which wanted to assess antibiotic prescribing patterns and utilization of microbiological test results to ascertain

the problem of irrational antibiotic use. There were a few related studies that were conducted before and below is the synthesis of the available literature.

2.2 Previous related studies on antibiotic prescribing patterns and utilization of microbiological test results in under five inpatients

Assessing antibiotic prescribing patterns helps to determine the problem of irrational antibiotic use. In the fight against antimicrobial resistance, studies have been conducted to establish inappropriate antibiotic use, by assessing antibiotic prescribing patterns and the use of diagnostic tests.

For instance, Chem et al. (1) conducted a cross-sectional retrospective study on antibiotic prescribing and associated factors of antibiotic prescription in primary health facilities, in North West Cameroon. The study reviewed 30096 prescriptions and found out that the overall rate of antibiotic prescriptions was 36.71%. Furthermore, the investigators observed the following findings: amoxicillin was the most prescribed antibiotic (29.9%); respiratory tract infection was the most indication for prescribing; all prescribed antibiotics were broad-spectrum, and that there was the prescription of Benzlypenicilin, Gentamycin, and Ceftriaxone for malaria cases. Generally, the investigators found misuse of antibiotics in a primary healthcare facilities in the study area and made recommendations that all primary healthcare facilities should be included in the Performance-Based financing and that prescribing should only be prepared by Physicians as they have adequate training (1).

A review conducted by, Klein et al. (19), looked at global increase and geographical convergence in antibiotic consumption between 2000 and 2015 and found out that global antibiotic consumption increased by 65% between 2000 and 2015, from 21.1 to 34.8 billion defined daily doses(DDDs), while the antibiotic consumption rate increased by 39%, from 11.3 to 15.7 DDDs per 1000 inhabitant per day over the study period(6). Based on their review findings, Klein et al. observed that the major driver of increased antibiotic consumption was rising incomes and high burden of infectious diseases in Low and Middle-Income Countries (LMIC) and it was imperative to keep tracking rates of antibiotic use because of well-quantified relation between antibiotic use and resistance (6).

Furthermore, another study conducted in India by Sharma et al. (1998)(20) on antimicrobial prescribing patterns found out that prescribing frequency of one antimicrobial per prescription was more common in the departments of surgery and urology (52.52%) and internal medicine (50.51%), whereas prescribing frequency of two antimicrobials per prescription was common in peaditric department (59.9%) (20).This was in contrast to another study in South Africa, which found relatively lower prescriptions rates than those described in the international literature on antibiotic use in the intensive care unit (21). Sharma et al., observed that there was a general tendency of prescribing newer antimicrobials and that in the majority of cases, the selection of antimicrobials was not based on microbiological confirmation. This was similar to the result of a study conducted by Chunnilall et al., who found a lack of microbiological verification in 38 % of its patients (21).The researchers suggested that the use of newer

and expensive antimicrobials should be kept reserved only for serious and life-threatening situations (20).

In Nepal, a similar study was conducted by Shankar et al. on prescribing patterns in peadiatric in a teaching hospital. The researchers observed high use of parenteral antibiotics and the predominant use of antibiotics for viral infections. Based on their findings the study investigators recommended the introduction of route conversions programs and the formulation of treatment guidelines for common infections (22). A similar study, conducted in South Western Nigeria by Fadare. et al. found related findings in which the investigators observed over-prescriptions (23).

In Kenya, a study was conducted by Momanyi et al., on antibiotic prescribing patterns. The researchers observed that there was a lengthy duration of prophylaxis, pervasive prescribing of broad-spectrum antibiotics, high rates of empirical prescribing, and lack of documenting the indication for antibiotics (24). Another study conducted in Saudi Arabia by Alakhali et al. also found a relatively high rate of broad-spectrum antibiotic prescriptions (25).

Sharma et al., conducted a retrospective chart review on the antibiotic prescribing patterns in peaditric emergency department at Georgetown Public Hospital Corporation in Guyana. The investigators found that one or more antibiotics were prescribed for 36.9% (n=299) of all the encounters and 90.83% of the antibiotic were prescribed from the essential drugs formulary list while 30% of the prescriptions had the generic name of

the drug. They also observed that the most frequently prescribed antibiotics were broad-spectrum B-Lactam penicillin which was 74.6% (299) of 360 antibiotic prescriptions. The investigators based on their findings concluded that there was; 1) higher than standard rates of antibiotic use, 2) polypharmacy, 3) good adherence to essential drug formulary (26).

A similar study was conducted in adults by Chunnilall et al., who did an evaluation of antibiotic prescribing patterns in adult intensive care units in private hospitals in Kwazulu-Natal, South Africa. The investigators looked at the dosing accuracy, frequency and duration of administration, microbiologically informed treatment, and de-escalation (21). The findings of their evaluation revealed a clear indication of antibiotic therapy in 58.5% (n=131) of the patients, of whom 70.2% of the prescribed treatment was consistent with guidelines and drug registration information. Furthermore, they found correct doses in 91.1% of the sample, 61.2% of the patients had confirmatory microbiological investigations, and de-escalation was observed in 13.1% of the patients. The evaluation found that the rate of antibiotic prescriptions was relatively lower compared to the ones described in the international literature on antibiotic use in the Intensive Care Unit. In addition, they found that 41.1% of the patients had antibiotic prescriptions without indication, 38.8% of the patients had no microbiological verification, 29. 8% of the patients had inaccurate drug choice 8.9% had incorrect dosing (21).

2.3 Conclusion

This chapter looked at literature review related to this study and eight articles were found and reviewed. Majority of the authors focused on antibiotic prescribing patterns. There was no article that had detailed information on both antibiotic prescribing patterns and utilization of laboratory results. The results of a laboratory test are crucial in making correct clinical diagnosis and thereby prescribed the correct antibiotic for the identified infection. More information is needed to link up the two, hence this study is trying to assess the antibiotic prescribing pattern and utilization of laboratory results of common bacterial infection in under five patients.

CHAPTER THREE: STUDY METHODOLOGY

3.1 Introduction

This chapter describes and justifies the methodology used for the study i.e. study design, the choice of the study area, sample size, data collection, and data analysis tools. Therefore the goals of this chapter are to:

a. Explain the rationale for the choice of the population/participants to be included in the study.
b. Justify the use of Statistical Package for Social Sciences (SSPS) V.20 and Microsoft EXCEL 2013 in the analysis of the study results.
c. Explain the details about the study design, inclusion and exclusion criteria, sample size, data collection, and data analysis.

3.2 Study design

This was a hospital-based study, designed as a prospective cross-sectional study. The study design was chosen because it was feasible to collect data over a short period and assess the outcomes of interest about the antibiotic prescribing patterns and utilization of microbiological test results in under five inpatients. The study tried to review the hospital records while the patient was still hospitalized because additional information was needed from the child's parents/ guardians which might have been missed on admission by the admitting clinician and also to avoid loss of patient's files.

3.3 Study setting

Ntchisi district hospital lies at latitude 13^{o} 22’ 0.12” S and longitude 34^{o} 0’ 0” E in the central region of Malawi. It is 96 km north of the capital city Lilongwe. It covers a total land area of 1,655km^2 and has a population of 317,069 people (10). The hospital has a bed capacity of 224 beds. It is housed with the following departments: Administration, Pediatrics medical & surgical, adult Medical & surgical, Obstetrics & Gynecology, laboratory, Pharmacy, Outpatient and radiology. This study was conducted in peaditric department which has a 52 bed capacity. According to Ntchisi Hospital crude statistics from July 2019 to June 2020, peaditric department admitted about 3188 under-five patients which are 266 under-five admissions per month. In addition the hospital had a district laboratory which was able to analyze microbiological tests (cerebral spinal fluid) though it lacked resources to perform culture and sensitivity. It was for this reason that, the researcher chose the site because the study population was enough to get the required sample size of 385 cases within a short time.

3.4 Study population

This study involved under-five children who were prescribed antibiotics and admitted at Ntchisi district hospital, peaditric department. Once the patient was admitted, the files were reviewed to establish whether the child was prescribed antibiotics or not. Below is the inclusion and exclusion criteria:

- ***Study inclusion criteria***
    - All children admitted to pediatric ward with medical conditions.
    - All inpatients children from 1 month to 59 months of age.
    - All inpatient children who were prescribed antibiotics on admission to pediatric department.
    - All children whose parents/guardians consented to collect information from their child's files/records.

- ***Study exclusion criteria***
    - All children were admitted to pediatric department with non-medical conditions.
    - All inpatients children under 1 month.
    - All inpatient children above 59 months.
    - All inpatient children without antibiotic prescription on admission to pediatric department
    - All inpatient children whose parents/guardians refused to consent to collect information from their child's hospital files or records.

3.5 Study duration

The study was conducted over 18months from October 2019 to April 2021. The first 8 months were the period for proposal development and approval by the College of Medicine Research and Ethics Committee (COMREC). Data collection was done for 3

months (September, October, and November 2020) and the remaining period was for data analysis and dissemination of study findings and publication.

3.6 Sample size

With a confidence level of 95%, standard deviate of 1.96, and the standard error of ±5%, a sample of 385 participants was calculated using Minimum Sample Size calculation (28) Since the prevalence of poor prescribing habits at Ntchisi hospital was unknown, the study used 50% as a standard proportion of patients who had inappropriate antibiotic prescribing pattern and utilization of microbiological tests results. Below is the formula:

$$n = \frac{Z^2 \times P(1-P)}{e^2}$$

Where n= sample size

Z= confidence level (95%) =1.96

P= estimated proportion (50%) =0.5

e= standard error (±5%) =0.05

The required sample size was as follows:

$$n = \frac{1.96^2 \times 0.5(1-0.5)}{0.05^2}$$

$$n = \frac{1.96^2 \times 0.5 \times 0.5}{0.05^2} = 384.16 \sim 385$$

3.7 Data collection

A structured questionnaire (appendix 2) was used to prospectively collect information from under five inpatients records/files. First, when the child came to the ward, from the outpatient department, the files/ patients records were screened for study eligibility. The screening process involved looking at age, prescription of antibiotics, and cause of admission. Thereafter, parents/guardians were asked for consent to allow the researcher to collect information from hospital admission files/ records of their children. After consent was granted, the researcher collected the information by filling the semi-structured questionnaire.

The participant was followed until discharge, once the information on initial contact was collected and recorded,. In summary, the collected information was regarding participant demographic, antibiotic prescribing and utilization of microbiological tests. That was performed to allow a proper assessment of the antibiotic prescribing pattern and utilization of microbiological laboratory tests results.

3.8 Data management

3.8.1 Data coding

Once the data collection was finished, all the information gathered was entered in Microsoft excel 2013 sheet on the computer. The variables were labeled and numerically coded to allow quantitative analysis of the collected information.

3.8.2 Data analysis

SPSS version 20.0 software and Microsoft Excel 2013 were used to analyze data. . The assessment of antibiotic prescribing pattern and utilization of Microbiological laboratory test results were analyzed using descriptive statistics. *Chi-square test* was used to compute p-values and the correlation between antibiotic prescribing patterns and utilization of microbiological test results using. Finally, the demographic information was analyzed using Excel.

3.9 Ethical considerations

Ethical approval was obtained from the College of Medicine Research and Ethics Committee (COMREC: P.06/20/3067), Ntchisi hospital research committee, and Ntchisi District Health Management Team (DHMT). Participation in the study was voluntary. Parents/guardians were asked for permission to collect information from the hospital charts of their children and also provide any other relevant information which was missing in the hospital charts. The participants were assured of privacy and confidentiality of their information as names were not used in the final analysis, instead, the participants were assigned a study Participant's identity (PID) number. The safety of participants was ensured as the study didn't involve any invasive procedures, only data collection from hospital case notes and interviews to generate missing information from the hospital records. See the informed consent form in appendix 1.

CHAPTER FOUR: STUDY RESULTS AND FINDINGS

4.1 Introduction

This chapter describes the study results and findings on the following objective: assessment of antibiotic prescribing pattern, evaluation of utilization of microbiological tests results, and finding out the correlation between antibiotic prescribing and utilization of microbiological results.

4.2 Demographic characteristics and common infection

Based on study sample calculation, 385 participants were targeted to be enrolled in the study, however, only 373 participants were enrolled representing 96.9% and 12 participants declined consent representing 3.1%. Among the enrolled under five inpatient participants, 45% were females and 55% were males. **Table 1**shows the prevalent infections and key demographic information about the study participants.

Table 1: ***Showing common infections and means of vital statistics***

Common Infections	**Number of Cases**	**Mean Age(Months) (SD:±14.01)**	**Mean Weight(KGs) (SD:±2.9)**	**Mean Temperature(^{o}C) (SD:±1.29)**
Sepsis	155(41.55%)	25.88	11.01	37.68
Meningitis	20(5.36%)	32.23	12.18	37.59
Pneumonia	111(29.76%)	19.18	9.80	37.23
Malaria	87(23.33%)	23.95	10.46	37.72
Grand Total	**373(100%)**	**23.77**	**10.58**	**37.55**

4.3 Pattern of Antibiotic prescribing

The study enrolled 373 the participants who were prescribed antibiotics. Among these participants, 76.68 %(286) were prescribed antibiotics based on MSTG and 23.32% (87) were inappropriately prescribed antibiotics (p=<0.001).The *Chi-square test* was used to compute p-values. The most frequently prescribed antibiotics were a combination of Benzylpenicillin and gentamycin 276(74.0%), followed by ceftriaxone 87(23.32%) and metronidazole 10(2.7%) *(*p=<0.001) as shown in table 2.

Table 2: Shows diagnosis and antibiotic prescribing

Prescribed antibiotic / **Diagnosis**				**Total**	***P*-value**
	Benzyl penicillin & Gentamycin	Ceftriaxone	Metronidazole		
Sepsis	119(76.8%)	31(20.0%)	5(3.2%)	155(41.6%)	<0.001
Meningitis	1(5.0%)	19(95.0%)	0(0.0%)	20(5.4%)	
Pneumonia	101(91.0%)	10(9.0%)	0(0.0%)	111(29.8%)	
Malaria	55(63.3%)	27(31.0%)	5(5.7%)	87(23.32%)	
Total	276(74.0%)	87(23.3%)	10(2.7%)	373(100%)	

4.4 Antibiotic prescribing versus qualification and experience of the prescribers

Table 3 is comparing prescribing habits among various clinicians based on their qualifications and experience. The majority of the prescribers were junior clinicians (certificate in clinical medicine) 68.63% (256) and among this category of prescribers, most of them adhered to Malawi standard treatment guidelines. Prescribers with experience between 1 to 5 years prescribed the most antibiotics 45.31% (169). There was no statistical significance whether qualification and experience influenced antibiotic prescribing of antibiotics (p=0.060), (p=0.193) respectively.

Table 3: Shows antibiotic prescribing Vs qualification & Experience of the prescribers

ANTIBIOTIC PRESCRIBING VS QUALIFICATION& EXPERIENCE OF PRESCRIBER						
Variables		Antibiotic Prescribing			Total	***P*-value**
		Benzyl penicillin & Gentamycin	Ceftriaxone	Metronidazole		
Qualification Of Antibiotic Prescriber	Certificate in clinical medicine	197(76.95%)	51 (19.92%)	8 (3.13%)	256 (68.63%)	0.060
	Diploma in clinical medicine	79 (67.52%)	36 (30.77%)	2(1.71%)	117 (31.37%)	
Total		276 (74.00%)	87(23.32%)	10 (2.68%)	373(100%)	
Experience Of Antibiotic Prescriber	Intern	87 (72.50%)	29 (24.17%)	4 (3.33%)	120 (32.17%)	0.193
	<1 Year	17 (56.67%)	12 (40.00%)	1 (3.33%)	30 (8.04%)	
	1-5Year	130 (76.92%)	34 (20.12)	5 (2.96%)	169 (45.31%)	
	>5Years	42 (79.25%)	12(22.22%)	0 (0.00%)	54 (14.48%)	
Total		276 (74.00%)	87 (23.32%)	10 (2.68%)	373 (100%)	

4.5 Utilization of microbiological test results in under five

The study found no utilization of microbiological test results of cerebral spinal fluid (CSF) that were analyzed at the laboratory. Out of 373 participants enrolled in the study, 318 (85.25%) cases had no microbiological tests requested and 55 (14.75%) cases had microbiological tests sent for laboratory analysis (p=<0.001). All microbiological samples sent to the laboratory were only Cerebral Spinal Fluid(CSF). Meningitis cases had the most microbiological tests sent to the laboratory. Out of 20 cases, 18(90.0%) samples were sent for microbiological analysis. Among these, no sample had confirmed disease causing microorganisms. Sepsis and malaria were second cases with most samples sent for microbiological tests. There were 155(41.55%) cases of sepsis and 87(23.32%) cases of malaria but only 18(11.61%) and 16(18.40%) cases respectively (p=<0.001) had their samples sent for microbiological analysis in the laboratory and no sample had confirmed presence of disease causing bacteria. Pneumonia had the least confirmatory microbiological test, out of 111(29.76%) cases, only 3(2.7%) cases had their samples sent for microbiological analysis (p=<0.001).

Despite having microbiological test results confirming no presence of bacterial infection, it was observed that the ward clinician didn't use the results that were available to evaluate the necessity to stop or maintain the prescribed antibiotics for the patient.

Table 4: Shows diagnosis and requested Microbiological tests and availability of microbiological test results

Diagnoses	Requested Microbiological Tests		Total		Availability Of Microbiological test Result		Total	*P*-value
	No	Yes			No	Yes		
Sepsis	137 (83.39%)	18 (11.61%)	155 (41.55%)		141 (90.97%)	14 (9.03%)	155 (41.55%)	<0.001
Meningitis	2 (10.00%)	18 (90.00%)	20 (5.36%)		5(25.00%)	15 (75.00%)	20 (5.36%)	
Pneumonia	108 (97.30%)	3 (2.70%)	111 (29.76%)		108 (97.30%)	3(2.70%)	111 (29.76%)	
Malaria	71 (81.60%)	16 (18.40%)	87 (23.32%)		73 (83.91%)	14 (16.09%)	8 (23.32%)	
Total	318 (85.25%)	55 (14.75%)	373 (100%)		327 (87.67%)	46 (12.33%)	373 (100%)	

4.6 Correlation between antibiotic prescribing and utilization of microbiological tests

The correlation between antibiotic prescribing and the utilization of microbiological test results was 0.055and p=0.288. It was hypothesized that there was a relationship between antibiotic prescribing and utilization of microbiological results. However, the null hypothesis was not rejected as the relationship was not statistically significant as shown in (

*Table **5**)* below.

Table 5: Shows Correlation between antibiotic prescribing and Utilization of Microbiological test on admission

Variables		Utilization Of Microbiological Results
Antibiotic Prescribing	Pearson Correlation	.055
	Sig. (2-tailed)	.288
	N	373

CHAPTER FIVE: DISCUSSION

5.1 Introduction

Antibiotics play a crucial role in the treatment of serious infectious diseases. Regular assessment of antibiotic prescribing and utilization of microbiological tests would help to know the magnitude of the problem of irrational antibiotic use, hence dealing with the fight against antimicrobial resistance. In this regard, this study looked at the antibiotic prescribing pattern, utilization of microbiological test results, and correlation between the two.

5.2 Antibiotic prescribing pattern

All the participants, in this study, were prescribed antibiotics regardless of admission indication. Generally, the majority of the participants were appropriately prescribed antibiotics, however, there were some discrepancies in antibiotic prescribing as 23.32% were not prescribed antibiotics according to Malawi standard treatment guidelines (MSTG) (17). The discrepancy found in this study was similar to a previous study conducted in South Africa, Durban by Chunnilall et al. who found 70.2% of participants were prescribed treatment consistent with guidelines or drug registration information (21). In the same way, another study conducted in Nepal by Shankar et al. (27), found the use of antibiotics in non-bacterial infections such as viral infections and fever under investigation. The only difference with this study is that malaria cases without co-existing infections were given antibiotics which included Benzyl penicillin, Gentamycin and Ceftriaxone, while in their study it was viral infections. According to Malawi standard treatment guidelines, the treatment for Malaria is antimalarial drugs (17).

Furthermore, according to Malawi Standard treatment Guidelines (MSTGs) (17) first-line treatment for sepsis and pneumonia is Benzyl penicillin and gentamycin which were appropriately prescribed in 76.8 % cases of sepsis and 91.0% cases of pneumonia respectively (p=<0.001). In this study pneumonia was the second highest indication for antibiotic prescriptions 29.76%, then Malaria followed with 23.33% and meningitis cases were the least 5.4%.This is in contrast with the study which was conducted in Nepal by Palinke (28) which found pneumonia as the most frequent diagnosis.

In the same way, first-line treatment for meningitis was Ceftriaxone which was appropriately prescribed in 95.0% of cases of meningitis (p=<0.001). Marked inappropriate antibiotic prescribing was observed in malaria cases as prescribed antibiotics did not follow the MSTGs (17). According to the findings, 23.2% (87) of malaria cases without co-existing conditions received antibiotics which include Benzyl penicillin, Gentamycin and Ceftriaxone, even though malaria is a non-bacterial infection (p=<0.001).

In addition, the most prescribed antibiotics were the combination of benzyl penicillin and gentamycin which was prescribed in 74% of the participants, followed by ceftriaxone which was prescribed in 23.3 % of the participants. This is different from a previous study conducted in Saudi Arabia by Khaled et al. (25) which found cephalosporin group as the most frequently (52%) prescribed antibiotic, followed by Aminoglycoside (17.3%) and penicillin's (12.5%). A similar observation was made in Nepal by Palinke (28) in

their study. This difference might be the result of different settings as well as differences in standard treatment guidelines.

In mitigation, for inappropriate antimicrobial use, WHO recommends that antibiotics should be prescribed based on antibacterial classification groups which are Access, Watch, Reserve (AWaRe) (29). This was developed as an antibiotic stewardship tool to assist in the classification of antibiotics and be used at the local, national, and global levels. Malawi as a country follows this antibiotic classification. According to Malawi standard treatment guidelines (MSTG), the first-line treatment for sepsis is the combination of benzyl penicillin and gentamycin (17). In this study, 76.8% (*Table 2:*) of the sepsis cases were started on first-line antibiotics, and out of 20 meningitis patients, 19 received ceftriaxone as the first-line treatment.

Generally, in this study, the majority of the cases were prescribed antibiotics based on standard treatment guidelines. In a few cases, there was a mixed up, as some patients were started on second line antibiotics who were supposed to receive first-line treatment. For example, 31% (N=155) of sepsis were prescribed second-line antibiotics before first-line treatment, 23.3% (N=87) of malaria were wrongly prescribed antibiotics instead of antimalarial. This was inappropriate antibiotic prescribing and this is in contrast to what Getachew et al. (30) found in their study in Ethiopia.

5.3 Utilization of microbiological test results

In this study, microbiological test results were not fully utilized. The majority of the patients were prescribed antibiotics based on the empirical clinical decisions, that is antibiotic prescriptions were made without microbiological tests 85.25% (*Table 4*). This is similar to a study done in Ethiopia by Feleke et al. (31), which found that antibiotic prescribing was done purely empirically. In this study, only 14.75% of participants had microbiological tests requested. Unfortunately among these, there was no utilization of the results. These findings were similar to a study done in Zambia by Hangoma (32) who found that only 31.4% (n=86) participants had microbiological tests ready at the time of the review of the participants.

Furthermore, the study observed that microbiological tests were not normally requested and in those tests that were requested, all results had no organism seen. The reluctance of prescribers not requesting the microbiological tests is a cause for worry because it means they are used to the routine way of doing this. Of course, the laboratory department had its challenges, like not doing culture and sensitivity but this could not stop prescribers requesting microbiological test, because the laboratory was able to do preliminary sample analysis, that is Gram's staining, India ink, CrAg, AAFB tests.

In addition, the laboratory could not provide full microbiological services due to a lack of equipment and supplies for culture and sensitivity. This was similar to a previous study done by Demoz et al. (33) which found that culture and sensitivity tests were not done in all participants that enrolled in their study. This could be one of the reasons why

prescribers opted for empirical diagnosis. As a way of mitigating insufficient utilization of microbiological test, this study suggests a new point of care diagnostic approach which would aid prescribers in making clinical diagnoses.

5.4 Correlation between antibiotic prescribing and utilization of microbiological tests

This study observed that there was no statistical significance in the association between antibiotic prescribing and utilization of microbiological tests results (correlation=0.055, significance level=0.288).

5.5 Limitations

The following study limitations were identified:

The prescribers were not interviewed to find out their experiences about antibiotic prescribing, only their qualification and years of work were recorded from patient files. However we believe that the lack of interviewing of the prescribers has not invalidated our findings, but gives an opportunity for future areas of research focus

The study was conducted in peaditric department only, other departments were not included, which may not be the same in the adult population. But this study still applies in the pediatric population and future studies could possibly include the adult population.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Introduction

This chapter provides a summary of the study findings and recommendations.

6.2 Conclusion

This study assessed the antibiotic prescribing patterns and utilization of microbiological test results of common bacterial infections in under-five inpatients at Ntchisi district hospital, Malawi. The findings of the study showed that, majority of the participants enrolled in the study had appropriate antibiotic prescribing. Furthermore, most prescribers followed Malawi standard treatment guidelines when prescribing antibiotics to their patient, and a few prescribers prescribed antibiotics to their participants inappropriately. The study also found out that there was no utilization of microbiological tests results by prescribers of antibiotics. Most diagnostic decisions were done empirically.

Finally, there was no correlation between antibiotic prescribing and the utilization of microbiological tests results.

6.3 Recommendations

Based on the study findings, it is being recommended that hospitals should introduce deliberate ways of enforcing the Malawi Standard Treatment Guidelines (MSTG) and Integrated Management of Childhood Illness (IMCI) guideline by health practitioners.

This can be done by making available individual copies of MSTG and IMCI guidelines to prescribers.

Even though there was a good adherence to MSTG, there is a need to introducean antimicrobial stewardship program to monitor antibiotic use. Among the function of the antimicrobial stewardship program, it has hadregular integrated antibiotic use audit meetings which should involve all key departments at the hospital that is clinical, pharmacy, nursing, and laboratory teams.

Our findings of lack of culture and sensitivity in the hospital might be a problem of several hospitals in Malawi. Therefore, there is need to strengthen the laboratory services so that they can be able to run necessary tests without problems.

In addition, for conditions like sepsis, the government can explore the integration of point of care biomarker-guided antibiotic therapy and empirical clinical algorithms to help reduce inappropriate antibiotic use.

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APPENDICES

Appendix 1: Draft manuscript submitted to Malawi Medical Journal

Assessing antibiotic prescribing patterns and utilization of microbiological test results for common bacterial infections in inpatients under-five children at Ntchisi District Hospital, Malawi.

Author's list:

Kondowe, Davie[1], BSc

Kamowa, Dina M.T.[2], MSc

Khuluza, Felix [2], PhD (ORCID no.: 0000-0002-8334-0160)

Author's affiliations list:

[1] Biomedical sciences department, Kamuzu University of Health Sciences, Blantyre, Malawi

[2] Pharmacy department, Kamuzu University of Health Sciences (formerly College of Medicine-University of Malawi), Blantyre, Malawi

Corresponding author's details

Email address: fkhuluza@kuhes.ac.mw or fkhuluza@cartafrica.org

Abstract

Background

Antibiotics are useful in the treatment of serious infectious diseases. Unfortunately, irrational antibiotic use has resulted in the emergence of antimicrobial resistance. The aim of this study was to assess antibiotic prescribing patterns and utilization of microbiological test results in common bacterial infections.

Methods

This was a prospective cross-sectional study, conducted at Ntchisi District Hospital, Malawi. The study used a structured questionnaire to record information prospectively from files of inpatients under-five children. Key information elicited were: 1) diagnosis, microbiological test requested; microbiological test received and whether they used the microbiological test results in coming up with the diagnosis. 2) antibiotic prescribing; type of prescribed antibiotics; appropriateness of the antibiotic with respect to dosage and duration; and whether the treatment was in line with Malawi Standard Treatment Guidelines or Integrated Management of Childhood Illness (IMCI) guidelines or WHO standard treatment guidelines. We enrolled all participants who were prescribed antibiotics in the pediatric ward into the study from September 2020 to November 2020 and the patients were followed until discharge from hospital.

Results

373 participants who were prescribed antibiotics were enrolled in the study. Major disease conditions identified were sepsis (41.6%), pneumonia (29.8%), malaria (23.3%) and meningitis (5.4%). The majority of recruited participants (76.8%, 276) were prescribed antibiotics appropriately (p=<0.001). The most prescribed antibiotics were a combination of Benzyl penicillin and gentamicin (276, 74.0%), followed by ceftriaxone (87, 23.2%) and metronidazole (10, 2.7%). There was no utilization of microbiological results in the prescribing of antibiotics. Antibiotic prescriptions were mostly done empirically (327, 87.6 %,). However, the majority of the antibiotic prescribing followed Malawi Standard Treatment Guidelines and Integrated Management for Childhood Illnesses guidelines, even though there was no confirmation of bacterial causing organism.

Conclusion

Antibiotic prescribing was appropriate as per recommended standard treatment guidelines. However, most of the antibiotic prescriptions were done empirically due to a lack of reliable laboratory services. It may be helpful to explore the integration of an empirical clinical algorithm with rapid test biomarker guided -antibiotic therapy.

Keywords: antibiotic prescribing, microbiological test, antimicrobial resistance

Introduction

Since Alexander Fleming made his historic breakthrough in the discovery of penicillin, eight decades ago, antibiotics have remained useful to human and animal health in the treatment of serious infectious diseases. Unfortunately, now there is a global health threat as widespread use, misuse, or inappropriate prescribing has resulted in the emergence of drug-resistant bacteria (1) One of the contributing factors to antimicrobial resistance is irrational antibiotic use (2) with clinical diagnoses of bacterial infections without confirmatory microbiological tests. Studies have reported positive relationships between antibiotic utilization and the level of antibiotic resistance (1). This study was conducted to assess the antibiotic prescribing pattern and utilization of microbiological test results to consider the possible need for a new point of care diagnostic tests for bacterial infections or enhancement of existing interventions for the improvement of rational use of antibiotics to mitigate the problem of antibiotic resistance.

It is estimated that globally every year 700, 000 deaths occur which are attributed to drug resistant bacterial infections (3, 4). Antimicrobial resistance has become a public health threat (5) that needs consultative efforts to overcome. It has been reported that the major driver of antimicrobial resistance is increased antibiotic usage resulting from many factors, one of which is irrational antibiotic use (2). For instance, a study in 2015 reported that the global antibiotic consumption was estimated at 42.3 billion defined daily doses (DDDs) or 15.8 DDDs per 1,000 inhabitants per day, and in Low and Middle-Income Countries it was 31.6 billion DDDs (6). Furthermore, it projected that the total global antibiotic use would increase by 15% between 2015 and 2030 (6).

According to a 2016 Review on Antimicrobial Resistance by Jimo (3), deaths from antimicrobial resistance could increase to 10 million each year by 2050, which would mean one person would die every three seconds. If antibiotic usage is not well managed, mortality in African countries could be more than four million lives per year. This projected loss of lives is huge, and thus reducing antibiotic usage to reduce antimicrobial resistance is most urgent.

In sub-Saharan Africa, the WHO has shown that the prevalence of infectious diseases is very high and the disease burden results in great demand for antimicrobial use and inconsequent antimicrobial resistance (7). Malawi, a country in southern Africa with the current population of 17,563,749(8), is one of the least-developed countries in the world (9) and is not spared from antimicrobial resistance. Makoka *et al.,* at Kamuzu Central Hospital, Malawi, in 2012, observed widespread resistance to almost all antibiotics that were empirically used (10). Eighty percent of the isolates were resistant to commonly used antibiotics (10). The resistance trends at Kamuzu Central Hospital are similar to Queen Elizabeth Central Hospital (11), which is not strange as both hospitals are in Malawi.

The WHO Antimicrobial Resistance Global Report on Surveillance showed high resistance rates in bacterial pathogens that cause common hospital, community and food-chain-related infections (7). The increasing prevalence of antibiotic-resistant bacterial infections seen in clinical practice stems from antibiotic use both within human health and veterinary medicine (12). In human medicine, the contributing factor is misuse and overuse of antibiotics whereas in veterinary medicine the contributing factor is use of antibiotics in livestock feed to promote faster growth (12-14). Additional factors that contribute to the problem of antimicrobial resistance include the availability of antimicrobial drugs without prescriptions and inappropriate physicians' prescriptions (15). The impact of irrational antibiotic use in pediatric population are drug-resistance, adverse drug reactions (ADRs) and unnecessary medical costs which leads to increased mortality and morbidity among the young children (16-18).

Unfortunately, there are few studies conducted to assess the antibiotic prescribing pattern and prudent utilization of microbiological test results of common bacterial infections in Malawi. Health care workers play a vital role in preserving the power of antimicrobial medicines (5). If they lack up-to-date information about AMR, they may not diagnose the infection before prescribing but, instead, will yield to patient pressure to prescribe antibiotics which may be inappropriate (5). In line with this, in 2015 the World Health Assembly endorsed a Global Action Plan (GAP) to tackle antimicrobial resistance, of which Malawi is a signatory (5). In 2017, Malawi developed and adopted the antimicrobial resistance strategy plan to provide guiding principles for the implementation of antimicrobial stewardship. This study was conducted to assess antibiotic prescribing patterns and utilization of microbiological test results of common bacterial infections in under-five year's old inpatients at Ntchisi District Hospital, Malawi to utilize the data in policy formulation for antimicrobial in Malawi.

Methodology

Study site and sample:

According to Malawi National Statistical Office 2018 data, Ntchisi had a general population of 317,069 of which 162,636 are children under the age of 16 years. This study was conducted in the pediatric ward at Ntchisi District Hospital, a 224-bed public hospital. The pediatric ward has a 54-bed capacity and admits about 3,944 children annually. This study enrolled inpatients aged 1-59 months, who were prescribed antibiotics in the pediatric ward. In-patients are those patients who were admitted due to the severity of their health conditions. Clinicians/physicians assess all patients on the severity of diseases from those that patronize Ntchisi hospital including those referred from the surrounding twelve primary health facilities within the Ntchisi district. For severe cases, the patients are initially admitted to the primary health facility and then referred as inpatients to Ntchisi District Hospital.

Study design and data collection tools:

This was a prospective cross-sectional hospital-based study and Davie Kondowe (the researcher) collected the data. A structured questionnaire was used to collect information prospectively from inpatient records/files. First, when the child came to the ward from the outpatient department, the files /patients records were screened for study eligibility. The eligibility criteria were a child between 1 and 59 months, having been prescribed an antibiotic, being admitted in the pediatric ward, and parent/guardian consent. Thereafter, parents/guardians were asked for consent to allow the researcher to collect information from hospital admission files/ records of their children. After consent was granted, the researcher collected the information by filling the structured questionnaire. Missing child demographic information in patients' files was obtained by asking parents/guardians. The participants were followed until discharge, once the information on initial contact was collected and recorded, Data were collected from September 2020 to November 2020.

Data collected included demographics (age, sex), body weight and temperature, antibiotic prescription information (antibiotic indication, antibiotic choice, dose and route of administration), utilization of microbiological test results (requests for microbiological tests, sample processing turnaround time, availability of microbiological test results, utilization of the microbiological results by the prescriber) and the qualification and experience of the prescriber. In addition, we checked the appropriateness of the antibiotic concerning the dosage and the duration, whether the treatment was in line with Malawi Standard Treatment Guidelines or Integrated Management of Childhood Illness (IMCI) guidelines.

Data analysis

SPSS IBM version 20.0 software and Microsoft Excel 2013 were used to analyze data. Descriptive statistics were used to determine the antibiotic prescribing pattern and utilization of microbiological laboratory test results. A *Chi-square test* was used to compute statistical significance between variablesand the correlation between antibiotic prescribing patterns and utilization of microbiological test results. Excel was used to analyze demographic information.

Ethical considerations

Ethical approval was obtained from the College of Medicine Research and Ethics Committee (COMREC) protocol number **P.06/20/3067.** Ntchisi Hospital Research Committee and Ntchisi District Health Management Team (DHMT) also provided support letters for the study. Participation in the study was voluntary. Parents/guardians were asked for permission to collect information from the hospital charts of their children and also provide any other relevant information which was missing in the hospital charts. The participants were assured of privacy and confidentiality of their information. Names were not used in the final analysis, instead, the participants were assigned a study Participants identity (PID) number. The safety of participants was ensured as the study didn't involve any invasive procedures or changes in management.

Results

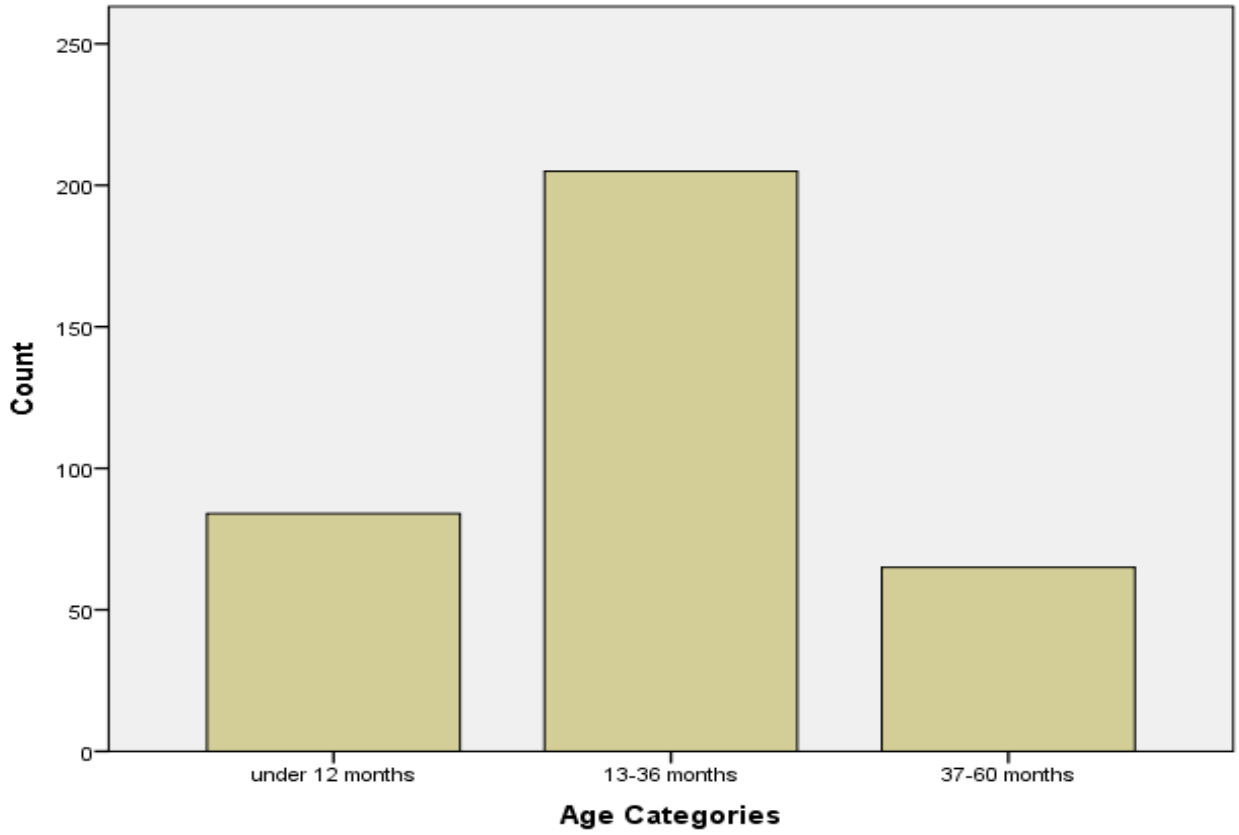
Demographic characteristics and common infection

Three hundred eighty five participants were approached to be enrolled in the study, but only 373 participants consented (96.9%). 168(45%) of participants were female and 205(55%) were male. **Error! Reference source not found.** shows the prevalent infections and key demographic information about the study participants. Majority of the participants were aged between 13 and 36 months (205 patients) as shown in figure 1.

Table 1: Showing common infections and vital statistics

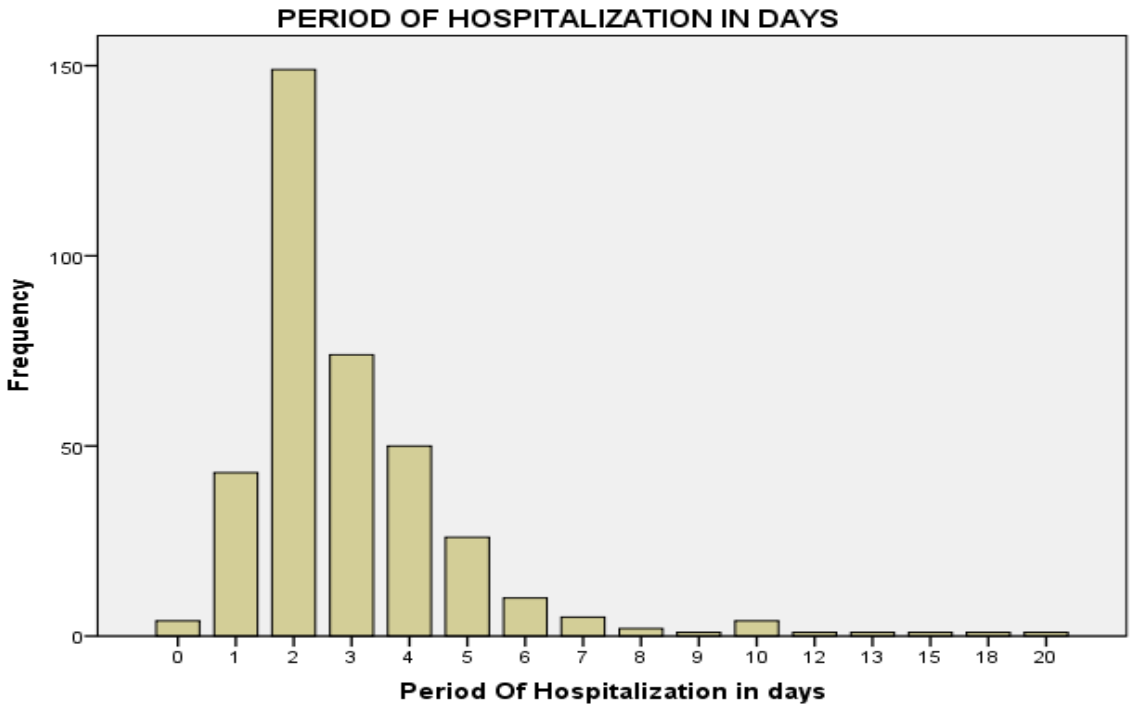
Common Infections	**Number of Cases**	**Mean Age (Months)**	**Mean Weight (Kgs)**	**Mean Temperature (^{o}C)**
Sepsis	155(41.6%)	25.9	11.0	37.7
Meningitis	20(5.4%)	32.2	12.2	37.6
Pneumonia	111(29.8%	19.2	9.8	37.2
Malaria	87(23.3%)	24.0	10.5	37.7
Grand Total	**373(100%)**	**23.8**	**10.6**	**37.6**

Figure 2: Bar chart showing the participants age range frequencies



The median hospital stay per child was 2 days with an interquartile range between 2 and 4 days. Very few patients were admitted beyond ten days, as shown in figure 2.

Figure 3: Bar Chart showing number of days of hospitalization per participant



Antibiotic prescribing pattern

The study enrolled 373 participants who were prescribed antibiotics. Among these participants, 76.7 %(286) were prescribed antibiotics in accordance to Malawi Standard Treatment Guidelines (MSTG-2015) or Integrated Management of Childhood Illnesses (IMCI) and 23.3% (87) were not (p=<0.001. The most frequently prescribed antibiotics were Benzyl penicillin and gentamicin 276(74.0%), followed by ceftriaxone 87(23.2%) and metronidazole 10(2.7%) as shown in table 2.

Table 2: Diagnosis and prescribed treatment on admission

Prescribed antibiotic / **Diagnosis**	Benzyl penicillin (ATC code: J01CE01)& Gentamicin (J01GB03)	Ceftriaxone (ATC=J01DD04)	Metronidazole (J01XD01)	**Total**
Sepsis	119(76.8%)	31(20.0%)	5(3.2%)	155(41.6%)
Meningitis	1(5.0%)	19(95.0%)	0(0.0%)	20(5.4%)
Pneumonia	101(91.0%)	10(9.0%)	0(0.0%)	111(29.8%)
Malaria	55(63.3%)	27(31.0%)	5(5.7%)	87(23.2%)
Total	276(74.0%)	87(23.3%)	10(2.7%)	373(100%)

Average number of prescribed drugs per patient was 2.8 with a minimum of 1 drug per patient and a maximum of seven prescribed drugs per patient. Antibiotics were prescribed by generic name and the frequency of duration of the antibiotic treatment is shown in the table 3 below. Majority of patients received antibiotics for three days.

Table 3: Showing duration of antibiotic treatment

Duration of antibiotic Treatment					
Number of day on antibiotics		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<1 day	47	12.6	12.6	12.6
	2-3 days	222	59.5	59.5	72.1
	4-5 days	77	20.6	20.6	92.8
	6-7 days	15	4.0	4.0	96.8
	8-14 days	9	2.4	2.4	99.2
	>14 days	3	.8	.8	100.0
	Total	373	100.0	100.0	

Table 44 shows prescribing habits among clinicians based on their qualifications and experience. There were seven clinicians who were involved in prescribing in the pediatric ward four of whom had Diploma in Clinical Medicine (senior prescribers) while three had Certificate in Clinical Medicine (junior prescribers). The majority of prescriptions were written by junior prescribers (68.6%, 256) and most of them adhered to MSTG/IMCI. Prescribers with 1 to 5 years' experience prescribed the most antibiotics (45.31%, 169).

Table 4: Prescriptions analyzed by Qualification & experience of prescriber

		Antibiotic Prescribing			Total	
		Benzyl penicillin & Gentamicin	Ceftriaxone	Metronidazole		
Qualification Of Antibiotic Prescriber	Certificate in clinical medicine	197(77.0%)	51 (19.9%)	8 (3.1%)	256 (68.6%)	
	Diploma in clinical medicine	79 (67.5%)	36 (30.8%)	2(1.7%)	117 (31.4%)	
Total		276 (74.0%)	87(23.3%)	10 (2.7%)	373(100%)	
Experience Of Antibiotic Prescriber	Intern	87 (72.5%)	29 (24.2%)	4 (3.3%)	120 (32.2%)	
	<1 Year	17 (56.7%)	12 (40.0%)	1 (3.3%)	30 (8.0%)	
	1-5Year	130 (76.9%)	34 (20.1)	5 (3.0%)	169 (45.3%)	
	>5Years	42 (79.3%)	12(22.2%)	0 (0.0%)	54 (14.5%)	
Total		276 (74.0%)	87 (23.3%)	10 (2.7%)	373 (100%)	

Utilization of microbiological test results

Most antibiotics were empirically prescribed. 318 of 373 cases (85.3%) had no microbiological tests requested, table 5. Only 55 (14.8%) cases had samples sent for laboratory analysis (p=<0.001). Eighteen (90%) out of twenty meningitis cases had microbiological tests sent to the laboratory but no sample had a confirmed disease-causing microorganism. Eighteen of 155 Sepsis cases (11.6%) and 16 of 87 malaria cases (18.4%) had samples sent for microbiological tests and no sample had a confirmed presence of disease-causing bacteria. Pneumonia cases had the fewest tests, 3 out of 111(2.7%, p=<0.001)

Despite microbiological test results failing to prove bacterial infection, the prescribed treatment was not changed by the prescribers.

Table 5: Microbiological tests according to diagnosis.

Diagnoses	Requested Microbiological Tests			Utilization Of Microbiological test Result		Total	P-value
	No	Yes		No	Yes		
Sepsis	137 (88%)	18 (12%)		153 (99%)	2(1%)	155(42%)	<0.001
Meningitis	2 (10%)	18 (90%)		19(95%)	1 (5%)	20 (5%)	
Pneumonia	108 (97%)	3 (3%)		110 (99%)	1(1%)	111 (30%)	
Malaria	71 (82%)	16 (18%)		79 (91%)	8 (9%)	87(23%)	
Total	318 (85%)	55 (15%)		361 (97%)	12(3%)	373 (100%)	

Discussion

Antibiotics play a crucial role in the treatment of serious infectious diseases. Regular assessment of antibiotic prescribing and utilization of microbiological tests would help to know the magnitude of the problem of irrational antibiotic use and hence deal with the fight against antimicrobial resistance. This study looked at the antibiotic prescribing pattern, utilization of microbiological test results, and correlation between the two. This is an even important study as it looked at the public/government health facility where treatment including medicines is provided to patients free of charge.

According to Malawi Standard treatment Guidelines (MSTGs) (19) and IMCI Guidelines: first-line treatment for sepsis and pneumonia is a combination of benzylpenicillin and

gentamicin which were appropriately prescribed in 76.8 % cases of sepsis and 91.0% cases of pneumonia respectively.

First-line treatment for meningitis was ceftriaxone which was appropriately prescribed in 95.0% of cases but prescribing for malaria did not follow the MSTGs (19). 23.2% of antibiotics were used in malaria cases without co-existing conditions being diagnosed (or noted on case file) by the clinicians. This is however lower than findings from Uganda which found 32% of prescriptions for malaria had an antibiotic prescribed without any bacterial infection (20). The lack of documentation of the reasons as to why antibiotics were prescribed in malaria cases is a worrying trend as people may assume that it was irrational use of antibiotics (even though in some cases it might be appropriate). This therefore, calls for policymakers to be conducting refresher courses on good prescribing habits.

The majority of the participants have appropriately prescribed antibiotics, but 23.3% were not prescribed antibiotics according to Malawi standard treatment guidelines (MSTG) (19). The non-adherence to guidelines found in this study was similar to studies in South Africa and Pennsylvania, USA that found the use of antibiotics in non-bacterial infections (21). According to Malawi standard treatment guidelines, the treatments for malaria are antimalarial drugs (19). However, in this study malaria cases were prescribed antibiotics without information on whether there was a co-morbidity with an infection. A study in India by Pradeekamur et al. (2017), found similar results albeit in a different country (22).

The most prescribed antibiotics were a combination of benzylpenicillin and gentamicin which was prescribed in 74% of the participants, followed by ceftriaxone which was prescribed in 23.3 % of the participants. This is different from a (2014) study in Saudi Arabia by Alakhali and Mohammad (23) which found cephalosporins to be the most frequently (52%) prescribed antibiotic, followed by aminoglycosides (17.3%) and penicillins (12.5%). A similar observation was made in Nepal by Palinke (2004) (24). This difference might be the result of different settings as well as differences in standard treatment guidelines.

To reduce inappropriate antimicrobial use, WHO recommends that antibiotics should be prescribed based on antibacterial classification groups which are Access, Watch, Reserve (AWaRe) (25,26). This was developed as an antibiotic stewardship tool to assist in the classification of antibiotics to be used at the local, national, and global level. Malawi follows this antibiotic classification. According to Malawi standard treatment guidelines (MSTG), the first-line treatment for sepsis is a combination of benzylpenicillin and gentamicin (19). In this study, 76.8% (Table 2)) of the sepsis cases were started on first-line antibiotics and out of 20 meningitis patients, 19 correctly received ceftriaxone as the first line treatment. Despite this, some cases were inappropriately prescribed metronidazole as first line antibiotic. 31% (N=155) of sepsis cases were prescribed second line antibiotic before first line treatment. 23.3% (N=87) of malaria patients were

prescribed antibiotics in addition to the antimalarial medicine without an additional diagnosis of infection.

Microbiological test results were not fully utilized in this study. 82% of antibiotic prescriptions were made without microbiological tests. Even in those cases where the clinician requested microbiological tests, there was no indication of the utilization of the result, neither was there any change in the prescribed antibiotic. This is similar to a study done in Ethiopia by Feleke et al. (2013) (27), which found that antibiotic prescribing was done purely empirically. In that study, only 14.75% of participants had microbiological tests requested. Unfortunately among those, there was no utilization of the results. These findings were similar to a study in Zambia by Hangoma (2014) who found that only 31.4% (n=86) participants had microbiological tests ready at the time of the review of the participants (28).

Our study showed that all microbiological samples were negative for bacteria by microscopy. This raises the competency of the laboratory capacity at the facility. Ntchisi hospital, being the secondary level-care facility responsible for the whole district, is supposed to have an improved laboratory capacity where the majority of microbiological testing should be done. However, the hospital did not have the capacity as such failing to do these basic microbiological tests which are key in aiding in rational antimicrobial prescribing. This raises questions about the reliability and value of the tests since culture and sensitivity testing is not available. This may explain the reluctance of prescribers to request tests or to change prescribing based on a negative finding.

As a way of mitigating insufficient utilization of microbiological test, we suggest a new point of care biomarker diagnostic approach that would aid prescribers in making clinical diagnoses. In terms of prescribing habits, our study findings of 2.8 prescribed drugs per patient is higher than the WHO indicators which recommends less than 2.0 prescribed drug per patient (29). This prescribing habit is higher than findings from several African countries, 2.14 in Ethiopia (30-32), 1.76 in Eritrea (33), 1.99 in Tanzania (34), 2.3 in Pakistan (35). The 2.8 prescribed drugs per patient might seem as poly pharmacy in WHO's categorization (36), but a closer look and comparison with other African, counties, there is a similar trend with a systematic analysis conducted in 2016 for African region finding that on average, African countries prescribes 3.1 drugs per patient per encounter (37). In addition majority of the studies on number of prescribed medicines per patient are those assessed on outpatient adult population, while our study was done on in-patients as well as pediatric patients, therefore a caution on this comparison should be understood.

Limitations

This study was in one department of one hospital and cannot be generalized to the whole of Malawi, or adults. Nonetheless, we believe it may reflect conditions more generally.

Conclusion

Generally, the study observed appropriate empirical antibiotic prescribing, but with limited utilization of microbiological tests. Further studies are required to explore the integration of biomarker-guided-antibiotic therapy into the empirical clinical algorithm.

Competing interests: The authors have declared that no competing interests exist.

Data Availability Statement: All relevant data are within the manuscript.

Author's contributions

Davie Kondowe, Felix Khuluza, Dina MT Kamowa - Conception and design, Acquisition of data, Analysis and interpretation of data

Davie Kondowe, Felix Khuluza - Drafting the article, Critical revision of the article

Felix Khuluza - Final write-up and approval of the version to be published

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Appendix 2: Consent form

INFORMED CONSENT FORM (English version)

Date_____

TITLE: Assessing antibiotic prescribing pattern and utilization of microbiological test results of common bacterial infection in under five inpatients at Ntchisi district hospital.

Principal Investigator: Davie Kondowe

Supervisors : Dr Felix Khuluza

Dina Kamowa

Institution : College of Medicine, Pathology department, University of Malawi.

Introduction

My name is_____ a postgraduate student, studying at University of Malawi College of medicine. I would like to collect information regarding your child's sickness of which s/he is admitted for.

What is the purpose of the study?

The purpose of this study is collect information regarding antibiotic prescribing and utilization of microbiological test results. It's a known fact that antibiotics are important in the treatment of serious infections that affect many people. In addition microbiological test results help clinicians to make certain decision in coming up with the correct diagnosis and treatment for their patients. However inappropriate antibiotic prescriptions

may result in antibiotic resistance. Therefore this study would like to gather information about antibiotic prescription and utilization of microbiological test results in order to assess irrational antibiotic use and suggest new ways to improve it.

What will happen in the study?

I will collect information regarding your child's sickness from the hospital admission file and at some point I will ask you some information that is missing on your child's hospital admission file. There will be no invasive procedures involved with the study. Laboratory test results will be from routine laboratory investigations that admitting clinician request. The information that will be collected include the following:

Demographics (location, age and sex)

Information regarding the prescribed antibiotics and its diagnosis.

Information regarding utilization of microbiological laboratory test results

Participation of your child is voluntary. You may wish not to participate or stop participation in the study at any time. Be assured there will be no penalty and this won't change the hospital care that your child may need.

Is there any benefit in participating in this study?

There is no direct benefit in participating in this study. However participation in the study will help the researcher to gather information that will help to assess the problem of irrational antibiotic use.

How will your privacy be protected?

Privacy and confidentiality of your child's information will be maintained at all times. The information collected from your child will be anonymized, (that is numbers will be used instead of names) so that s/he won't be recognized in the database. The information that will be collected will be used only for the purpose of this study

Who should you contact if you have questions or you need more information about the study?

Further information about this study or regarding your rights as study subject can be obtained from the Institutional Review Board (College of Medicine Research and Ethics Committee) by contacting:

The Chairman

College of Medicine Research and Committee, University of Malawi.

Private Bag 360,

Chichiri, Blantyre, Malawi

Cell: + 265888118993

To report any injury or harm that you feel is due to your participation in this study, please contact:

The principal investigator (Davie Kondowe),

University Of Malawi College of Medicine –Pathology Department,

Private Bag 360,

Chichiri, Blantyre 3

Cell: +265993465284PART A: LITERATE PARTICIPANT SIGNATURE: DATA COLLECTION INFORMED CONSENT

TITLE: Assessing antibiotic prescribing pattern and utilization of microbiological laboratory results in under five in patient at Ntchisi district hospital.

Principal Investigator: Davie Kondowe

Supervisors : Dr Felix Khuluza

Dina Kamowa

Parent's/Guardian's Agreement:

If you have read this informed consent or have had it read or explained to you, and understand the information and you voluntarily give permission to allow your child to participate in this study please sign your name or make a mark below.

_____

Printed name of participant (child)

_____

Printed name of parent/guardian

_____ _____

Signature of parent/guardian Date

OR

PART TWO:

ILLITERATE PARENT/GUARDIAN SIGNATURE: DATA COLLECTION INFORMED CONSENT

TITLE: Assessing antibiotic prescribing pattern and utilization of microbiological laboratory results in under five in patient at Ntchisi district hospital.

Principal Investigator: Davie Kondowe

Supervisors : Dr Felix Khuluza

Dina Kamowa

Parent's /guardian's Agreement:

If you have read this informed consent or have had it read or explained to you, and understand the information and you voluntarily give permission to allow your child to participate in this study please sign your name or make a mark below.

_____

Printed name of participant (child)

_____

Printed name of parent/guardian

_____ _____

Thumb print of parent/guardian Date

Witness of illiterate parent/guardian:

I attest that the information contained in this written consent form have been read and explained to participant's parent/guardian's/he appears to understand purpose, procedures, risk and benefits of data collection and has voluntarily accepted to participate in the study.

For those placing a thumbprint: I attest that the parent/guardian who states that his/her name is_____ has placed his/her thumbprint on this consent form of his/her own free will on this day_____

_____ _____

Name of witness Date

Staff:

I have explained the purpose of the study to the participant's parents/guardians and have responded to all the questions that were asked. I believe to the best of my knowledge the parents/guardians understands the purpose, procedures, risks and benefits of the study.

_____ _____

Study staff conducting consent discussion Study staff signature and date

INFORMED CONSENT FORM (Chichewa version)

KALATA WA CHILOLEZO

Tsiku_____

Kafukufuku IRB# Kalata wa chilolezo: version 1.0 27 February 2020

Mutu wa Kafukufuku: Kufufuza m'mene mankhawala amapelekedwera ndi m'mene zotsatira zoyezetsa matenda zimagwiritsidwira ntchito kwa ana odwala ochepera zaka 5 amene agonekedwa pa chipatala cha Ntchisi ku Malawi

Otsogolera Kafukufuku: Davie Kondowe -mwana wa sukulu ku sukulu yaukachenjede yosula madokotala ku Malawi ya College of medicine.

Otsogolera Kafukufuku ena: Dr Felix Khuluza Mphunzitsi wamkulu ku sukulu yaukachenjede yosula madokotala ku Malawi ya College

of Medicine

Ms Dina Kamowa Mphunzitsi wamkulu ku Sukulu yaukachenjede yosul Madokotala Ku Malawi ya College

of medicine

Opereka thandizo la chuma: College of Medicine

Nambala ya foni ya wopanga kafukufuku: +265993465284

Mawu Oyamba

Dzina langa ndi_____ mwana wa sukulu amene ndikuphunzira ku sukulu yosula madokotala ya ku Malawi ya College of medicine. Ndikufuna kutolera uthenga wokhuzana ndi mankhwala ndi matenda amene mwana wanu adotokotala amulembera.

Cholinga cha kafukufuku

Cholinga cha kafukufuku uyu ndikutolera uthenga m'mene mankhwala amaperekedwera ndi m'mene zotsatira zoyedzetsa matenda zimagwiritisdwira ntchito ndimadokotala. Ndifundo yodziwikiratu kuti mankhwala ndiwofunika pochiza matenda ovuta kwambiri amene amakhuza anthu ambiri. Moonjedzera, zotsatira zoyeza matenda zimathandiza madokotala popanga chiganizo chosimikizika kuti apeze matenda ndi mankhwala enieni awodwala. Ngakhale izi zili chomwechi, kusagwiritsa ntchito bwino mankhwala ku kubweretsa vuto loti mankhwala sakuthanso kuchiza matenda m'mene ziyenera kukhalira.Nchocho kafukufukuyu akufuna kutolera uthenga m'mene mankhwala amaperekedwera ndiponso m'mene zotsatira zoyedzetsa matenda zimagwiritsidwira ntchito ndi madotokotala kuti tione m'mene vuto losagwiritsa ntchito bwino mankhwala lili ndi kuganiza za njira za tsopano zothesera vuto limeneli.

Kodi chizachitike ndi chani mkafukufukuyu?

Ndizatolera uthenga okhuza matenda a mwana wanu pa chikalata chake chachipatala ndipo nthawi zina ndizakufunsani uthenga womwe ukusowekera pa chikalata chachipatala cha mwana wanu. Mkafukufukuyu simkhala ndondomeko zoti zinga

phweteke mwana wanu. Zotsatira za zoyeza ku laboratore zizichokera ku zoyetsa za kulaboratore zomwe a chipatala amapanga kale. Uthenga umene uzatoleredwe ndi uwu:

Kuziwa zaka za mwana and ndikumene akukhala ndiponso kuziwa kuti mwana ndiwamuna kapena wamkazi

Uthenga wokhudzana ndi mankhwala ndi matenda womwe a dokotala amulembera mwana wanu.

Uthenga wokhudzana ndi m'mene zotsatira zoyedzetsa matenda zimagwiritsidwira ntchito ndi madokotala.

Kutenga nawo mbali mkafukufukuyu ndikufuna kwanu. Mkhoza kusankha kusatenga nawo mbali mkafukufukuyu kapena kusiwa kutenga nawo mbali nthawi yina yiliyonse. Muliolimbikitisidwa kuti mkatero palibe chilango china chili chonse ndipo chithandizo chanu chachipatala sichizasintha.

Kodi pali phindu lina lililonse potenga nawo mbali mkafukufukuyu?

Palibe phindu lodziwikiratu potenga nawo mbali mkafukufukuyu. Komabe kutenga nawo mbali kwanu mkafukufukuyu, kudzathandiza ofufuza kuti apeze uthenga womwe udzathandizire kuona vuto losagwiritsa ntchito bwino mankhwala ndiku thandizira amene amakonza ndondomeko zakagwiritsidwe kabwino kamankhwala kuti apange ziganizo zabwino zakagwiritsidwe kabwino ka mankhwala.

Kodi chinsinsi chanu chizasungidwa bwanji?

Nchinsi cha uthenga wa mwana wanu chizakhala chotetezedwa nthawi zonse. Uthenga womwe uzatoleledwe kwa mwana wanu uzabisidwa pogwiritsa ntchito manambala m'malo mwa mayina ndicholinga choti wina asazindikire. Uthenga womwe uzatoleledwe uzagwiritsidwa ntchito mkafukufukuyu basi.

Kodi mkhoza kulumikizana ndi ndani ngati muli ndi mafunso kepena mkufuna kudziwa zambiri za kafukufukuyu?

Uthenga owonjezera wokhuzana ndi kafukufukuyu kapena uthenga wokhuzana ndi ufulu wanu ngati wotenga nawo mbali mkafukufuku, mkhoza kuupeza kuchokera ku mbungwe loyang'anira kafukufuku la Institutional Review Board(College of Medicine research and Ethics committee) powalembera kalata pa keyala iyi:

Wapampando

College of Medicine Research and Ethics Committee, University of Malawi,

Private Bag 360,

Chichiri, Blantyre 3,

Cell: +265888118993

Kuti mpereke uthenga wokhuzana ndi kuvulala kapena kupwetekeka komwe inu mkuganiza kwabwera chifukwa chakafukufukuyu, chonde dziwitsani:

Wamkulu wakafukufuku

University of Malawi, College of Medicine- Pathology department

Private Bag 360,

Chichiri, Blantyre 3

Tel: +2651871911 cell: +265993465284

GAWO A: SAYINI YA WOTENGA MBALI MKAFUKUFUKU WOZIWA KULEMBA NDI WERENGA

Mutu wa Kafukufuku: Kufufuza m'mene mankhawala amapelekedwera ndi m'mene zotsatira zoyezetsa matenda zimagwiritsidwira ntchito kwa ana odwala ochepera zaka 5 amene agonekedwa pa chipatala cha Ntchisi ku Malawi

Otsogolera Kafukufuku: Davie Kondowe mwana wa sukulu ku sukulu yaukachenjede yosula madokotala ku Malawi ya College of medicine.

Otsogolera Kafukufuku ena: Dr Felix Khuluza Mphunzitsi wamkulu ku sukulu yaukachenjede yosula madokotala ku Malawi ya College of Medicine

Ms Dina Kamowa Mphunzitsi wamkulu ku Sukulu yaukachenjede yosula madokotala Ku Malawi ya College of medicine

Mgwirizano ndi kholo/woyang'anira

Ngati mwawerenga chikalata chachilolezochi kapena mwawerengeredwa kapena kufotokozeredwa ndipo mwamvetsa uthengayu ndipo mwakufuna kwanokha mwapereka chilolezo kuti mwana wanu atenge nawo mbali mkafukufukuyu, chonde sayinani dzina lanu kapena yikani chidzikilo m'msimu:

_____

Lembani Dzina la mwana

_____

Lembani Dzina la Kholo/oyanga'nira

_____ _____

Sayini Tsiku

KAPENA

GAWO B: SAYINI YA WOTENGA MBALI MKAFUKUFUKU WOSAZIWA KULEMBA NDI KUWERENGA

Mutu wa Kafukufuku: Kufufuza m’mene mankhawala amapelekedwera ndi m’mene zotsatira zoyezetsa matenda zimagwiritsidwira ntchito kwa ana odwala ochepera zaka 5 amene agonekedwa pa chipatala cha Ntchisi ku Malawi

Otsogolera Kafukufuku: Davie Kondowe mwana wa sukulu ku sukulu yaukachenjede yosula madokotala ku Malawi ya College of medicine.

Otsogolera Kafukufuku ena: Dr Felix Khuluza Mphunzitsi wamkulu ku sukulu yaukachenjede yosula madokotala ku Malawi ya College of

Medicine

Ms Dina Kamowa Mphunzitsi wamkulu ku Sukulu yaukachenjede yosula madokotala Ku Malawi ya College of

Medicine

Mgwirizano ndi kholo/woyang’anira

Ngati mwawerenga chikalata chachilolezochi kapena mwawerengeredwa kapena kufotokozeredwa ndipo mwamvetsa uthengayu ndipo mwakufuna kwanokha mwapereka chilolezo kuti mwana wanu atenge nawo mbali mkafukufukuyu, chonde sayinani dzina lanu kapena yikani chidzikilo m’msimu:

_____

Lembani Dzina la mwana

_____

Lembani Dzina la Kholo/oyanga’nira

_____ _____

Chidindi cha chala cha kholo/oyanga’nira Tsiku

Ogwira ntchito:

Ndafotokozera cholinga chakafukufuku kwa makolo/oyanga’nira wotenga nawo mbali mkafukufuku ndipo ndayankha mafunso onse omwe anafunsidwa. Ndili ndichikhulupiliro mmene ndimadziwira kuti makolo/oyanga’nira amvetsetsa cholinga, ndondomeko, chiopsezo ndi ubwino wotenga nawo mbali mkafukufukuyu.

_____ _____ _____

Dzina la ogwira ntchito Sayini Tsiku

Mboni Ya kholo/oyanga’nira wosaziwa Kuwerenga

Ine ndikuperekera umboni kuti uthenga umene uli mchikalata chachivomelezochi wawerengedwa ndi kufotokozeredwa kwa makolo/oyanga’nira otenga mbali mkafukufuku, ndipo akuonetsa kuti amvetsa cholinga, ndondomeko, chiopsezo ndi ubwino otolera uthenga ndipo mwakufuna kwaokha amvomereza kutenga nawo mbali mkafukfukuyu.

Kwa amene akuyika chidindo chachala: Ndikuperekera umboni kuti kholo/oyanga’nira amene akunena kuti dzina lake ndi _____ wayika chidindo chachala pakalalata yachivomelezochi mwakufuna kwayekha pa tsiku la _____

Dzina la mboni	Sayini	Tsiku

Appendix 3: Structured questionnaire

Demographics

Name of hospital_____ admission Number_____

Age (in months)_____

Sex: Male ☐ Female ☐

Date of birth:____/_____/_____

Date of admission____/_____/_____ Time of admission_____

Screening and enrollment (circle or fill in blank spaces the correct answer)

Is any antibiotic prescribed for the child on admission to the hospital?

Yes

No

If the response is "YES" then proceed to QUESTION 3; if the response is "NO" then stop.

Is consent/permission obtained from the parents/guardians to collect information from their child's admission form and laboratory results sheets?

Yes

No

If the response is “YES” then proceed with the enrollment process of the child but, if the response is “NO” stop the enrollment process.

Assign Participant ID_____

Patient admission

Was body temperature measured on hospital admission?

Yes

No

If yes, what was the body temperature, on admission?._____

Was the weight of the child measured?

Yes

No

If yes, What was the weight of the child?_____

Was the initial diagnosis of child made on admission?

Yes

No

If Yes, What was the initial diagnosis of child on admission?

_____

What is the type of infection?

Bacterial

Viral

Fungal

Helminths

Other

Was the initial antimicrobial agents prescribed based on the preliminary diagnosis?

Yes

No

Utilization of microbiological test results

Was microbiological test requested to confirm the identified diagnosis?

Yes

No

What is the requested microbiological test?

_____

Was the microbiological test analyzed?

Yes

No

If the response is "YES" indicate the results _____

_____

If the response is "NO" give a reason why the requested bacteriological test was not performed by selecting one or more of the following?

Lack of equipment

Lack of reagent

Lack of laboratory personnel

Other

Did the results confirm bacterial infection?

Yes

No

If "YES" did the prescribing clinician utilize the bacteriological test result to change or maintain the initial diagnosis?

Yes

No

Antibiotic prescribing

Was antibiotic prescribed for the patient for the identified diagnosis on admission?

Yes

No

What is/are the name(s), route of administration and dosage of the prescribed antibiotic?

Name_____

Route_____

Dosage_____

What is the type of antibiotics?

_____

Was the duration of the prescribed antibiotic indicated?

Yes

No

What is the indicated duration of the prescribed antibiotics?

_____

Summary of antibiotic prescribing

Was the choice of the prescribed antibiotic correct based on Malawi Standard Treatment Guidelines (MSTG)

Yes

No

Was dosage of prescribed antibiotic correct based on MSTG?

Yes

No

Was the duration of the prescribed antibiotics correct based MSTG?

Yes

No

What is the qualification of the prescribing clinician/doctor?

Certificate in Clinical Medicine

Diploma in Clinical Medicine

Degree in Clinical Medicine

Doctor (MBBS)

Others (specify)

What is the experience of the prescribing clinician/doctor?

Intern

<1 year

1-5 years

>5 years

Discharge summary

What is the final diagnosis of the child on discharge?

_____

What is the duration of hospital admission of the child in days?

_____

Was the course of the prescribed antibiotic completed on discharge?

Yes

No

Are bacteriological laboratory results for the child available on discharge?

Yes

No

If the results are available on discharge, what was turnaround time? (select one of the following)

0-6 Hours

>6-24 Hours

> 24 Hours

What is discharge outcome of the child?

Alive

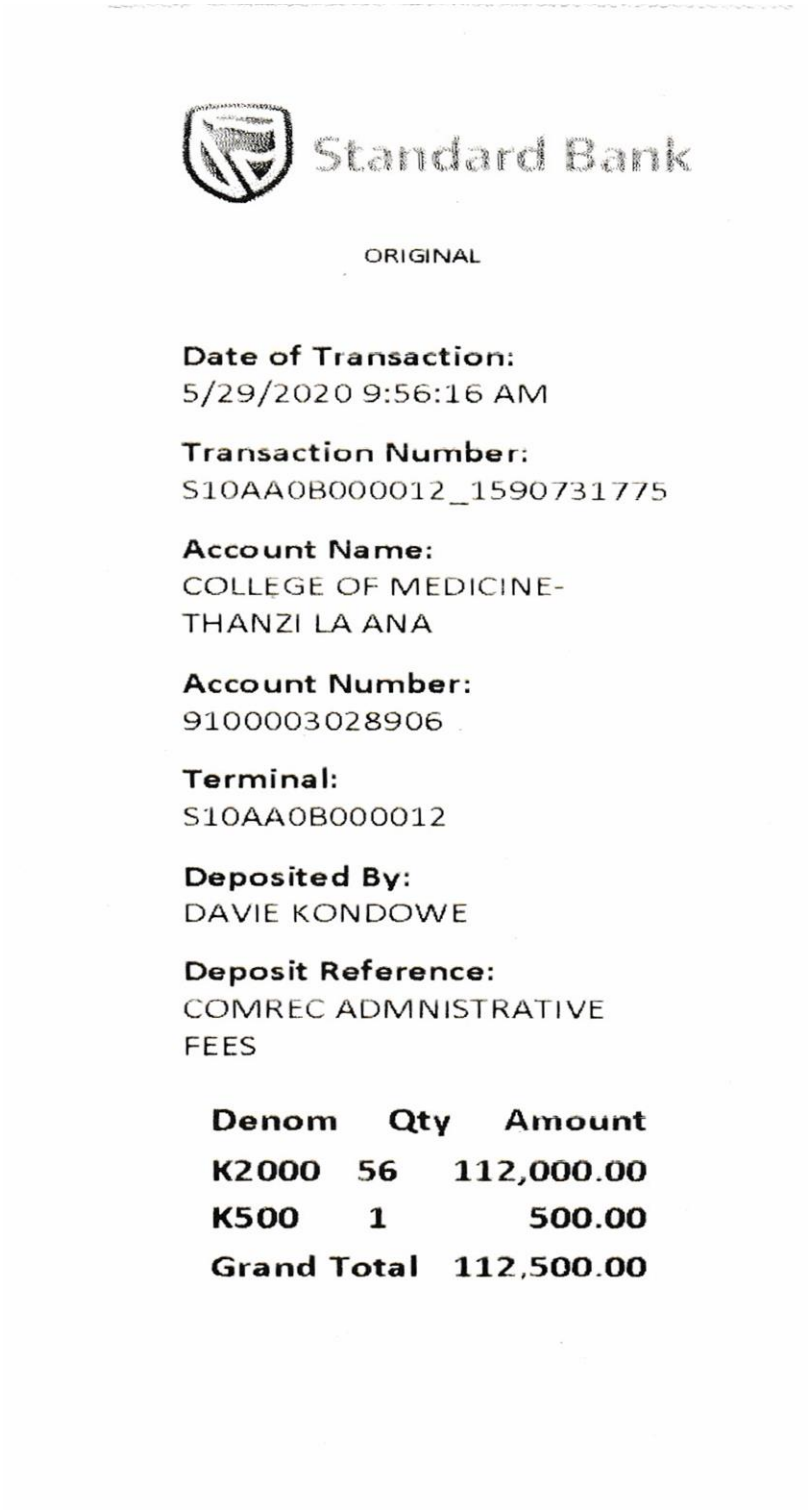
Abscond

Died

Referred

Record the discharge date _____/_____/_____

Appendix 4: COMREC administrative fee receipt



Standard Bank

ORIGINAL

Date of Transaction:
5/29/2020 9:56:16 AM

Transaction Number:
S10AA0B000012_1590731775

Account Name:
COLLEGE OF MEDICINE-
THANZI LA ANA

Account Number:
9100003028906

Terminal:
S10AA0B000012

Deposited By:
DAVIE KONDOWE

Deposit Reference:
COMREC ADMNISTRATIVE
FEES

Denom	Qty	Amount
K2000	56	112,000.00
K500	1	500.00
Grand Total		112,500.00

Appendix 5: Letter of support from College of Medicine-Pathology Department

COLLEGE OF MEDICINE

Principal

Dr M H C Mipando

Our Ref.:

Your Ref.:

College of Medicine
Private Bag 360
Chichiri
Blantyre 3
Malawi
Telephone: 01 871911
01 874107
Fax: 01 874 70

PATHOLOGY DEPARTMENT

Dr Eric Umar
Chairperson of COMREC
COMREC
University of Malawi
College of Medicine
P/Bag 360
Chichiri
Blantyre 3.

18 May, 2020

Re: Letter of Support for Mr David Kondowe protocol titled: Assessing Antibiotic Pattern and Utilisation of Microbiological Test Result of Common Bacterial Infections in Under Five Children at Ntchisi District Hospital.

I write to support the submission of Mr. David Kondowe protocol to COMREC for ethical clearance. Mr Kondowe is a student at College of Medicine pursuing a Master of Science in Health Sciences - Antimicrobial Stewardship. Mr. Kondowe's protocol aims to prospectively 1) assess the antibiotic prescribing pattern, 2) assess the utilization of microbiological test results and 3) assess the correlation between antibiotic prescribing and utilization of microbiological test results. Mr Kondowe has developed his protocol with support from his supervisors; Dr. Felix Khuluza and Ms. Dina Kamowa and they have recommended submission for ethical clearance. The department of Pathology will support Mr kondowe's project implementation on condition that he is granted clearance by COMREC.

I look forward to your favorable response.

University of Malawi
College of Medicine
18 MAY 2020
Pathology Dept
P/Bag 360, Blantyre

Yours sincerely

Dr Tonney Nyirenda
Course Coordinator

Appendix 6: Letter of support from Ntchisi District Hospital

NTCHISI DISTRICT COUNCIL

All correspondence to be addressed to:

Ntchisi District Health Office
P.O. Box 44, Ntchisi
Phone No.: (265) 994046010
(265) 0882644335

Our Ref:
Your Ref:
Date: March 31, 2020

Email: ntchisidho@gmail.com

The Chairperson,
COMREC
College of Medicine
P/Bag 360, Chichiri,
Blantyre 3, MALAWI

Dear Sir/Madam

LETTER OF SUPPORT FOR A RESEARCH STUDY TITLED: ASSESSING ANTIBIOTIC PRESCRIBING PATTERNS AND UTILIZATION OF MICROBIOLOGICAL TESTS RESULTS OF COMMON BACTERIAL INFECTIONS IN UNDER-FIVE INPATIENTS AT NTCHISI DISTRICT HOSPITAL, MALAWI

I am writing this letter in full support for the research to be conducted by **Mr. Davie Kondowe** and collaborators. The study is expected to reveal that inappropriate antibiotic prescribing is facilitating irrational antibiotic use that in turn accelerates antibiotic resistance in hospital setting. The study has been designed to complement the Malawi antibiotic resistance strategic plan

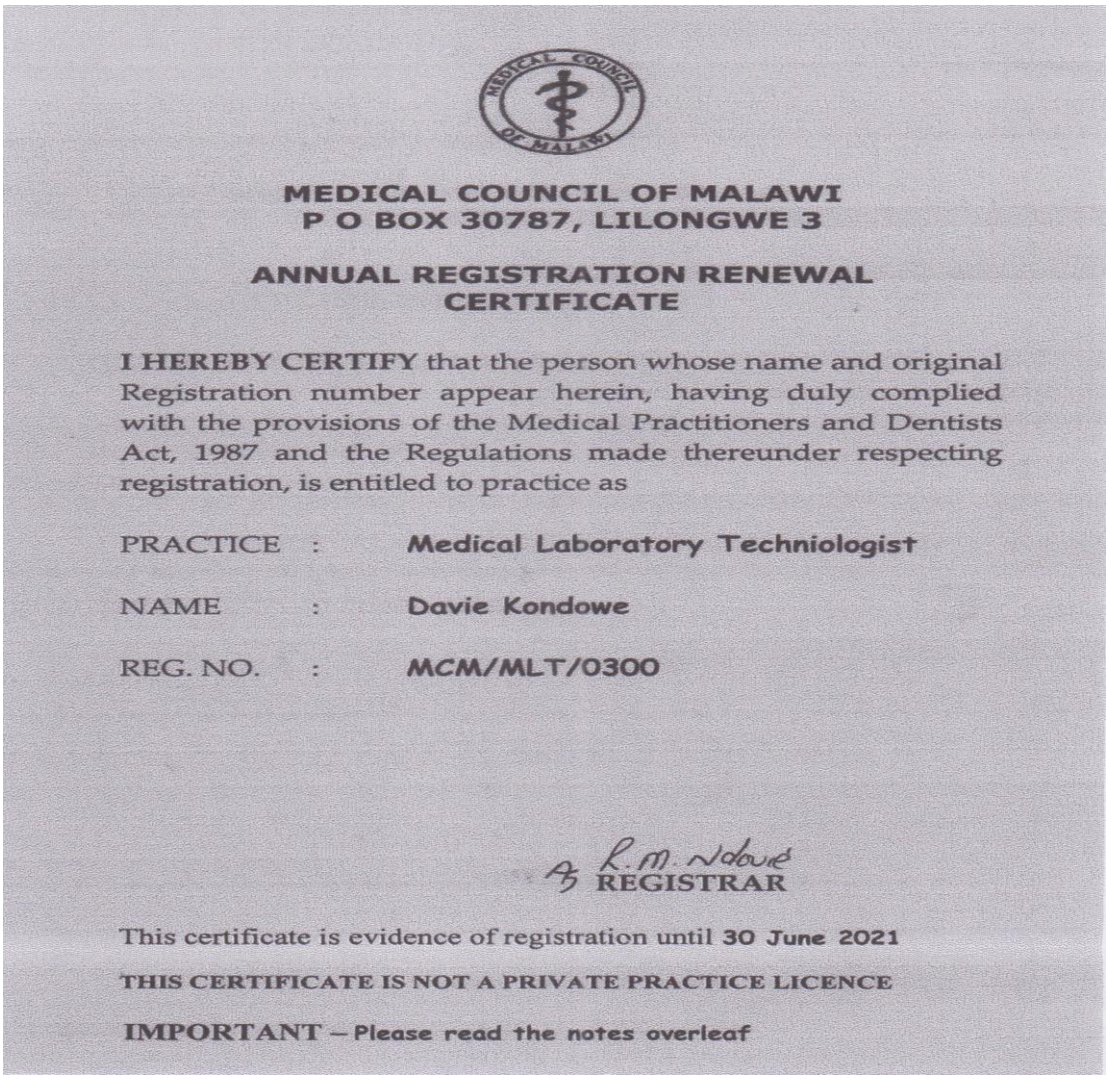
I foresee no conflicts or risks involved with this study, should any concerns arise I shall report to the COMREC.

Yours faithfully,

Dr. Zondwayo Ng'oma
Director of Health and Social Services
Cell: +265 999 375 692
Email: zdngoma@gmail.com

THE DISTRICT HEALTH OFFICER
NTCHISI DISTRICT HOSPITAL
MAR 2020
P.O. BOX 44
NTCHISI

Appendix 7: Evidence of current registration with Medical Council of Malawi



MEDICAL COUNCIL OF MALAWI
P O BOX 30787, LILONGWE 3

ANNUAL REGISTRATION RENEWAL CERTIFICATE

I HEREBY CERTIFY that the person whose name and original Registration number appear herein, having duly complied with the provisions of the Medical Practitioners and Dentists Act, 1987 and the Regulations made thereunder respecting registration, is entitled to practice as

PRACTICE : Medical Laboratory Techniologist

NAME : Davie Kondowe

REG. NO. : MCM/MLT/0300

L.M. Ndovie
REGISTRAR

This certificate is evidence of registration until 30 June 2021

THIS CERTIFICATE IS NOT A PRIVATE PRACTICE LICENCE

IMPORTANT – Please read the notes overleaf