DETERMINANTS OF ADHERENCE TO ANTI-TUBERCULOSIS TREATMENT AMONG PAEDIATRIC PATIENTS IN URBAN KENYA

A DISSERTATION SUBMITTED IN PARTIAL FULLFILMENT OF REQUIREMENTS FOR MASTERS OF PHARMACY IN CLINICAL PHARMACY DEGREE OF UNIVERSITY OF NAIROBI

DR. MARION NYAMOKAMI ONG'AYO

DEPARTMENT OF PHARMACEUTICS AND PHARMACY PRACTICE, UNIVERSITY OF NAIROBI

NOVEMBER 2010

DECLARATION

This dissertation is my original work and has not been presented for a degree in any other university.

Name: Dr. Marion Nyamokami Ong'ayo

Signature:  **Date:** 16TH NOVEMBER 2010

SUPERVISORS' APPROVAL

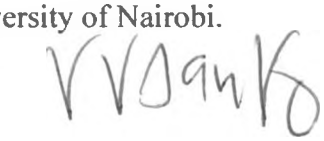
This dissertation has been submitted for examination with our approval as university supervisors.

Name: Dr. George O. Osanjo

Department of Pharmacology and Pharmacognosy,

School of Pharmacy,

University of Nairobi.

Signature:  **Date:** 16/11/2010

Name: Dr. Margaret Oluka

Department of Pharmacology and Pharmacognosy,

School of Pharmacy,

University of Nairobi.

Signature:  **Date:** 16/11/2010

DEDICATION

I am grateful to the Almighty God for giving me strength and knowledge to carry out this work. I would like to dedicate this dissertation to my family, my husband Jarred, my son Andrew and my daughter Maria for their constant love, support and patience throughout the study.

I dedicate this dissertation to my parents Mr. Samuel Ong'ayo and Mrs. Joyce Ong'ayo for their advice, love and encouragement throughout the study. This study is also dedicated to my siblings Anita, Evelyn, Davis and Gerald for their constant support and encouragement.

I dedicate this study to my in-laws Mr. John Nyakiba, Mrs. Agnes Nyakiba and Phyllis Nyakiba for their encouragement throughout the study.

ACKNOWLEDGEMENTS

I am very grateful to the following people whose contributions have made this study a success:

- My supervisor Dr. George O. Osanjo for his generous contribution of the INH test strips which were used to conduct this study and also for his guidance and supervision throughout the study.
- Dr. Margaret Oluka, my supervisor for her guidance, support, encouragement and supervision throughout the study period.
- Kenyatta National Hospital Ethics and Research Committee for reviewing and approving the study to be carried out at the hospital.
- Prof David Scott for his guidance especially during the initial stages of developing the project proposal.
- KNH staff for their assistance and cooperation during data collection.
- My colleagues Dr(s) J.O Nyakiba, P.N. Karimi, S.A. Opanga, G.K. Kenyatta, B. Ogolla, L. Wafula, A. Okeyo, J. Were and M. Kodhiambo for their constant encouragement and moral support during the study.
- Gerald Ong'ayo for his role in data entry
- Mr. Moses Mwangi of Centre for Public Health Research for his role in the data analysis.

TABLE OF CONTENTS

DECLARATION ii

DEDICATION iii

ACKNOWLEDGEMENTS iv

TABLE OF CONTENTS v

LIST OF TABLES viii

LIST OF FIGURES x

ACRONYMS xi

DEFINTION OF TERMS xii

ABSTRACT xiii

CHAPTER ONE: INTRODUCTION 1

CHAPTER TWO 9

2.0: Literature review 9

2.1: Problem statement 15

2.2: Justification 16

2.3: General objective 17

2.3.1: Specific objectives 17

2.4: Research questions 18

CHAPTER THREE: DESIGN AND METHODOLOGY 19

3.1: Area of study 19

3.2: Research design 19

3.3: Target population 19

3.4: Inclusion and exclusion criteria 19

3.5: Ethical consideration.....20

3.6: Sampling procedure and size.....21

3.7: Data collection method.....22

3.8: Determination of isoniazid in urine.....22

3.9: Data management and analysis.....24

3.10: Data quality control.....25

CHAPTER FOUR: RESULTS.....26

4.1 Demographics of the study group.....26

4.1:1 Baseline characteristics of the patients.....26

4.1:2 Level of education among patient's care-givers.....27

4.1:3 Marital status of the patients' care-givers.....28

4.1:4 Occupations of the care-givers and their spouses.....29

4.1:5 The average monthly income of the families.....30

4.2 Rate of adherence to anti- tuberculosis medication at KNH.....31

4.3 Factors contributing to non-adherence to anti-TB medication.....32

4.3.1 Relationship between adherence to TB treatment and baseline characteristics of the patients.....32

4.3.2 Relationship between adherence to anti-TB medication and economic and structural factors of the care-givers.....34

4.3.3 Relationship between adherence to TB medication and patient/caregiver related factors.....36

4.3.4 Relationship between adherence to anti-TB medication and regimen complexity.....47

4.3.5 Relationship between adherence to TB treatment and supportive relationship between health care provider and the caregiver.....50

4.3.6: Relationship between adherence to TB medication and pattern of healthcare delivery.....54

4.3.7: Multivariate analysis of association between marital status and medicine administration at 24 hour intervals and treatment adherence.....56

CHAPTER FIVE: DISCUSSION.....59

5.1: Rate of adherence to anti-TB medication.....59
5.2: Factors contributing to non-adherence to anti-TB medication.....59
5.2.1: Baseline characteristics of the patients.....59
5.2.2: Economic and structural factors contributing to non-adherence to anti-TB medication.....60
5.2.3:Patient/caregiver related factors contributing to non-adherence to anti-TB medication.....62
5.2.4: Regimen complexity factors.....65
5.2.5: Relationship between healthcare provider and caregiver.....66
5.2.6: Pattern of healthcare delivery.....68
5.3: Limitations of the study.....68

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS.....70

REFERENCES.....73

APPENDICES

Appendix I: Questionnaire.....78

Appendix II: Consent and consent information form.....88

Appendix III: Letter of approval from the ethics committee.....92

LIST OF TABLES

Table 1: Level of education of the care-givers.....28

Table 2: Occupation of the care-givers and their spouses.....29

Table 3: Rate of adherence to anti-TB medication as determined by Taxo-INH urine test strips.....31

Table 4: Relationship between adherence to anti-TB medication and baseline characteristics of the patient.....33

Table 5: Relationship between adherence to TB medication and economic and structural factors of the caregivers.....35

Table 6: Respondents knowledge and awareness on TB.....37

Table 7: Communities perception towards TB patients.....39

Table 8: TB treatment administration factors.....41

Table 9: Reasons for missing anti-TB medication.....42

Table 10: Relationship between adherence to TB treatment and knowledge of TB and communities perception towards TB patients.....44

Table 11: Relationship between adherence to TB treatment and TB medication administration.....46

Table 12: Regimen complexity factors which contribute to non-adherence to TB medication.....48

Table 13: Relationship between adherence to anti-TB medication and regimen complexity factors.....49

Table 14: Supportive relationship between healthcare providers and caregivers factors that affect adherence to anti-TB medication.....51

Table 15: Relationship between adherence to TB medication and supportive relationship between the healthcare provider and the caregiver.....53

Table 16: Pattern of healthcare delivery factors that influence adherence to TB medication.....55

Table 17: Relationship between adherence to TB treatment and pattern of healthcare delivery..56

Table 18: Multivariate logistic regression model determining factors associated with anti-TB medication non-adherence.....57

LIST OF FIGURES

FIGURE 1: Age and gender distribution of the patients.....27

FIGURE 2: Marital status of the care-givers.....28

FIGURE 3: Families average monthly income.....30

FIGURE 4: Association between administration of medicine at 24 hour intervals and adherence to medication.....58

FIGURE 5: Association between marital status and adherence to medication.....58

ACRONYMS

AIDS	Acquired immune-deficiency syndrome
BCG	Bacillus Calmette-Guerin
CXR	Chest x-ray
DLTLD	Division of leprosy tuberculosis and lung disease
EPTB	Extra-pulmonary tuberculosis
HIV	Human immunodeficiency virus
INH	Isonicotinyl hydrazide
KG	Kilogram
KNH	Kenyatta National Hospital
KSH	Kenyan shilling
ML	Millilitre
NLTP	National Leprosy and Tuberculosis Programme
PTB	Pulmonary tuberculosis
TB	Tuberculosis
WHO	World Health Organization

DEFINITION OF TERMS

Adherence: it is the consistency and accuracy with which a patient follows the regimen prescribed by a physician or other health professional.

Caregiver: refers to the person who takes care of the child and is responsible for administering drugs to the child.

ABSTRACT

Background

Tuberculosis is an infectious bacterial infection caused by *Mycobacterium tuberculosis.* It remains a major cause of morbidity and mortality worldwide and is the most common cause of death from a single infectious disease particularly in children.

The management of TB involves the use of multi-drug regimens for a period of six months. Adherence to the long course of TB treatment is a complex, dynamic phenomenon with a wide range of factors impacting on treatment taking behavior. Adherence to anti-tuberculosis medication is extremely important if the treatment for TB is to be successful.

Objective

To determine the rate of patient adherence to anti-tuberculosis treatment and to determine the factors which affect adherence to treatment in TB paediatric patients.

Method

This was a hospital based cross sectional study which was carried out at the Kenyatta National Hospital (KNH) TB clinic. The convenient sampling technique was used to sample 55 caregivers of children aged 0 to 14 years who met the inclusion criteria. The sampled caregivers were interviewed using a structured questionnaire. After the interview the patients were requested to provide a urine sample which was tested for the presence of INH or its metabolites using Taxo-INH urine strips to verify adherence to anti-tuberculosis medication.

Results

The rate of adherence to anti-TB medication as determined by the INH urine test strips was 91.8%. Marital status, an economic and structural factor that was found to be significantly associated with adherence to medication. Among the patient/caregiver factors, administration of medicine at 24 hour intervals was significantly associated with adherence to medication. Bivariate analysis showed that patients whose caregivers were married or administered medication at 24 hour intervals were more likely to adhere to medication. The ORs (95% CIs) were 4.57(1.04-20.11) and 7.70(1.85-33.33) respectively. In multivariate analysis, administration of medication at 24 hour intervals was significantly associated with adherence to medication (OR: 6.47; 95% CI 1.44-29.10). There was no significant association between regimen complexity factors, relationship between health care provider and patient/caregiver, pattern of healthcare delivery and adherence to medication.

Conclusion

The adherence rate to anti-TB medication in the study population was found to be generally high. The high rate of adherence observed was probably due to free anti-TB drugs, extensive distribution of TB treatment services in various health facilities up to the community level and the sustained training of health care workers to promote adherence to treatment at community level and to improve TB case management also at the community level.

The marital status of the caregiver which was an economic and structural factor and administration of medication at 24 hour intervals, a patient/caregiver related factor were

significantly associated with adherence to anti-TB medication. Relationship between healthcare provider and patient/caregiver, regimen complexity and pattern of healthcare delivery were not significantly associated with adherence to anti-TB medication.

CHAPTER ONE: INTRODUCTION

BACKGROUND

Tuberculosis (TB) is an infectious bacterial infection caused by *Mycobacterium tuberculosis*. Transmission occurs through exposure to tubercle bacilli in airborne droplet nuclei produced by people with pulmonary or respiratory tract tuberculosis during expiratory efforts such as coughing or sneezing. Most infections are acquired from adults with post primary pulmonary tuberculosis. Between 90 to 95% of cases of tuberculosis in children are non-infectious[1].

Global picture of TB prevalence

Tuberculosis causes about 2 million deaths worldwide each year and one-third of the world's population is infected with the tubercle bacillus. It is becoming the leading cause of death in people with HIV[1].

TB is the most common cause of death from a single infectious disease particularly in children. Nearly 40 million children are likely to be exposed to the risk of TB and nearly 3 to 4 million children below age 5 years are estimated to be infected and may progress to disease worldwide[2].

Kenyan picture of TB prevalence

Kenya ranks 13th on the list of the 22 high burden TB countries in the world and has the fifth highest burden in Africa. According to the World Health Organization's (WHO's) Global TB

control report 2009, Kenya had approximately more than 132,000 new TB cases and an incidence rate of 142 new sputum smear positive cases per 100,000 population[3].

The incidence of childhood TB in Kenya is estimated to be amongst the highest in the world but limited data are available from both Kenya and elsewhere due to difficulties in diagnosing TB in chidren[4].

Paediatric TB

Paediatric TB is different from that in adults in several ways: the diagnosis of TB is more difficult in children due to the non-specific or complete absence of symptoms and difficulty in confirming the diagnosis microbiologically. Young children suffer more extra-pulmonary and disseminated TB than adults. Treatment for TB in children is challenging due to the lack of paediatric drug formulations and challenges in monitoring for toxicity. Children should be TB skin tested only if they have a risk for TB infection or are likely to progress to active TB or are suspected to be having active TB. Unlike adults, all children should be treated for latent TB infection if identified. Young children are not contagious with active TB and acquire their disease from shared airspace with adolescents or adults with pulmonary TB[5].

Young children once infected are at increased risk of TB disease and progression to extra-pulmonary disease. Primary disease and its complications are more common in children than in adults leading to differences in clinical and radiographic manifestations. Difficulties in diagnosing children stem from the low yield of mycobacteriology cultures and the subsequent

reliance on clinical case definitions. Inadequately treated TB infection and TB disease in children today is the future source of disease in adults[6].

Classification of childhood TB[2]

Childhood TB can be classified as follows:

- Asymptomatic mantoux positive
- Symptomatic mantoux positive
- Primary pulmonary complex
- Progressive pulmonary disease
- Disseminated TB
- Cervical and abdominal TB
- Tubercular meningitis
- Progressive bacillus Calmette-Guerin (BCG) disease
- Congenital tuberculosis

Diagnosis of TB in children

There are no specific features on clinical examination that can confirm that the presenting illness is due to pulmonary TB. In clinical assessment, there are three important clues to TB in children and they are: contact with an adult or older child with smear-positive PTB, failure to thrive or weight loss (growth faltering) and respiratory symptoms such as cough lasting more than two weeks in a child who has received a course of broad-spectrum antibiotics.

A tuberculin skin test should be done as it may provide supportive evidence. A negative tuberculin test does exclude TB[7].

Chest X-ray (CXR) is a common investigation in suspected PTB or miliary TB. The most consistent specific feature on CXR is nodal enlargement and this will be present in many children with PTB. Cavitations may be seen in older children and adolescents, who will often be sputum smear positive. A normal CXR can be useful to exclude PTB or miliary TB in a child with suggestive symptoms, such as persistent fever, night sweats and failure to thrive. A child presenting with persistent cough should receive a course of broad-spectrum antibiotics, with a follow-up CXR at least one month later.

Definitive diagnosis of extra-pulmonary TB is often difficult. Diagnosis may be presumptive, provided you can exclude other conditions. Patients usually present with constitutional features (fever, night sweats, weight loss) and local features related to the site of disease. Helpful special diagnostic investigations include microscopy of fluid (e.g. pleural fluid, cerebrospinal fluid, ascitic fluid) and TB culture, specialized X-rays, biopsy and histology[7].

Treatment of childhood TB

The decision to start TB treatment in a child is an active process, which involves weighing up the clinical evidence and investigation findings, careful thought, and often a period of observation[7]. Kenya subscribes to the internationally accepted WHO strategy in TB control and treatment has been tailored from WHO recommended regimes. The regimen for children younger than 15 years is rifampicin, isoniazid and pyrazinamide for the first two months (intensive phase) and

rifampicin, isoniazid for the remaining four months (continuation phase). This is the regimen for both PTB and EPTB[8].

Adherence to anti-tuberculosis treatment

Adherence can be defined as the consistency and accuracy with which a patient follows the regimen prescribed by a physician or other health professional[9]. It can also be defined as the extent to which a person's behavior (taking medication, following a diet and/or executing lifestyle changes) corresponds with agreed recommendations from a health care provider[10].The therapeutic regimens recommended by WHO have been shown to be highly effective for both preventing and treating TB, but poor adherence to anti-TB medication is a major barrier to its global control. TB is a communicable disease, thus poor adherence to a prescribed treatment increases the risks of morbidity, mortality and drug resistance at both the individual level and community level[10]. Adherence to the long course of TB treatment is a complex, dynamic phenomenon with a wide range of factors impacting on treatment taking behavior. Patient's adherence to their medication regimens can be influenced by the interaction of a number of these factors[11].

Measurement of adherence

There is no "gold standard" for measuring adherence behavior. There is use of a variety of strategies. One measurement approach is to ask providers and patients for their subjective ratings of adherence behavior. However when providers rate the degree to which patients follow their recommendations, they overestimate adherence. The analysis of patients' subjective reports has

been problematic as well. Patients who reveal they have not followed treatment advice tend to describe their behavior accurately, whereas patients who deny their failure to follow recommendations report their behavior inaccurately[10].

Other subjective means for measuring adherence include standardized, patient administered questionnaires. Typical strategies have assessed global patient characteristics or "personality" traits, but these have proven to be poor predictors of adherence behaviour. There are no stable factors that reliably predict adherence. However questionnaires that assess specific behaviours that relate to specific medical recommendations may be better predictors of adherence behaviour[10].

Although objective strategies may initially appear to be an improvement over subjective approaches, each has drawbacks in the assessment of adherence behavior. Remaining dosage units can be counted at clinic visits; however counting inaccuracies are common and typically result in overestimation of adherence behavior, and important information (e.g. timing of dosage and patterns of missed dosages) is not captured using this strategy. A recent innovation is the electronic monitoring device (medication event monitoring system-MEMS) which records the time and date when a medication container was opened, thus better describing the way patients take their medications. Unfortunately the expense of these devices preludes their widespread use[10].

Pharmacy databases can be used to check when prescriptions are initially filled, refilled over time and prematurely discontinued. One problem with this approach is that obtaining the

medicine does not ensure its use. Also, such information can be incomplete because patients may use more than one pharmacy or data may not be routinely captured[10].

Biochemical measurement is a third approach for assessing adherence behaviours. Non-toxic biological markers can be added to medications and their presence in blood or urine can provide evidence that a patient recently received a dose of the medication under examination. The drawbacks of this method include misleading findings which are influenced by a variety of individual factors including diet, absorption and rate of excretion. A multi-method approach that combines feasible self-reporting and reasonable objective measures is the current state of the art in measurement of adherence behavior[10].

Factors that influence adherence to treatment[10]

Many factors have been associated with adherence to TB treatment including patient characteristics, the relationship between health care provider and the patient, the treatment regimen and the health care setting. Factors that are barriers to TB drugs adherence can be classified as:

- Economic and structural factors.
- Patient-related factors.
- Regimen complexity.
- Supportive relationship between the health care provider and the patient.
- Pattern of health care delivery.

Strategies to improve adherence to treatment[10]

The interventions for improving adherence rates may be classified into the following categories:

- Staff motivation and supervision- includes training and management processes aimed at improving the way in which providers care for patients with TB.
- Defaulter action- the action to be taken when a patient fails to keep a pre-arranged appointment.
- Prompts- routine reminders for patients to keep pre-arranged appointments.
- Health education- provision of information about TB and the need to attend for treatment.
- Incentives and reimbursements- money or cash in kind to reimburse the expenses of attending the treatment centre, or to improve the attractiveness of visiting the treatment centre.
- Contracts- agreements (written or verbal) to return for an appointment or course of treatment.
- Peer assistance- people from the same social group helping someone with TB to return to the health centre by prompting or accompanying him or her.
- Directly observed therapy (DOT) - an identified, trained and supervised agent (health worker, community volunteer or family member) directly monitors patients swallowing their anti-TB drugs.

CHAPTER TWO: LITERATURE REVIEW

The therapeutic regimens recommended by WHO have been shown to be highly effective for both preventing and treating TB, but poor adherence to anti-tuberculosis medication is a major barrier to its global control.

TB is a communicable disease, thus poor adherence to a prescribed treatment increases the risks of morbidity, mortality and drug resistance at both the individual and community levels[10]. Adherence to treatment requires the active participation of the patient in self management of the treatment and co-operation between the patient and the health care provider. TB therapy requires high (>90%) compliance to facilitate cure[12].

In a study carried out in China, data was obtained from 670 patients amongst whom non-adherence was 12%. Non-adherence was found to be lowest amongst patients whose treatment was given under direct observation (6%), and highest amongst those whose treatment was self administered (24%). Illiterate patients were also more likely to be non-adherent (20%). The main reasons for non-adherence given by patients were: adverse drug reactions to anti-TB drugs (38%), relieved symptoms (27%), long course regimen and large dose of drugs (16%), worry about dangers of drugs (16%), other disorders (16%), financial burden and medical expenditures (16%) [13].

In another study carried out in South Africa to determine adherence to anti-tuberculosis chemoprophylaxis and treatment in children, adherence to treatment was 82.6% and adherence to chemoprophylaxis was 44.2%. Adherence to a 3 month chemoprophylaxis regimen of isoniazid and rifampicin was significantly better than adherence to a 6 month regimen of isoniazid only

(69.6% versus 27.6%). The study concluded that although adherence to treatment was good, adherence to unsupervised chemoprophylaxis was poor[14].

In a study carried out in Malawi to determine adherence to the different treatment options for TB, in-patients showed the highest adherence rate. Adherence was measured at 2, 4, and 8 weeks after onset of TB treatment. Patients on guardian-based DOT showed 94% adherence, while patients on health centre based DOT showed more non-adherent behavior: 11% according to monitoring forms, 14% according to tablet counts and 16% according to urine tests. The study concluded that decentralized care is a feasible option for anti-tuberculosis treatment and that guardians can supervise TB treatment just as well as health workers during the intensive phase of TB treatment[15].

In a study carried out in Iran in 2007, 30% of the patients were non-compliant with treatment regimen which was more frequent than presumed. After the first month of treatment, adherence rate was 96%. In the second, fourth and sixth month, the whole adherence rates were 56%, 76% and 81% respectively[16]. In another study carried out in Kampala, Uganda involving 127 adults and 109 children, 21.2% admitted to non-adherence to treatment during the previous month. An additional 15 patients (6.8%) were detected through urine testing. 39.7% of the patients started on treatment did not complete the regimen[17].

There are a number of factors that are barriers to adherence to TB treatment. There are economic and structural factors, patient-related factors, regimen complexity, supportive relationship between the health provider and the patient and pattern of health care delivery.

Economic and structural factors: TB usually affects people who are hard to reach such as the

homeless, the unemployed and the poor. Lack of effective social support networks and unstable living circumstances are additional factors that create an unfavourable environment for ensuring adherence to treatment[10].

Patient related factors: ethnicity, gender and age have been linked to adherence in various settings. Knowledge about TB and a belief in the efficacy of the medication will influence whether or not a patient chooses to complete the treatment. In addition, cultural belief system may support the use of traditional healers in conflict with allopathic medicine[10].

Regimen complexity: the number of tablets that need to be taken as well as their toxicity and other side-effects associated with their use may act as a deterrent to continuing treatment. Supportive relationships between the health provider and the patient: patient satisfaction with the significant provider of heath care is considered to be an important determinant of adherence but empathic relationships are difficult to forge in situations where health providers are untrained, overworked, inadequately supervised or unsupported in their tasks, as commonly occurs in countries with a high TB burden[10].

Pattern of health care delivery: the organization of clinical services, including availability of expertise, links with patient support systems and flexibility in the hours of operation, also affects adherence to treatment. Many of the ambulatory health care settings responsible for the control of TB are organized to provide care for patients with acute illnesses and staff may therefore lack the skills required to develop long term management plans with patients. Consequently, the patient's role in self-management is not facilitated and follow up is sporadic[10].

In a study carried out by Munro *et al* (2007), the researchers identified eight major factors associated with adherence to treatment. These included: health service factors such as the organization of treatment and care; social context (family, community and household influences); and the financial burden of treatment. The study concluded that adherence to TB treatment is influenced by four interacting sets of factors: structural factors (including poverty and gender discriminations), social context factors, health service factors and personal factors (including attitudes towards treatment and illness) [11].

Studies have been conducted on socioeconomic and behavioural factors affecting adherence. In Hong Kong, China, a study of 102 defaulters matched to 306 controls indicated that tobacco smoking, a history of prior treatment default or a poor adherence, treatment side effects and subsequent hospitalization were associated with treatment default[12]. A study in Fujian, China that combined quantitative and qualitative methods reported that treatment adherence was associated with the intention of patients and the behaviour of health service providers but not with gender, age, career, education level or social stigma[13].

In a study carried out in Zambia to investigate factors contributing to treatment non-adherence in-order to design a community based intervention to promote compliance, the major factors leading to non-compliance were patient beginning to feel better, lack of knowledge on the benefits of completing a course (25.7%), lack of food at home (11.4%), running out of drugs at home (25.4%), and drugs too strong (20.2%). The study established that 29.8% of TB patients failed to comply with TB drug taking regimen once they started feeling better[18].

In a study conducted in Egypt to determine the compliance of patients to TB treatment, two-thirds of the males (64.5%) and females (66.7%) complied with their anti-TB regimens, giving an overall compliance rate of 65.1%. Chi-squared distribution showed no association between age of the patient and compliance (Chi^2=7.78). Work was not found to be statistically associated with compliance (Chi^2=6.01). More than half the patients were either illiterate or could just read and write. Education was not found to be statistically associated with compliance (Chi^2=4.65). As regarding the presenting symptoms of TB, patients with cough and night sweats were more likely to comply with treatment (odds ratio=3.27 and 3.03 respectively). Those who presented with anorexia were less likely to comply (odds ratio=0.61). Presence of other associated disease e.g. diabetes, decreased compliance (odds ratio=0.63). Patients hospitalized at the start of treatment, patients who received instructions about the use and the importance of the drugs from drug providers, patients with good knowledge about TB, and patients who reported a positive family history of TB were found to have been more compliant[19].

In a study carried out in Nepal, the overall objective was to explore factors affecting treatment adherence under DOTS among TB patients in Nepal. Socioeconomic position was found to affect adherence to TB treatment. According to bivariate analysis, people who were illiterate, unemployed or in a low status occupation with a lower income had a statistically significant higher risk of being non-adherent. Respondents burdened with having to spend money on travel to reach the TB treatment facility as well as difficulty in financing treatment were also associated with non-adherence. Non-adherence to anti-TB treatment was found to be significantly associated with poor socioeconomic position such as unemployment (OR=9.2), low status occupation (OR=4.4), cost of travel to reach the treatment facility (OR=3.0), and low annual

income (OR=5.4). In a multivariate analysis, three variables were found to be significant risk factors with respect to non-adherence. They were: past experience with TB in the household (OR=3.3), discontinuity in taking drugs due to the appearance of side effects (OR=7.0) and inadequate knowledge about duration of treatment (OR=7.5). In this study, poor behaviour by health examiners and dispensers was found to be associated with non-adherence; however, the trend was not statistically significant. Lack of information about side effects, was found to be significantly related to non-adherence. Lack of sufficient time and attention provided by dispensers was associated with non-adherence. Poor quality of communication (OR=11.2) was significantly associated with treatment non-adherence rather than fair and good communication quality (OR=2.7)[20].

In a study carried out at Freegold mines, South Africa to determine the prevalence of non-compliance with tuberculosis treatment, the overall prevalence of non-compliance was 14.6+/- 3.3%. This was a cross-sectional study which involved collecting urine samples and testing for rifampicin and/or isoniazid metabolites. Non-compliance was defined as a negative urine test result for these drugs in participants whose treatment regimens included one or both. The mean prevalence of non-compliance established by rifampicin and isoniazid tests were 19.5+/- 5.3% and 9.8+/- 3.9% respectively, and these were significantly different (Chi^2=7.44). The study concluded that attendance at the clinics does not accurately reflect compliance[21].

In a study carried out in the Western Cape, South Africa to evaluate the effectiveness of voluntary health workers in enhancing adherence of TB patients to treatment, the supervision provided by volunteers or at a nursery for children achieved higher adherence results than the

health centre. The study involved 203 children and 148 adults. The volunteer group supervised the treatment regimen of 82 (23%) of the patients and the rest of the patients were supervised by the primary health care centre nurse or designated persons at workplaces, schools or nurseries. Adherence was defined as the patient taking 75% or more of the prescribed medication during the 6 months of treatment. The overall mean adherence rate for all types of supervision was 68% (73% among children and 62% among adults). Among adults, no one supervision option performed significantly better than any other[22].

In a study conducted in Kenya involving two centres, Mbagathi district hospital and Kibera health centre, the adherence to treatment was 96.5%. The study involved 147 patients. Those was patients whose urine isoniazid was detected were termed as adherent and those who isonazi s to not detected were non-adherent. The reasons for non-adherence were; not having enough pi l last until appointed date, delays due to work or family reasons, need to seek money for trans ort and losing some pills[24].

2.1: STATEMENT OF THE PROBLEM

TB has re-emerged as a major public health problem in the world. TB is an important cause f new childhood illness and death worldwide. TB in children is both common with nearly a million cases estimated each year. Young children are at particularly high risk of severe disease and death following infection. The incidence of childhood TB in Kenya is estimated to be among st the highest in the world[4].

The therapeutic regimens recommended by WHO have been shown to be highly effective for both preventing and treating TB, but poor adherence to anti-tuberculosis medication is a major barrier to its global control. TB is a communicable disease, thus poor adherence to a prescribed treatment increases the risks of morbidity, mortality and drug resistance at both individual and community levels[10].

Data on childhood TB has been limited therefore the rate of adherence to anti-TB medication in this group of patients is not known. Factors which influence adherence behavior among patients have been identified in studies that have been carried out in other countries but such studies have not been done locally especially for the paediatric patients.

2.2: JUSTIFICATION

TB is a major contributor to the global burden of disease and has received considerable attention in recent years, particularly in low and middle income countries where it is closely associated with HIV/AIDS. Poor adherence to treatment is common despite various interventions aimed at improving treatment completion. Lack of a comprehensive and holistic understanding of barriers to and facilitators of treatment adherence is currently a major obstacle to finding effective solutions. By carrying out this study, the rate of adherence to anti-TB medication was determined and it provided information on the extent of non-adherence to medication in our setting. This study also identified the factors that hinder and those that facilitate adherence to anti-TB medication and therefore proved instrumental in determining that patient/caregiver interventions

were needed to promote adherence and greater attention to structural factors was required to improve treatment adherence.

2.3: Objectives

2.3.1: General objective

- To determine the rate of adherence to anti-TB drugs and the factors that contribute to non-adherence in paediatric patients at KNH.

2.3.2: Specific objectives

- To determine the rate of adherence to anti-TB medication in paediatric patients.
- To determine which economic and structural factors contribute to non-adherence to anti-TB medication.
- To determine which patient/caregiver related factors contribute to non-adherence to anti-TB medication.
- To determine which regimen complexity factors contribute to non-adherence to anti-TB medication.
- To determine if the nature of the relationship between the healthcare provider and the patient/caregiver affects adherence to anti-TB medication.
- To determine if the pattern of health care delivery affects patient's adherence to anti-TB medication.

2.4: Research questions

- What is the rate of adherence to anti-TB drugs among paediatric patients at KNH?
- Which economic and structural factors contribute to non-adherence to anti-TB medication?
- Which patient/caregiver related factors contribute to non-adherence to anti-TB medication?
- Which regimen complexity factors contribute to non-adherence to anti-TB medication?
- Does the nature of the relationship between the health care provider and the patient affect adherence to anti-TB drugs?
- Does the pattern of health care delivery affect the patients' adherence to anti-TB medication?

CHAPTER THREE: DESIGN AND METHODOLOGY

3.1: AREA OF STUDY

The study was carried out at Kenyatta National Hospital in TB clinic.

3.2: RESEARCH DESIGN

The study was a cross-sectional study which was questionnaire based face-to-face interview using patient self report method. Taxo-INH urine strips were used to test for the presence of INH and its metabolites in the urine of the patients to confirm if the patient was adherent to medication.

3.3: TARGET POPULATION

The target population was children diagnosed with TB from age 0-14 years and who were on treatment with anti-TB drugs.

3.4.1: INCLUSION CRITERIA

- Children between the ages of 0 to 14 years who had been diagnosed with TB and were on treatment with anti-TB drugs.
- Children who had been on treatment for more than two months.
- Children whose caregivers consented to participate in the study.

3.4.2: EXCLUSION CRITERIA

- Children who were 15 years or older.

- Children who had been on treatment for less than 2 months.
- Children whose caregivers did not consent to participate in the study.

3.5: ETHICAL CONSIDERATIONS

3.5.1: Approval to carry out the study

Permission to carry out the study was sought from the Ethics and Research Committee at KNH.

3.5.2: Informed consent

Consent from the caregivers of the children who met the inclusion criteria was sought and the caregivers who consented were included in the study.

3.5.3: Confidentiality

The caregivers were interviewed in a private area at the TB clinic and all the information obtained was treated with confidentiality. Serial numbers were assigned and were used instead of the child's name to protect the patient's identity. The serial numbers were used during data analysis. The data collecting material were kept in a locked cabinet in the house of the investigator during the entire study period.

3.5.4: Risks involved

There were no risks to the patients involved in the study.

3.5.5: Benefits from the study

- Care givers with children who were non-adherent were counseled on the importance of adherence and how they could improve on adherence.
- All the caregivers were given an opportunity to ask questions or raise any concerns they had concerning their child's treatment and their questions were answered and their concerns addressed immediately.
- The results of the study will be communicated to the relevant health care providers to contribute to improving the quality of management and care of children with TB.

3.6: Sampling procedure/size

Caregivers of the children who met the inclusion criteria were interviewed consecutively as they were seen at the TB clinic at KNH.

The sample size was calculated using the Fischer's formula:

$n=Z^2 \times p\,(1-p)/d^2$

n= sample size

Z=1.96 which is the Z-value corresponding to a significance level of 0.05.

P=0.965 which is the estimated prevalence rate of adherence to anti-TB treatment (Kenyan study[24])

d=0.05 which is the desired degree of accuracy for the study.

$n=1.96^2 x\ 0.965\ x\ 0.035/0.05^2$

$n=51.9$

From the calculation the sample size was set at 55 patients to cater for non-responders.

3.7: Data collection method

The data collection was divided into two parts. The first part of data collection was done using standardized questionnaire (appendix 1) based face-to-face interviews with the caregivers of the children on TB treatment from May to July 2010 at the TB clinic. The interviews were carried out by the principal investigator. Most of the caregivers were more comfortable communicating in Swahili therefore the questions were translated into Swahili when carrying out the interviews but the responses were translated back into English when filling in the questionnaire.

3.8: Determination of isoniazid in urine

The second part of the data collection involved collection of urine to test for the presence of isonicotinic acid and its metabolites in urine. The results obtained from the urine test were used as a measure of adherence whereby a patient with a positive test result was termed as adherent and a patient with a negative test result was termed as non-adherent.

The materials that were required to carry out the urine test were BBL Taxo INH test strips, BBL Taxo INH test control, plastic container (15ml), test tubes, de-ionized water, scissors and latex gloves.

3.8.1: Specimen collection and handling

The patients were provided with a 15ml plastic container with a lid to collect their urine in. The patients/caregivers were instructed to provide urine quantities that filled at least two thirds of the plastic container so as to provide at least 10ml of urine. Once the urine was collected, it was handed over to the principle investigator for testing.

3.8.2: Preparation of reagents

A positive control for the test was prepared by placing a BBL Taxo INH test control disc in 2mls of de-ionized water in a test tube. The test tube was shaken three times over a 15 minute period to assure extraction of INH into the water.

BBL Taxo INH test strips were obtained from their jar and one corner of the plastic tube at the arrow end of the strip was cut.

Half an inch of the plastic tube of the INH test strip was squeezed at the end opposite the arrow between the thumb and forefinger. While squeezing the tube, the open end of the tube was inserted below the surface of the urine specimen and pressure was released from the other end of the tube to allow the specimen to rise in the tube to cover the arrow on the strip. The tube was left to float in the urine container for 15-30 minutes then observations were made and results were recorded.

The same test was performed using the BBL Taxo INH test control which had been prepared in the test tube parallel with the urine sample.

If the appearance of the test strip after 15-30 minutes was a blue, purple or green colour indicating the presence of INH or its metabolites in the urine specimen, the results were positive. If the colour of the urine remained on the test strip after 30 minutes of testing, the results were negative. INH and its metabolites are detectable in the specimen within 24 hours after the last intake of isoniazid.

3.8.3: Quality control of tests

When the observations for the urine sample were being made, observations for the INH test control were also made. The INH test control tube contained INH extracted into water and therefore gave a positive result when tested with the urine test strips. The positive results obtained from the INH test control indicated that the test strips were in good condition and were able to detect the presence of INH and its metabolites. If the results of the INH test control were negative, it meant that the urine test strips were unable to detect INH and its metabolites and could not give accurate results when used in urine specimen. By concurrently carrying out the urine test and INH test control the quality of the test strips was ascertained and this ensured that accurate results were obtained.

3.9: Data management

3.9.1: Data processing and analysis

The data collected was entered into SPSS (Statistical Package for Social Sciences) version 12.0 software for analysis. Skewed numerical data was summarized as medians while categorical data was summarized as percentages and frequencies. The rate of adherence was computed as the

percentage of patients whose results for the INH urine test was positive over the whole sample size. Association between the various factors and non-adherence was estimated using the odds ratio (OR) and their 95% confidence intervals (CI) from a logistic regression model. Predictive variables that were independently significantly associated with adherence to medication in bivariate analysis were included in a multivariate logistic regression model to determine if they were independent predictors of non-adherence. The criterion for significance was set at $p<0.05$ based on a two sided test. The qualitative data was analyzed manually and was used to explain the results obtained from quantitative data analysis.

3.9.2: Data quality control

Data entered into the database was routinely checked for accuracy and completeness and any errors and omissions were rectified. On completion of data entry, data cleaning was done to correct any mistakes that might have been made during data entry.

4.0: RESULTS

This study was carried from May to July 2010. During the study period, 55 patients who met the inclusion criteria for the study were recruited to participate in the study. Therefore 55 patients and their caregivers participated in this study. However 6 patients were unable to provide a urine sample which was required for testing for adherence using the INH urine test strips. Therefore data from 49 patients and their caregivers was analyzed in this study. There was no significant difference in the results obtained for 49 patients compared to those of the calculated sample size of 52 patients.

The INH urine test strips were used to determine the rate of adherence to medication within 24 hours since the last intake of medication. Adherence to mediation throughout the course of treatment was determined through caregiver self report using a standardized questionnaire (Appendix 1).

4.1 DEMOGRAPHICS OF THE STUDY GROUP

4.1:1 Baseline characteristics of the patients

The median age of the patients who participated in this study was 3.5 years. The inter-quartile ranges were 2 to 7.8 years. Majority of the patients were below 5 years, 28(57.1%) and the rest were 5years and above, 21(42.9%). Female patients accounted for 55.1% (n = 27) of the study participants while male patients accounted for 44.9% (n = 22).

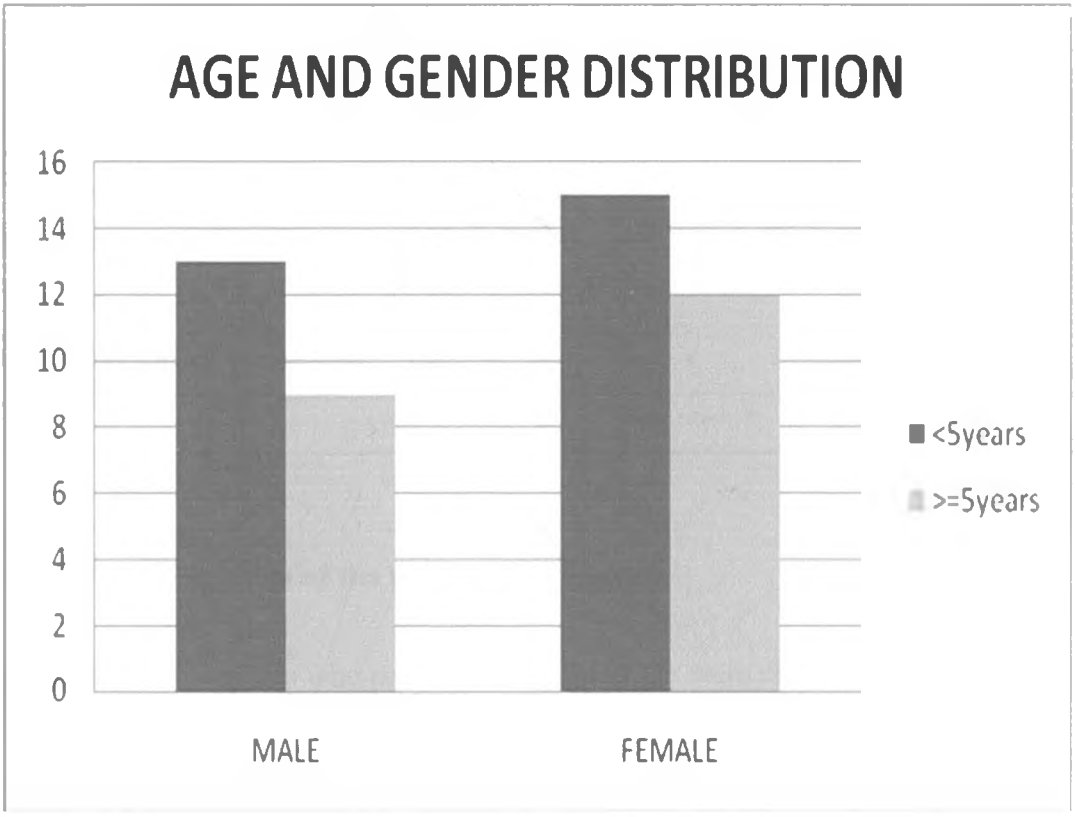


FIGURE 1: Age and gender distribution of the patients

4.1:2 Level of education among patient's care-givers

A total of 13(26.5%) of the care-givers had received primary school education. 23(46.9%) had received secondary school education and 11(22.4%) had received tertiary education (either diploma or degree courses). A small number of the participants 2(4.1%) had not received any formal education.

Table 1: Level of education of the care-givers

EDUCATION	N = 49	PERCENTAGE (%)
Primary	13	26.5
Secondary	23	46.9
Tertiary	11	22.4
Others(no formal education)	2	4.1
TOTAL	49	100

4.1:3 Marital statuses of the patients' care-givers

Most of the care-givers who participated in the study were married 38(77.6%). 5 (10.2%) were single and 3(6.1%) were either divorced or separated. 3(6.1%) were widowed.

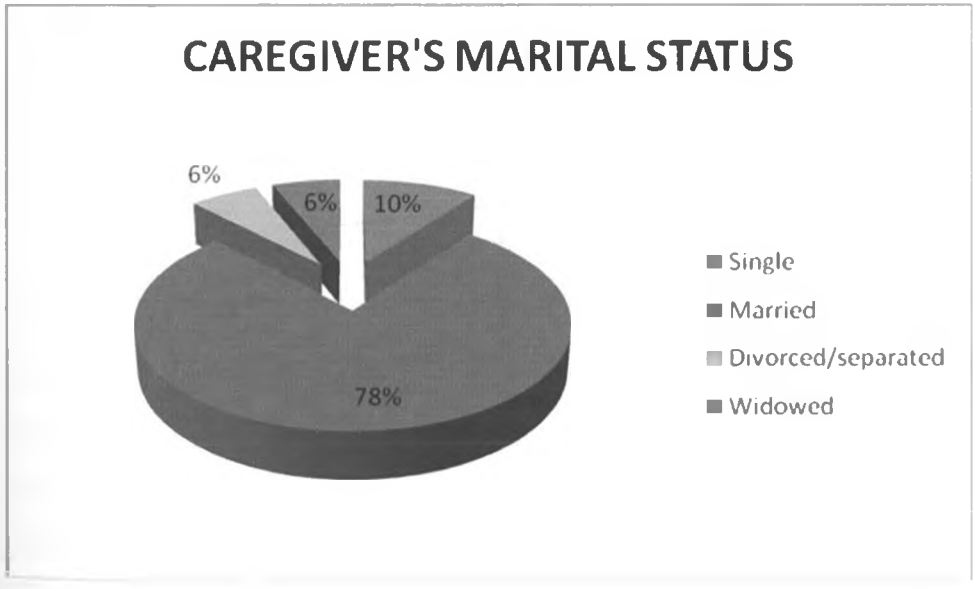


FIGURE 2: Marital status of the care-givers

4.1:4 Occupations of the care-givers and their spouses

The occupations of the care-givers and their spouses were categorized into 7 major groups. Among the care-givers, 4(8.2%) were in professional/technical occupations. Clerical had 5(10.2%) of the care-givers while sales and services had 7(14.3%). Skilled/unskilled manual also had 7(14.3%) while domestic services had the majority 15(30.6%). 8(16.3%) of the caregivers were in agriculture and 3(6.1%) were unemployed. Among the spouses, 6.1% were in professional/technical occupations while 8.2% were in clerical. Majority of the spouses were in sales and services (32.7%) followed by skilled/unskilled manual at 18.4%. Agriculture accounted for 12.2% of the spouses' occupation.

Table 2: Occupation of the care-givers and their spouses

CARE-GIVER'S OCCUPATION	NUMBER(N)	PERCENTAGE (%)
Professional/technical	4	8.2
Clerical	5	10.2
Sales and services	7	14.3
Skilled/unskilled manual	7	14.3
Domestic services	15	30.6
Agriculture	8	16.3
Unemployed	3	6.1
SPOUSES' OCCUPATION		
Professional/technical	3	6.1
Clerical	4	8.2
Sales and services	16	32.7
Skilled/Unskilled manual	9	18.4
Agriculture	6	12.2
Not applicable(no spouses)	11	22.4

4.1:5 Average monthly income of the families

The average monthly income of the families ranged from less than KSH 5,000 to more than KSH 20,000. 16.3% earned less than 5,000 shillings a month and 22.4% earned 5,000-10,000 shillings a month. 26.5% earned 10,000-20,000 shillings a month and another 26.5% earned over 20,000 shillings a month.8.2% either declined to disclose how much they earned or were unemployed and being supported by relatives and therefore did not have this information.

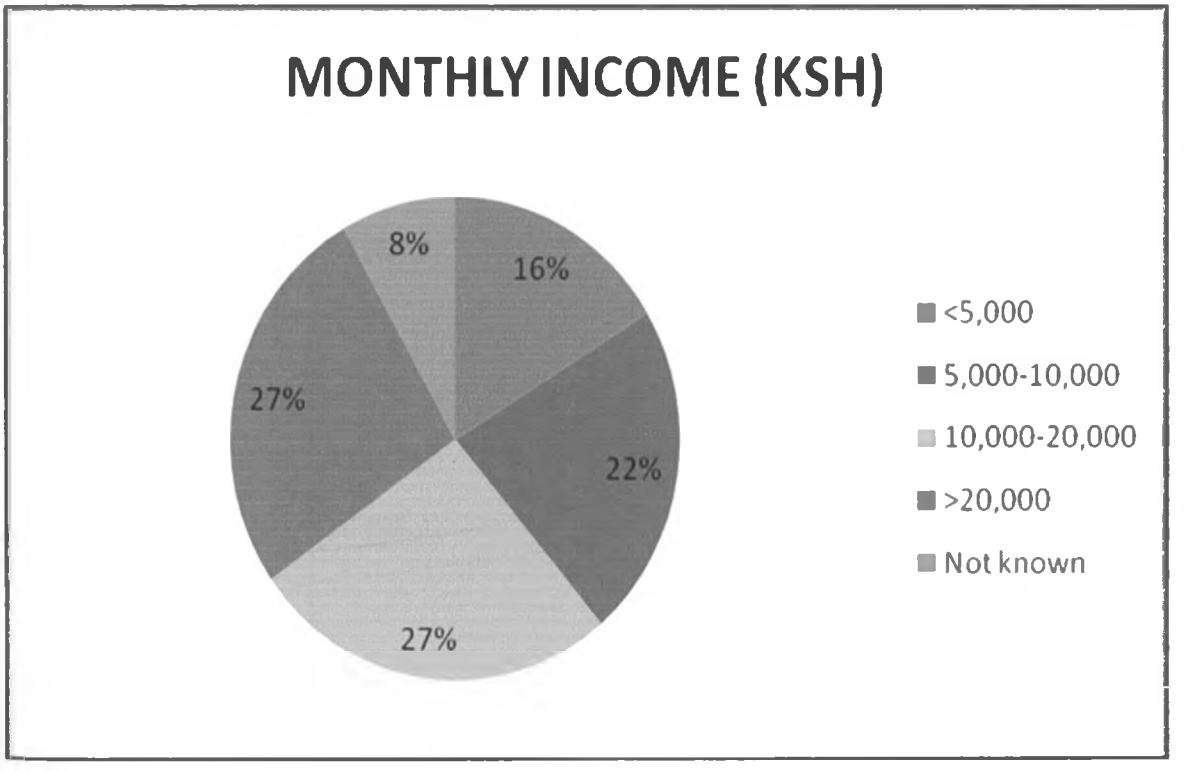


FIGURE 3: Families average monthly income

4.2 RATE OF ADHERENCE TO TUBERCULOSIS MEDICATION AT KNH

The rate of adherence to TB medication was determined using the Taxo-INH urine test strips. Urine isoniazid (INH) was detected in 45(91.8%) of the 49 patients who took part in the study.

Table 3: Rate of adherence to anti-TB medication as determined by Taxo-INH urine test strips

Characteristics	**INH positive, N (%)**	**INH negative, N (%)**	**Total**
GENDER			
Male	21 (95.5)	1 (4.5)	22
Female	24 (88.8)	3 (1.2)	27
AGE GROUP			
<5 years	25 (89.2)	3 (10.8)	28
≥5 years	20 (95.2)	1 (4.8)	21
WEIGHT			
<20kgs	29 (90.6)	3 (9.4)	32
≥20kgs	16 (94.1)	1 (5.9)	17

4.3 FACTORS CONTRIBUTING TO NON-ADHERENCE TO ANTI-TB MEDICATION

Adherence to anti-TB medication throughout the course of treatment was determined using self-report from the care-givers. 44.9% of the patients had missed taking their medication at some point during the treatment period. For purposes of determining the factors that contribute to non-adherence to medication the adherence rate determined from the questionnaire was used. Patients who had missed medication at some point in their course of treatment were termed as non-adherent to medication.

4.3.1 Relationship between adherence to TB treatment and baseline characteristics of the patients

There was no significant association between the baseline characteristics and adherence to TB medication ($P>0.05$). However, adherence to TB medication was 1.21 [95% CI= 0.39-3.78] times more in female patients aged < 5 years (57.1%) compared to those aged ≥ 5 years (52.4%). Adherence was 1.45 times more in females (59.3%) compared to males (50.0%) and 1.64 times more in those weighing less than 20kgs (59.4%) compared to those weighing 20kgs or more (47.1%).

Table 4: Relationship between adherence to anti-TB medication and baseline characteristics of the patient

	Adherent (n=27)		Non-adherent (n=22)			95% CI of OR		P
Variables	**n**	**%**	**n**	**%**	**OR**	**Lower**	**Upper**	**value**
Age in years;								
< 5 years	16	57.1	12	42.9	1.21	0.39	3.78	0.740
>= 5 years	11	52.4	10	47.6	1.00			
Gender;								
Female	16	59.3	11	40.7	1.45	0.47	4.52	0.517
Male	11	50.0	11	50.0	1.00			
Weight in kgs;								
< 20	19	59.4	13	40.6	1.64	0.50	5.38	0.409
>= 20	8	47.1	9	52.9	1.00			

4.3.2 Relationship between adherence to anti-TB medication and economic and structural factors of the care-givers.

There was a statistically significant association between marital status and adherence to TB medication (P= 0.046). Patients with married caregivers (63.2%) were 4.57 times more likely to adhere to TB treatment compared to those whose caregivers were not married (27.3%).

Considering primary education as a reference category, patients whose caregivers had attained secondary education (56.5%), were 1.49 times more likely to adhere to TB medication compared to those whose caregivers had acquired primary education (46.7%). The likelihood increased to 2 times for caregivers who had attained tertiary level of education (63.6%). The relationship between adherence to TB medication and the caregiver's level of education was not statistically significant (P = O.557 for secondary education and P = 0.400 for tertiary level).

There was no significant relationship between the family's average monthly income and adherence to TB medication. However using the group whose monthly income was less than 5,000 shillings as a reference category; those who earned 5,000-10,000 shillings were 1.68 times more likely to adhere to medication. The likelihood of adhering to medication increased to 2.24 times for those who earned 10,001- 20,000 shillings and also for those who earned more than 20,000 shillings.

Caregivers who resided outside Nairobi were 2.34 times more likely to adhere to TB medication compared to those who resided within Nairobi. However the relationship between the area of residence and adherence to medication was not statistically significant (P= 0.181).

Table 5: Relationship between adherence to TB medication and economic and structural factors of the caregivers

Variables	Adherent (n=27)		Non-adherent (n=22)		95% CI of OR			P value
	n	%	n	%	OR	Lower	Upper	
Level of education;								
Tertiary	7	63.6	4	36.4	2.00	0.31	13.45	0.400
Secondary	13	56.5	10	43.5	1.49	0.33	6.75	0.557
Primary	7	46.7	8	53.3	1.00			
Marital status;								
Currently married	24	63.2	14	36.8	4.57	1.04	20.11	**0.046***
Not married	3	27.3	8	72.7	1.00			
Family's average monthly income;								
>20,000	8	61.5	5	38.5	2.24	0.34	15.46	0.330
10,001 - 20,000	8	61.5	5	38.5	2.24	0.34	15.46	0.330
5,000 - 10,000	6	54.5	5	45.5	1.68	0.24	12.29	0.546
<5,000	5	41.7	7	58.3	1.00			
Area of residence;								
Outside Nairobi	11	68.8	5	31.3	2.34	0.66	8.23	0.181
Within Nairobi	16	48.5	17	51.5	1.00			

4.3.3 Relationship between adherence to TB medication and patient/caregiver related factors.

Among the caregivers who participated in the study, 95.9% reported that they had knowledge on TB and 4.1% reported to lack knowledge on TB. 6.1% of the caregivers were able to describe TB very well and 53.1% were able to describe it fairly well. 36.7% of the caregivers described TB poorly and 4.1% were unable to describe it.

The signs and symptoms that were listed by the caregivers included coughing, fever, night sweats, weight loss, poor appetite and others like chest pain and coughing blood. 79.6% of the caregivers mentioned coughing while 65.3% of the caregivers mentioned night sweats. 49% mentioned fever while 51% mentioned weight loss. 4.1% mentioned poor appetite while 10.2 % mentioned other signs and symptoms including chest pain and coughing blood. 2% did not mention any signs and symptoms.

87.8% of the caregivers stated that they knew the mode of transmission of TB and 77.6% of the caregivers were able to describe the mode of transmission correctly. All of the caregivers knew that TB was curable. 93.9% of the caregivers knew the length of time of TB treatment and 95.9% knew the importance of finishing TB medication and were able to explain the importance of finishing medication well.

Table 6: Respondents knowledge and awareness on TB

Variables	N=49	
Self reported knowledge on TB;		
Known	47	95.9%
Not known	2	4.1%
Description of TB;		
Poorly describe it	18	36.7%
Describe it fairly well	26	53.1%
Describe it very well	3	6.1%
Could not describe	2	4.1%
Sign and symptoms listed;		
Coughing	39	79.6%
Fever	24	49%
Night sweats	32	65.3%
Weight loss	25	51%
Poor appetite	2	4.1%
Others	5	10.2%
Don't know	1	2%
Mode of transmission;		
Known	43	87.8%
Not known	6	12.2%
Description of mode of TB transmission;		
Correct	38	77.6%
Incorrect	11	22.4%
TB curability;		
Curable	49	100%
Length of treatment;		
6 months	46	93.9%
Others	3	6.1%
Importance of finishing treatment;		
Known	47	95.9%
Not known	2	4.1%
Importance of finishing treatment (explanation);		
Well explained	47	95.9%
Not well explained	2	4.1%

The community's perception towards TB patients was explored as one of the patients /caregivers' factors affecting adherence. The relatives and friends to 53.1% of the TB patients were not aware of the patients TB status. The caregivers gave various reasons as to why their relatives and friends were not aware of the children's TB status. 18.4% of the caregivers felt that it was not necessary to tell other people about the TB status of the child, 6.1% said that they had not had a chance to tell their relatives and friends, 8.2% said that the matter had not come up, 6.1% felt that people might stay away from the child once they found out their status, 8.2% felt that people might stay away from their home, 8.2% said that people might think that they have AIDS and 2.0% said that people would not want them to visit them.

The presence of friends or relatives was found to interfere with drug administration in 49.0% of the cases. The caregivers had come up with 2 ways of dealing with drug administration in the presence of friends or relatives. 36.7% of the caregivers took the child to a different room to administer the medicine when people were around while 12.2% waited for the visitors to leave before administering the drugs.

The community had different ways of relating to TB patients in the area of residence. 10.2% of the caregivers said that TB patients were avoided in their area of residence, 22.4% said that people suspected them of having AIDS, 12.2% said that people did not share things like utensils with them, another 12.2% said that they did not have any TB patients in their area of residence and were therefore not aware of the nature of the relationship between the community and TB patients and 26.5% of the caregivers said that they did not know how the community related to

TB patients.18.4% of the caregivers said that people related normally to TB patients in their area of residence.

Table 7: Communities perception towards TB patients

Perception on TB patients	**N=49**	
Family and friends awareness about the child TB status;		
Aware	23	46.9%
Not aware	26	53.1%
Reasons for not being aware;		
Don't think it is necessary	9	18.4%
Not had a chance to tell them	3	6.1%
The matter has not come up	4	8.2%
They might stay away from the child	3	6.1%
Might stay away from our home	4	8.2%
They might think we have AIDS	4	8.2%
They will not want us to visit them	1	2.0%
Not applicable	23	46.9%
Presence of friends or relatives interfere with drug administration;		
Agreed	24	49.0%
Disagreed	25	51.0%
Coping with presence of friends or relatives interfering with drug administration;		
Take child to different room and administer the drugs	18	36.7%
Wait till the visitors leave	6	12.2%
Not applicable	25	51.0%
People relationship with TB patients in the area of residence;		
Don't know	13	26.5%
People avoid them	5	10.2%
People suspect that they have AIDS	10	22.4%
People don't share things with them e.g. utensils	6	12.2%
There are no TB patients	6	12.2%
People relate to them normally	9	18.4%

Among the patients who were taking part in the study, 38.8% of them were in their third month of treatment, 34.7% were in their fourth month of treatment and 26.5% were in their fifth month

of treatment.

Drug administration was done by the mother only in 63.3% of the patients and in the other 36.7% it was done by the mother and/or other people. Drug administration was done before meals in 14.3% of the patients while in 83.7% of the patients it was done after meals. 2.0% of the patients took their drugs with their meals. 46.9% of the children sometimes refused to take their medication and the caregivers had come up with various ways of ensuring that the children took their medicine. 8.2% of the caregivers promised to reward their children if they took the medicine while 18.4% forced the children to take the medicine. 12.2% mixed the drug with food or sweet fluids while 8.2% gave the medicine with plenty of juice or milk.

Side effects including nausea, vomiting and abdominal discomfort were experienced in 42.9% of the patients. 46.9% of the patients took their drugs in the morning and the rest (53.1%) took theirs in the evening. 71.4% of the caregivers reported that they usually administered medicine at 24 hour intervals while the others (28.6%) administered in intervals which were either greater than or less than 24 hours. 95.9% of the caregivers had administered TB medicine within 24 hours before participating in the study. The remaining 4.1% had not administered the TB medicine. 87.8% of the caregivers employed some way of remembering that it was time to administer the drugs to the child and this included using an alarm clock , having someone to remind the caregiver that it was time to administer the medicine and synchronizing administration of the medicine with certain events e.g. meal time. The other 12.2% did not employ any method to remind them of the time to administer the medicine.

Table 8: TB treatment administration factors

Characteristics	N=49	
Drug administration		
Duration of treatment (months);		
3	19	38.8%
4	17	34.7%
5	13	26.5%
Drug administrator;		
Mother only	31	63.3%
Mother and/or others	18	36.7%
Drug administration done;		
Before meals	7	14.3%
After meals	41	83.7%
With meals	1	2.0%
Child's refusal to take the medication;		
Sometimes	23	46.9%
Does not refuse	26	53.1%
Ways of ensuring the child takes the medicine;		
Promise to reward the child	4	8.2%
Force the child	9	18.4%
Mix the drug with food or sweet fluids	6	12.2%
Give with plenty of juice or milk	4	8.2%
Does not refuse	26	53.1%
Experience on problems immediately after taking the		
Always experienced	14	28.6%
Sometimes experienced	7	14.3%
Not experienced	28	57.1%
Time of administering drugs;		
Morning	23	46.9%
Evening	26	53.1%
Medicine administered at 24 hour intervals;		
Administered	35	71.4%
Not administered	14	28.6%
Administration of medicine in the past 24 hours;		
Administered	47	95.9%
Not administered	2	4.1%
Way of remembering that it is time to administer medicine;		
Employed	43	87.8%
Not employed	6	12.2%

From the questionnaires, 44.9% of the participants admitted that the patients had missed medication at some point during the course of treatment. 72.7% of those who had missed medication admitted to have missed medication ≤ 5 times. 22.7% had missed 6-10 doses of their medication and 1(4.5%) had missed medication for 2 weeks and had to be restarted on treatment. Various reasons for missing medication were given and are shown in table 9. Some caregivers gave more than one reason for missing drugs.

Table 9: Reasons for missing anti-TB medication

REASON	NUMBER	PERCENTAGE (%)
Forgot to administer the drugs	9	40.9
Ran short of drugs	8	36.4
Child refused to take the medicine	2	9.1
Health of child improved	2	9.1
Was away from home/ had travelled up-country	4	18.2
Drugs made the child feel worse	1	4.5

Association between adherence to anti-TB medication and patient/caregiver factors

There was no statistically significant association between majority of the patient/caregiver factors and adherence to TB medication. However, patients whose caregivers had adequate knowledge on TB were 2.04 times more likely to adhere to medication compared to those who had inadequate knowledge.

In terms of community's perception towards TB patients, those whose relatives and friends were aware of the child's TB status were 1.11 times more likely to adhere to medication compared to those whose relatives and friends were not aware. Those who the presence of relatives and friends did not interfere with drug administration were 1.50 times more likely to adhere to medication compared to those whose family and friends' presence interfered with drug administration. Considering communities which had a positive attitude towards TB patients as reference group, patients from communities with a negative attitude were 1.38 times more likely to adhere to medication and those from communities whose attitude towards TB patients was not known were 2.14 times more likely to adhere to medication.

Table 10: Relationship between adherence to TB treatment and knowledge of TB and communities perception towards TB patients

	Adherent (n=27)		Not adherent (n=22)			95% CI of OR		P
Variables	**n**	**%**	**N**	**%**	**OR**	**Lower**	**Upper**	**value**
Knowledge score categories;								
Adequate	17	63.0	10	37.0	2.04	0.65	6.42	0.220
Inadequate	10	45.5	12	54.5	1.00			
Family and friends awareness about the child TB status;								
Aware	13	56.5	10	43.5	1.11	0.36	3.45	0.851
Not aware	14	53.8	12	46.2	1.00			
Presence of friends or relatives interfering with drug administration;								
Disagreed	15	60.0	10	40.0	1.50	0.48	4.65	0.482
Agreed	12	50.0	12	50.0	1.00			
People relationship with TB patients in the area of residence;								
Undecided	12	63.2	7	36.8	2.14	0.33	14.65	0.432
Negative attitude	11	52.4	10	47.6	1.38	0.22	8.70	0.695
Positive attitude	4	44.4	5	55.6	1.00			

Patients who were on their third month of treatment were 1.2 times more likely to adhere to medication compared to those who had been on treatment for more than 3 months. Patients who had only the mother administering the medicine to them were 1.39 times more likely to adhere to

medication compared to those whose mothers and/or other people administered the medicine. Where drug administration was done after meals, patients were 1.78 times more likely to adhere to medication compared to where drug administration was done before meals. Children who did not refuse to take medicine were 2.46 times more likely to adhere to medication compared to those who sometimes refused to take the medication.

Children who did not experience any side-effects on taking the medication were 1.7 times more likely to adhere to medication compared to those who experienced side-effects on taking the medication. Children who took their medication in the morning were 1.11 times to more likely to adhere to medication compared to those who took their medication in the evening. Children whose caregivers employed ways of remembering that it was time to administer the medication were 2.78 times more likely to adhere to medication compared to those whose caregivers did not employ any method.

There was a statistically significant association between administering medication at 24 hour intervals and adherence to TB medication ($P = 0.003$). Patients whose caregivers administered medication at 24 hour intervals were 7.70 times more likely to adhere to medication compared to those who did not administer at 24 hour intervals.

Table 11: Relationship between adherence to TB treatment and TB medication administration

Variables	Adherent		Not adherent		OR	95% CI of OR		P
	n	%	n	%		Lower	Upper	value
Duration of treatment (months);								
3	11	57.9	8	42.1	1.20	0.32	4.50	0.757
> 3	16	53.3	14	46.7	1.00			
Drug administration done;								
Mother only	18	58.1	13	41.9	1.39	0.43	4.35	0.584
Mother and/or	9	50.0	9	50.0	1.00			
Drug administration done;								
After meals	24	57.1	18	42.9	1.78	0.28	11.77	0.685
Before meals	3	42.9	4	57.1	1.00			
Child's refusal to take the medication;								
Does not refuse	17	65.4	9	34.6	2.46	0.77	7.79	0.124
Sometimes	10	43.5	13	56.5	1.00			
Experience side-effect								
Not experienced	17	60.7	11	39.3	1.70	0.47	6.27	0.367
Experienced	10	47.6	11	52.4	1.00			
Time of administering								
Morning	13	56.5	10	43.5	1.11	0.36	3.45	0.851
Evening	14	53.8	12	46.2	1.00			
Administer medicine at 24 hour interval;								
Administered	24	68.6	11	31.4	7.70	1.85	33.33	**0.003***
Not administered	3	21.4	11	78.6	1.00			
Ways of remembering time to administer								
Employed	25	58.1	18	41.9	2.78	0.46	16.67	0.360
Not employed	2	33.3	4	66.7	1.00			

4.3.4 Relationship between adherence to anti-TB medication and regimen complexity

All the patients who were taking part in the study were in the continuation phase of treatment and were therefore on rifampicin and isoniazid fixed dose combination tablets. 51% of the patients were taking less than 2 tablets a day, 40.8% were taking 2 tablets a day and 8.1% were taking more than 2 tablets a day. There were 2 drug formulations available and they were the tablet form and the dispersible tablet form. 44.9% of the patients were on the tablet form while 55.1% were on the dispersible tablets form.

A number of caregivers experienced problems when administering drugs to their children. The type of problems encountered included difficulty in swallowing tablets (12.2%) and refusal to take the medicine (24.5%). 63.3% of the caregivers did not experience any problem when administering the drugs to the children.

The caregivers who were experiencing problems when administering drugs to their children had come up with various ways of dealing with the problems. Where the children had difficulty swallowing the tablets, the caregivers crushed the tablets (22.2%) or instructed the child to chew the tablets (11.1%). Where children refused to take the medicine, the caregivers either forced them to take the medicine (50%) or gave the medicine in small portions slowly (17.7%).

Table 12: Regimen complexity factors which contribute to non-adherence to TB medication

Characteristics	N=49	
Number of tablets the patient is taking		
<2	25	51.0%
2	20	40.8%
>2	4	8.1%
Type of drug formulation		
Tablet	22	44.9%
Dispersible tablets	27	55.1%
Problems encountered		
Problems when administering;		
Experienced	18	36.7%
Not experienced	31	63.3%
Types of problems; n=18		
Difficulty in swallowing tablets	6	33.3%
Refusal to take	12	66.7%
Dealing with the problem; n=18		
Crush the tablets	4	22.2%
Child chews the tablets	2	11.1%
Force the child to take the medicine	9	50.0%
Give in small portions slowly	3	16.7%

There was no statistically significant relationship between adherence to TB medication and regimen complexity factors. However patients who were taking one tablet were 1.47 times more likely to adhere than those who were taking more than one tablet. Patients who were taking the dispersible tablets were also 1.45 times more likely to adhere than those who were taking the tablets. The patients whose caregivers did not experience any problems when administering the medication were twice as likely to adhere to medication compared to those who experienced problems when administering the medication.

Table 13: Relationship between adherence to anti-TB medication and regimen complexity factors

	Adherent (n=27)		Not adherent (n=22)		95% CI of OR			P
Variables	**n**	**%**	**n**	**%**	**OR**	**Lower**	**Upper**	**value**
Number of tablets the patient is taking;								
One	11	61.1	7	38.9	1.47	0.45	4.80	0.519
More than one	16	51.6	15	48.4	1.00			
Type of drug formulation;								
Dispersible tablets	16	59.3	11	40.7	1.45	0.47	4.52	0.517
Tablet	11	50.0	11	50.0	1.00			
Problems when administering;								
Not experienced	19	61.3	12	38.7	1.98	0.61	6.43	0.253
Experienced	8	44.4	10	55.6	1.00			

4.3.5 Relationship between adherence to TB treatment and supportive relationship between health care provider and the caregiver.

Among the study participants, 98% felt that they got to speak privately to the healthcare provider and 91.8% felt that they spent enough time with the healthcare provider. 63.3% felt that they were always assisted by the healthcare provider whenever they had a problem while 34.7% felt that they were sometimes assisted and 2% felt that they were not assisted. 16.3% said that they were scolded whenever they failed to follow the healthcare provider's instructions especially when they failed to keep the appointment date. 14.3% said that the healthcare provider did not address their failure to follow instructions while 26.5% said that the healthcare provider explained to them the importance and consequences of not following the set instructions. Only 34.7% felt that the healthcare provider provided all the necessary information on the disease and medication.

Table 14: Supportive relationship between healthcare providers and caregivers factors that affect adherence to anti-TB medication

Characteristics	N=49	
Health providers support		
Caregiver get to speak privately to healthcare provider;		
Yes	48	98.0%
No	1	2.0%
Amount of time spent with healthcare provider;		
Enough	45	91.8%
Not enough	4	8.2%
Healthcare provider assist when there's a problem;		
always Assists	31	63.3%
Sometimes assists	17	34.7%
Does not assist	1	2.0%
Healthcare provider's response to failure to follow instructions;		
Scolds the caregiver	8	16.3%
Does not address the matter	7	14.3%
Explains importance & consequences	13	26.5%
Others	21	42.9%
Provision of information on the disease & drugs by healthcare provider;		
Provides	17	34.7%
Does not provide	32	65.3%

There was no significant association between the supportive relationship between the healthcare provider and the caregiver and adherence to TB medication (P=0.05). However, adherence to TB medication was 4.17[95% CI=0.40-5.00] times more in those who felt that they spent enough time with the healthcare provider compared to those who felt that they did not spend enough time with the healthcare provider. Adherence was relatively the same in those who felt that the healthcare provider assisted when there was a problem and those who felt that they were not assisted when there was a problem (P=0.962). Considering healthcare provider scolding caregiver for failure to follow instructions as a reference category, caregivers who felt that their failure to follow instructions was not addressed by the healthcare providers were 2.22 times more likely to adhere to medication and those who were explained to the importance and consequences of not following instructions were 2.67 times more likely to adhere to medication. Caregivers who felt that the healthcare provider provided all the necessary information on the disease and the medication were 1.26 times more likely to adhere compared to those who felt that not all of the necessary information was provided.

Table 15: Relationship between adherence to TB medication and supportive relationship between the healthcare provider and the caregiver

Variables	Adherent (n=27)		Not adherent (n=22)		95% CI of OR			P value
	n	%	n	%	OR	Lower	Upper	
Caregiver get to speak privately to healthcare provider;								
Yes	27	56.3	21	43.8	UD	UD	UD	0.449
No	0	0.0	1	100.0	1.00			
Amount of time spent with healthcare provider;								
Enough	26	57.8	19	42.2	4.17	0.40	50.00	0.314
Not enough	1	25.0	3	75.0	1.00			
Healthcare provider assist when there's a problem;								
Does not assist	10	55.6	8	44.4	1.03	0.27	3.88	0.962
Assist	17	54.8	14	45.2	1.00			
Healthcare provider's response to failure to follow instructions;								
Addresses	8	61.5	5	38.5	2.67	0.32	24.85	0.387
Does not address	16	57.1	12	42.9	2.22	0.35	15.05	0.434
Scolds caregiver	3	37.5	5	62.5	1.00			
Provisions of information on the disease & drugs by healthcare provider;								
Provides	10	58.8	7	41.2	1.26	0.33	4.89	0.706
Does not provide	17	53.1	15	46.9	1.00			

UD= undefined

4.3.6: Relationship between adherence to TB medication and pattern of healthcare delivery

Various healthcare delivery pattern factors were explored to determine whether they influenced adherence to TB medication. They included waiting time at the clinic, availability of drugs at the clinic, suitability of clinic operating days and time of attending the clinic.

Among the caregivers, 4.1% felt that the waiting time at the clinic was always long while 55.1% felt that the waiting time was sometimes long.40.8% felt that the waiting time was not long. All the caregivers said that the TB drugs were always available at the clinic and they all felt that the time they attended the clinic was suitable. 65.3% preferred attending the clinic early in the morning while 34.75 preferred attending the clinic in the late morning. 75.5% of the caregivers felt that the clinic operation days were suitable while 24.5% felt that they were not suitable. The ones who found the clinic operation days unsuitable cited difficulty in getting time off from work as a major reason.

Table 16: Pattern of healthcare delivery factors that influence adherence to TB medication

Characteristics	N=49	
Clinic operations		
Clinic operation days;		
Suitable	37	75.5%
Not suitable	12	24.5%
Reasons why clinic operation days not suitable;		
Difficult to get time off	12	24.5%
Suitable	37	75.5%
Time of attending clinic;		
Early morning	32	65.3%
Late morning	17	34.7%
Time for attending clinic suitable	49	100%
Waiting time at the clinic;		
Always long	2	4.1%
Sometimes long	27	55.1%
Not long	20	40.8%
TB drugs always available at the clinic;	49	100%

There was no significant association between the pattern of healthcare delivery and adherence to TB medication. Adherence was relatively the same among those who found the waiting time at the clinic to be long and those who did not find the waiting time long (OR= 1.01). Those who

found the clinic operation days not suitable were 1.90 times more likely to adhere to TB medication, compared to those who found the days suitable. Most of the caregivers who found the clinic days unsuitable were those in formal employments and had to seek time off work.

Table 17: Relationship between adherence to TB treatment and pattern of healthcare delivery

	Adherent (n=27)		Not adherent (n=22)			95% CI of OR		P
Variables	**n**	**%**	**n**	**%**	**OR**	**Lower**	**Upper**	**value**
Clinic operation days;								
Not suitable	8	66.7	4	33.3	1.90	0.49	7.40	0.354
Suitable	19	51.4	18	48.6	1.00			
Waiting time at the clinic;								
Long	16	55.2	13	44.8	1.01	0.27	3.69	0.991
Not long	11	55.0	9	45.0	1.00			

4.3.7: Multivariate analysis of association between marital status and medicine administration at 24 hour intervals and treatment adherence

Binary logistic regression was used to model adherence to TB treatment using two candidate predictive factors, namely marital status and medicine administration at 24 hour intervals. These factors were significantly associated (independently) with adherence to TB treatment at bivariate analysis. Upon adjustment in multivariate analysis, the resulting model is as shown in table 16.

Table 18: Multivariate logistic regression model determining factors associated with anti-TB medication non-adherence

	Bivariate analysis				Multivariate analysis	
Predictors	N (%)	N (%)	OR (95% CI)	P value	Adj. OR (95% CI)	P value
Marital status: Currently married	24 (63.2)	14 (36.8)	4.57 (1.04 – 20.11)	**0.046**	3.06 (0.61 – 15.37)	0.173
Medicine administration: 24 hrs interval	24 (68.6)	11 (31.4)	8.00 (1.85 – 34.54)	**0.003**	6.47 (1.44 – 29.10)	**0.015**

Adjusting for interval of administration of medicine, marital status emerged not significantly associated with adherence to TB treatment (P=0.173). However, a child raised by a married couple was 3.06 times more likely to adhere to treatment compared to one raised by a single caregiver.

Upon adjusting for marital status, administration of medicine at 24 hours interval was significantly associated with adherence to TB treatment (P=0.015). A Child given medication at 24 hour interval was 6.47 times more likely to adhere to treatment compared to one given at a shorter interval.

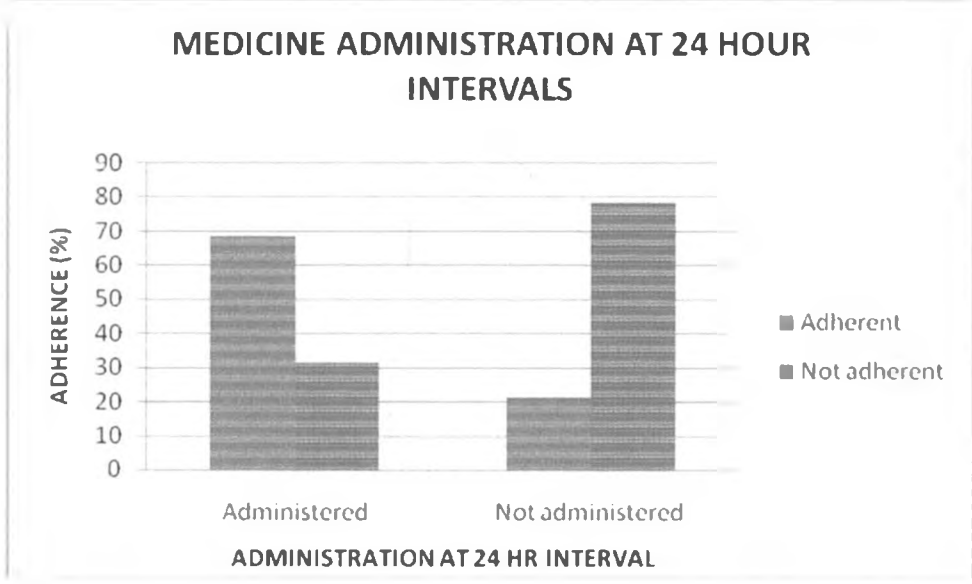


FIGURE 4: Association between administration at 24 hour intervals and adherence

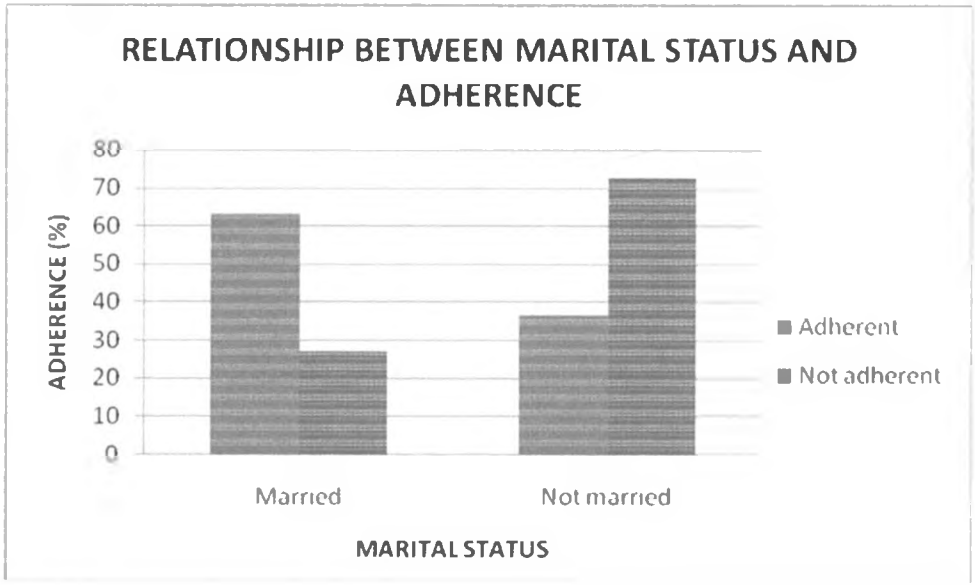


FIGURE 5: Association between marital status and adherence to medication

DISCUSSION

5.1: Rate of adherence to anti-TB medication

The rate of adherence to anti-TB medication as determined by INH test strips was 91.8%. This adherence rate was slightly lower than that observed in a similar study whose study population was predominantly adults, which was carried out in Kibera and Mbagathi hospital, Nairobi where the adherence rate was 96.5%[24]. A number of similar studies which also used urine isoniazid testing to determine the rate of adherence had been carried out in Uganda and the rate ranged from 72%-80% [17,25,27,28]. In other studies, adherence rates were 72% [26], 71.5% [29] and 82% [30]. The high adherence rate compared to most of the other studies could have been attributed to structures which have been put in place by DLTLP in an effort to control TB.

The INH test strips proved to be of value as a tool for detecting non-adherence. If the strips were to be used periodically for the TB patients during their visits to the clinic, it could aid in identifying non-adherent patients at any point in the course of treatment and promoting adherence among such patients. However the test strips are very costly and unaffordable for routine use in developing countries.

5.2: Factors contributing to non-adherence to anti-TB medication

5.2.1: Baseline characteristics of the patients

The age, sex and weight of the patients had no statistically significant association with adherence to medication. These findings were consistent with the findings in other similar studies which also concluded that age and sex of the patient had no significant association with adherence [13,25,32,33,34,36,37]. However, a study carried out in rural Turkey showed females to be more adherent

than males[35]. Another study carried out in Thailand also found sex of the patient to be significantly associated with adherence[38]. In the two studies that found a significant association, the participants were adult patients. No significant association was found in all the studies which involved paediatric patients. This could be attributed to the fact that in paediatric patients, adherence is highly dependent on the caregivers of the children therefore the baseline characteristics of the patients may fail to reflect their association with patient's adherence to medication.

5.2.2: Economic and structural factors contributing to non-adherence to anti-TB medication

Marital status of the caregiver was the only structural factor that had a statistically significant association with adherence to medication (P = 0.046) in the bivariate analysis. Patients whose caregivers were married were 4.57 times more likely to adhere to treatment compared to those whose caregivers were not married. However when adjusted for in the multivariate analysis, it was not statistically significant. The trend that emerged showed that a child whose caregiver was married was 3.06 times more likely to adhere to medication compared to one whose caregivers was not married. However, other studies did not find a significant association between marital status and adherence to medication[25,32,33,34]. For most of the married couples, if the primary caregiver had difficulty keeping the clinic appointment, the spouse could attend the clinic and therefore collect the medicine on time. The spouses of the caregivers also played a role in reminding the caregiver that it was time to administer the drugs to child. Such support went a long way in ensuring that the patient adhered to their medication. Therefore, the higher

adherence rate among children of married caregivers could be explained by the fact that marriage offers good structural support.

Although the level of education did not have a statistically significant relationship with adherence, the rate of adherence seemed to increase with the level of education whereby those who had secondary education were 1.49 times more likely to adhere those who had primary education and those who had tertiary education were twice as likely to adhere compared to those who had primary education. The findings were in line with those of a Chinese study[13] and an Egyptian study[19] which also found no significant association between the level of education and adherence to medication. The trend that emerged whereby there was an increase in adherence with increase in the level of education could be attributed to a better understanding of the nature disease, the treatment requirements and the consequences of poor adherence in those with higher levels of education. Most of the caregivers who had tertiary education had sought for more information on the disease apart from that which was provided at the clinic and had a better understanding of the consequences of not of adhering to medication.

The family's average monthly income had no statistically significant relationship with adherence to medication. This was consistent with the findings of a Malaysian study [34] which found no significant association between the family income and adherence to medication. However, in a study carried out in China[13], the average income of the patient was significantly associated with adherence. This was because TB treatment had many additional costs which where unaffordable to low income earners. In Kenya, the structure that has been put in place is such that TB treatment is free and therefore accessible to all who present themselves to the hospital for

treatment. This could explain why there was no significant relationship between the average family income and adherence to medication.

There was no significant association between the rate of adherence and the area of residence of the patients. This was in line with the findings in a Ugandan study[25] which also found no significant association. However, other studies[17,31,32,37] found the area of residence to significantly affect adherence since the distance to the healthcare facility depended on the patient's area of residence. In those studies, patients who lived far from the health facility had significantly higher odds of being non-adherent. In Kenya, TB treatment is delivered through 2,318 healthcare facilities which are spread out and are located at the community level. All of the caregivers who were interviewed stated that there was a facility in their locality which had a TB clinic that they could easily access and get their medication. They also stated that the healthcare facility was either within a walking distance or at a distance which required an affordable amount of money for transport. Most of the patients from outside Nairobi were those who had been referred to KNH for some medical follow up at the clinic which could not be done at their local facilities. The widespread set up of TB clinics has gone a long way in promoting accessibility to TB treatment in TB patients. This has played a major role in improving adherence to anti-TB medication.

5.2.3:Patient/caregiver related factors contributing to non-adherence to anti-TB medication

The caregiver's knowledge on TB had no significant association with adherence to medication. The findings were similar to the findings of Naing *et al*[37] who also did not find any significant association between knowledge on TB and adherence to medication. However, other studies found a significant association[18,20,25,32]. In a Ugandan study by Amuha *et al*[25], knowledge of TB

was associated with adherence at bivariate analysis however there was no significant association at multivariate analysis. In a study carried out in Eastern Nepal[32], majority of the non-adherents were not well informed about their disease, effects and treatment. 95.9% of the caregivers reported that they knew about TB. Most of them were able to describe it but the extent of the description varied from poor to very well. The ones who described it very well were those who had sought extra information about it apart from what they had been told at the clinic. Most the caregivers were able to list some signs and symptoms of the disease and knew how it was transmitted. However the caregivers of extra-pulmonary TB patients kept on inquiring on how TB was transmitted to other parts of the body. The nature of extra-pulmonary TB either had not been brought out by the healthcare provider or it had not been understood by the caregivers. All of the caregivers knew that TB is curable and most of them quoted an advertisement in Kiswahili which states that "TB ina tiba" which means that TB is curable. Most of the caregivers (95.9%) understood the importance of completing TB treatment. The national TB program by DLTLD has laid emphasis on patient education at the TB clinics to ensure that they are informed on the disease and the nature of treatment. Several posters on TB have also been put up in various sections of the hospital to provide information not only to TB patients but also to the general public. The advertisement on the curability of TB seemed to have reached many people and had improved the perception people had of TB. The efforts of DLTLD have gone a long way in improving general awareness of TB therefore many people have some knowledge on the disease. This could explain why the findings on the association between knowledge on TB and adherence were not significant.

Disclosure to family and friends about the TB status of the child had no significant association with adherence. Presence of friends or relatives interfering with drug administration and how people in the patient's area of residence related to TB patients also had no significant association with adherence. These factors were picked as indicators for stigmatization in TB patients therefore stigmatization was not significantly associated with adherence to medication. However in a study that was carried out in China[13], there was a lot of stigma attached to TB and this lead to patients hiding their diagnosis from others and defaulting on their medication. In this study, an element of stigmatization came out from the caregivers' various responses on why they had not disclosed the children's diagnosis and how the community related to TB patients. From the responses, AIDS was strongly associated with TB by some people and TB was seen as a highly contagious disease which required people to keep off the patient. To deal with stigma, DLTLD has been carrying out trainings and sensitizing health workers on stigma reduction in TB. Failure to find a significant association between stigma and adherence to medication could be attributed to reduced stigmatization of TB patients.

There was no statistically significant relationship between side-effects to medication and adherence to anti-TB medication. The findings were similar to those of a Ugandan study[25] and a South African study[26]. Other studies however found a significant association between the occurrence of side-effects or adverse reactions and adherence[13,20,30,32,38]. Failure to find an association between the occurrence of side-effects and adherence to medication could be attributed to the fact that the side-effects that were experienced were minor e.g. vomiting, abdominal discomfort and nausea. The caregivers had come up with ways of dealing with these

side-effects therefore their occurrence did not significantly affect the patient's adherence to medication.

Medicine administration at 24 hour intervals had a statistically significant association with adherence to medication both at bivariate and multivariate analysis. Children whose caregivers had a specific time for administering medication were 6.47 times more likely to adhere to medication compared to those whose caregivers did not administer the medication at 24 hour intervals. Caregivers who had a specific time for administering medication were less likely to forget to administer the medication because they often employed ways of reminding them when it was time to administer the medication. Some of them used alarm clocks which went off when it was time to administer drugs while others had someone to remind them that it was time to administer the drugs. Those caregivers who had no specific time for administering medication usually administered the medication any time during the morning hours for those who administered medication in the morning or any time during the evening hours for those who administered medication in the evening. These caregivers therefore ended up administering the drugs earlier than or later than usual on some days and sometimes they forgot to administer the drugs. Adherence to medication can be improved by advising all the caregivers to pick the most suitable time for them to administer medication and to ensure that they administer the medication at that specific time every day. This will encourage them to employ various methods of reminding them that it is time to administer the medicine hence promote adherence.

5.2.4: Regimen complexity factors

There was no statistically significant association between the pill burden and adherence to medication. The findings were consistent with those of a Ugandan study[25] which also had no

significant association. However, in an Indian study, there was a significant association and patients were likely not to take their medication if the pills were too many[31]. Failure to find a significant association between the pill burden and adherence could be attributed the fact that the drugs for TB come in fixed dose combination whereby all the drugs are combined and formulated into a one tablet. Therefore instead of the patients taking two different tablets for the two different drugs, the patient takes only one tablet. This goes a long way in reducing the pill burden hence promoting adherence.

The type of drug formulation had no significant association with adherence to medication. However a trend emerged which showed that those patients who were taking dispersible tablets were more likely to adhere than those who were taking tablets. This could be attributed to the fact that the dispersible tablets were easy to administer compared to the tablets. Some of the children who were receiving tablets experienced some difficulty in swallowing the tablets and this could have had an impact on adherence. The introduction of dispersible tablets for paediatric patients has gone a long way in improving drug administration in this group of patients hence promoting adherence. However not all the patients who could benefit from using the dispersible tablets are able to access them since priority is given to the very young patients.

5.2.5: Relationship between healthcare provider and caregiver

Most of the caregivers (91.8%) felt that they spent enough time with the healthcare providers when they attended the clinic. The caregivers felt that they did not need to spend a lot of time at the clinic especially after the child's health had improved and all they needed to do was collect the medication for the month. 63.3% of the caregivers felt that they were always assisted when they had a problem and 34.7% felt that sometimes they were assisted. Only 2.0% felt that they

were not assisted. 65.3% of the caregivers felt that the healthcare provider did not provide all the information on the disease and drugs while the rest felt that the information was provided. 16.3% of the caregivers reported that when they failed to follow instructions they were scolded by the healthcare provider while 26.5% said that they were explained for the importance and consequences of failing to follow the instructions. 14.3% felt that the healthcare provider did not address the matter. The patients of the caregivers who were explained for the importance of following the instructions were shown to be 2.67 times more likely to adhere compared to those who were scolded. The amount of time spent with the caregiver, assistance by healthcare provider when there's a problem, healthcare provider's response to failure to follow instructions and provision of information on the disease and treatment by healthcare workers were used as parameters of determining the nature of the relationship between the healthcare provider and the caregivers and also for determining the attitude of the healthcare providers towards the patients and the caregivers. There was no significant association between all of the above factors and adherence to medication, therefore in this study the nature of relationship between the healthcare provider and the caregiver and the attitude of the healthcare provider towards the caregiver had no significant association with adherence. The findings are similar to those of a Ugandan study[25] which found no significant association between the attitude of the healthcare provider towards the patient and adherence to medication. However other studies have found a significant association between the attitude of the healthcare worker and adherence to medication[20,31,32]. These studies found that a breakdown in the healthcare provider-patients relationship lead to significant levels of non-adherence.

5.2.6: Pattern of healthcare delivery

There was no significant association between the waiting time at the clinic and adherence to medication. The findings were similar to those of a Ugandan study[25] but conflicted results from other studies that showed significant association[17,31,32]. The clinic operation days were not suitable for 24.5% of the caregivers. These caregivers were mainly those who were employed and therefore needed to take time off work to attend the clinic. They said that it was difficult to get time off work every month without explaining why they needed the time off and would have preferred to attend the TB clinic over the weekend. The other caregivers who had no employers to answer to had no problem with the clinic operation days. Failure to find an association between the pattern of healthcare delivery and adherence to medication could be attributed to a generally good pattern of healthcare delivery whereby drugs are always available at the clinic, the clinic operates throughout the week and the waiting time is not so long at the clinic. Kenya has a good pattern of healthcare delivery compared to the other countries which had significant association between the pattern of healthcare delivery and adherence to medication.

5.3: LIMITATIONS OF THE STUDY

In the study several factors which had no statistically significant association with adherence to medication had trends emerging which indicated that they had an effect on adherence to medication. Failure to detect significant associations could have been due to the small sample size used in the study which might have been unable to detect some associations.

Data on treatment history and the factors that influence adherence to medication were based on self reports given by the patient's caregivers. This could have lead to some recall bias in the study.

The INH urine test strips can only determine rate of adherence over a period of 24 hours therefore other methods e.g. patient self report are required to determine adherence over a long period of time.

CONCLUSION AND RECOMMMENDATIONS

The adherence rate as determined by the urine isoniazid test was generally high compared to the rates in other countries where similar studies have been carried out. The high rate of adherence observed was probably due to free anti-TB drugs, extensive distribution of TB treatment services in various health facilities up to the community level and the sustained training of health care workers to promote adherence to treatment at community level and to improve TB case management also at the community level.

The INH test strips proved to be of value in determining the rate of adherence in patients taking anti-TB medication. The test strips were easy to use and the results were easily observed. The INH test strips could be particularly relevant for evaluating adherence to self-administered treatment especially in cases whereby there is no improvement in a patient who has been on treatment for a while or in those patients who are suspected to be non adherent to medication. However, the costs of these tests remain high and advocacy is necessary to make this test accessible to the national TB programme in Kenya.

Among the economic and structural factors that were looked into, marital status was found to be significantly associated with patient adherence to anti-TB medication. Marriage seemed to provide structural support to the caregiver which seemed to promote adherence to medication. Provision of structural support to the caregivers who are not married could promote adherence to medication. This can be achieved by encouraging such caregivers to involve close friends or relatives in the child's treatment so that they are able to support the caregiver whenever there's a need. Caregivers who are not willing to seek the support of their friends and relatives can be encouraged to join or form patient support groups with other caregivers of TB patients. The aim

of support groups is to bring together people going through the same problem so that they can encourage and assist each other to get through their problem and such support can promote adherence.

Only one of the patient/caregiver factors was found to be significantly associated with adherence to anti-TB medication. This factor was administration of medication at 24 hour intervals. Administration of medicine at 24 hour intervals meant that the caregiver had a set hour at which medication was administered and methods of reminding the caregiver when it was time to administer the medication were employed. All caregivers should be advised to set a specific time for administering medication and should be educated on the various methods they can use to remind them when it is time to administer the medicine. This intervention could promote patient adherence to medication.

Regimen complexity factors were not significantly associated with adherence to anti-TB medication. This could be attributed to the use of fixed dose combination tablets which reduce the pill burden of the patient and availability dispersible tablets for paediatric patients which makes it easier to administer the drugs to children. However, greater quantities of the dispersible tablets should be supplied to the health facilities so that all the paediatric patients who require them can access them hence promote adherence among them.

The relationship between the health care provider and the patient/caregiver was not significantly associated with adherence to anti-TB medication. This could be attributed to a generally positive relationship between the healthcare provider and the patient/caregiver which has been brought about by the sustained training by DLTLD of the health care workers on the better case management of the TB patients and sensitization on TB/HIV stigma reduction.

The pattern of health care delivery was not significantly associated to adherence to anti-TB medication. This could be attributed to decentralization by DLTLD of TB control services down to the community level to increase access to this services and timely supply of drugs to all health facilities to ensure that drugs are always available at the facilities.

In this study, trends indicating that some factors had an effect on adherence were observed but they were not statistically significant. Similar studies should be carried out in future using large sample sizes so as to detect important associations between such factors and adherence to anti-TB medication which this study was unable to detect due to the sample size.

Similar studies should be carried out in different provinces to determine if the adherence rates are comparable to those in Nairobi and the factors affecting adherence in the different areas.

Studies should be done to determine if our population is made up of slow or fast acetylators and how it affects the plasma isoniazid levels. This would provide useful information on whether our population is appropriately dosed for isoniazid, if the occurrence of side effects is associated with the rate of acetylation of isoniazid in the patient and if development of resistance to anti-TB drugs especially isoniazid is associated with the rate of acetylation of isoniazid in the patient.

REFERENCES

1. Nehaul L.K (2007): Tuberculosis, Clinical pharmacy and therapeutics, 4th edition. Churchill Livingstone Elsevier; pp555-557.
2. Tuberculosis profile. Available on http://www.usaid.gov/our-work/global-health/id/tuberculosis/countries/africa/kenya.pdf
3. Childhood tuberculosis. Available on www.kemri-welcome.org/people/researchers/andrewbrent
4. Brent AJ, Anderson ST, Kampmann B (2008). Childhood tuberculosis: Out of sight out of mind? Trans R Soc Trop Med Hyg; **102**: 217-218.
5. Feja K, Saiman L (2005). Tuberculosis in children. Clin Chest Med; **26(2)**: 295-312.
6. Mubarik M, Nabi B, Ladakhi GM, *et al* (2000). Childhood tuberculosis (part 1) Epidemiology, pathogenesis, clinical profile. JK pract;**7(1)**:12-5
7. WHO TB/HIV a clinical manual 2nd edition, Geneva 2004.
8. www.nltp.co.ke
9. Mwendwa JN (2008). Disclosure of HIV/AIDS and adherence to HAART among HIV infected children. *A dissertation submitted in partial fulfillment for master of pharmacy in clinical pharmacy UON.*
10. World Health Organization. Adherence to long term therapies: Evidence for action. Geneva 2003.
11. Munro SA, Lewin SA, Smith H, *et al* (2007). Patient adherence to tuberculosis treatment: A systematic review of Qualitative research. PLoS Med;**4(7)**:e238

12. Awofeso N (2008). Anti-tuberculosis medication side-effects constitute major factor for poor adherence to TB treatment. Bull WHO 2008 March; **86 (3)**: B-D.

13. Xu W, Lu W, Zhou Y, *et al* (2009).Adherence to anti-tuberculosis treatment among pulmonary tuberculosis patients. A qualitative and quantitative study. BMC Health Serv Res; **9**:169.

14. Van-Zyl S, Marais BJ, Hesseling AC, *et al* (2006). Adherence to anti-tuberculosis chemoprophylaxis and treatment in children. Int J. Tuberc lung dis; **10(1)**: 13-18.

15. Manders AJ, Banerjee A, VandenBorne HW, *et al* (2001). Can guardians supervise TB treatment as well as health workers? A study on adherence during the intensive phase. Int J Tuberc Lung Dis; **5(9)**:838-42.

16. Khalili H, Dashti-Khavidaki S, Sajadi S, *et al* (2008). Assessment of adherence to tuberculosis drug regimen. DARU; **16(1)**:47-50.

17. Meissner PE, Musoke P, Okwera A, *et al* (2002). The value of urine testing for verifying adherence to anti-tuberculosis chemotherapy in children and adults in Uganda. Int J Tuberc Lung Dis; **6(10)**:903-908.

18. Kaona FA, Tua M, Sizya S, *et al* (2004). An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. BMC Public Health; **4**:68.

19. Ashry G, Ahmed MAM, Sherif AA, *et al* (1997). Compliance with anti-tuberculosis drugs among tuberculosis patients in Alexandria, Egypt. Eastern Mediterranean Health Journal; **3(2)**:244-250.

20. Pranaya Mishra; Adherence to tuberculosis treatment under Directly Observed Treatment, short-course (DOTs) in Nepal: Quantitative and Qualitative studies. Available at www.farma.ku.dk/idex.php/Pranaya-Mishr/2776/01. Accessed on November 20th 2009.

21. Mqoqi NP, Churchyard GA, Kleinschmidt I, *et al* (1997). Attendance versus compliance with tuberculosis treatment in an occupational setting-a pilot study. S Afr Med J; **87(11)**:1517-21.

22. Dick J, Schoeman JH, Mohammed A, *et al* (1996). Tuberculosis in the community: Evaluation of a volunteer health worker programme to enhance adherence to anti-tuberculosis treatment. Tuber Lung Dis; **77(3)**:274-9.

23. Stop TB partnership Childhood TB subgroup. WHO, Geneva Switzerland. Chapter 2: Anti-tuberculosis treatment in children. Int J Tuberc Lung Dis; **10(11)**:1205-1211.

24. Raguenaud M, Zachariah R, Massaquoi M, *et al* (2008). High adherence to anti-tuberculosis treatment among patients attending a hospital and slum health centre in Nairobi, Kenya. Global Public Health; **3(4)**: 433-439.

25. Amuha MG, Kutyabami P, Kitutu FE, *et al* (2009). Non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mbarara Hospital Uganda: Prevalence and associated factors. African Health Sciences; **9(51)**:S8-S15.

26. Szakacs TA, Wilson D, Cameron DW, *et al* (2006). Adherence with isoniazid for prevention of tuberculosis among HIV infected adults in South Africa. BMC Infect Dis; **6:**97.

27. Pekovic V, Mayanja H, Vjecha M, *et al* (1998). Comparison of three composite compliance indices in a trial of self-administered preventive therapy for tuberculosis in HIV infected Ugandan adults. J Clin Epidemiol; **51**: 597-607.

28. Lugada E.S, Watera C, Nakiyingi J, *et al* (2002). Operational assessment of isoniazid prophylaxis in a community AIDS service organization in Uganda. Int J Tuberc Lung Dis; **6**: 326-331.

29. Eidlitz-Markus T, Zeharia A, Baum G, *et al* (2003). Use of the urine colour test to monitor compliance with isoniazid treatment of latent tuberculosis infection. Chest; **123**: 736-739.

30. Skukla SJ, Warren DK, Woeltje KF, *et al* (2002). Factors associated with the treatment of latent TB infection among health-care workers at a Midwestern teaching hospital. Chest; **122**: 1609-1614.

31. Jaiswal A, Singh V, Ogden JA, *et al* (2003). Adherence to tuberculosis treatment, lessons from the urban setting of Delhi, India. Tropical Medicine and International Health; **8(7)**: 625-633.

32. Wares DF, Singh S, Acharya AK, *et al* (2003). Non adherence to TB treatment in the eastern Tarai of Nepal. International Journal of Tuberculosis and Lung Disease; **7(4)**: 327-335.

33. Mc Donell M, Turner J, Weaver TM, *et al* (2001). Antecedents of Adherence to Anti-tuberculosis therapy. Public Health Nursing; **18(6)**: 392-400.

34. Nuwaha F. (1999). Control of Tuberculosis in Uganda, a tale of two districts. Int Journal of Tuberc and Lung Disease; **3(2)**: 224-230.

35. Balbay O, Annakkaya NA, Arbak P, *et al* (2005). Which patients are able to adhere to Tuberculosis treatment? A study in rural area in the Northwest Part of Turkey. International Journal of Infectious Diseases; **58**: 152-158.

36. Caylà JA, Rodrigo T, Ruiz-Manzano J, *et al* (2009). Tuberculosis treatment adherence and fatality in Spain. Respiratory Research; **10**: 121.

37. Naing NN, D'este C, Isa AR, et al (2001). Factors contributing to poor compliance with anti-tuberculosis treatment among tuberculosis patients. Southern Asian Journal of Tropical Medicine Public Health; **32(2)**: 369-382.

38. Ngamvithayapong J, Uthaivoravit W, Yanai H, *et al* (1997). Adherence to tuberculosis preventive therapy among HIV-infected persons in Chiang Rai, Thailand. AIDS; **11**: 107-112.

APPENDIX I

QUESTIONNAIRE

A.BIODATA

Study number: Date:

Age:

Gender:

Weight:

B.GENERAL KNOWLEDGE ON TB

1. Do you know what TB is? Yes ☐ No ☐

If yes, briefly state what it

is.....

.....

.....

2. How do you know that someone has TB?

.....

.....

3. Do you know how it is transmitted? Yes ☐ No ☐

If yes,

explain.....

.....

4. Does it have a cure? Yes ☐ No ☐

5. How long is the treatment?.....

6. Do you know why it is important to finish the treatment?

Yes ☐ No ☐

If yes,

explain.....

.....

.....

C. ADHERENCE TO MEDICATION

1. When was the child started on TB treatment? (dd/mm/yy).....

2. Which drugs is the child currently taking for TB?

.....

.....

3. How have you been giving the drugs to the child?

Drug name	Dose	Frequency	Dosage	Formulation

4. Who administers the drugs to the child?

.....

5. When do you give the drugs?

- Before meals ☐
- After meals ☐
- With meals ☐

6. Does the child sometimes refuse to take the medication?

Yes ☐ No ☐

If yes, how do you ensure that the child takes the medicine?

- Promise to reward the child ☐

- Force the child ☐
- Mix the drug with food or fluids which have a sweet taste ☐
- Give with plenty of juice or milk ☐
- Others,

specify.....

7. Does the child experience any problem immediately after taking the medicines?

Yes ☐ No ☐

If yes, what type of problem.....

.....

How do you handle it.....

.....

8. Are there any circumstances that have led to the child missing TB medication in the past?

Yes ☐ No ☐

If yes, how many times has the child missed taking their medication?

.....

What were the circumstances?

- Forgot to administer ☐
- Ran short of drugs ☐

- Child refused to take ☐
- Health of the child improved ☐
- Was away from home ☐
- Other,

specify.....

.....

9. At what time do you usually administer the drug? .....

10. Are there occasions whereby you administer the drugs earlier than or later than usual?

Yes ☐ No ☐

If yes, explain.....

11.Did the child take their medication in the last 24hrs?

Yes ☐ No ☐

12. Are those in close contact with you (friends and relatives) aware that the child has TB?

Yes ☐ No ☐

If no, why?.....

13. Does the presence of friends or relatives visiting you at home interfere with the way you give the drugs to the child?

Yes ☐ No ☐

If yes, what do you normally do?

Take the child to a different room and administer the drugs

Wait till the visitors leave

Other.....

14. In your opinion or from experience, how do people in your area of residence relate to TB patients?.....

.....

15. Do have a way of remembering that it is time to administer the drug?

Yes No

If yes, how do you always remember to give the drug on time?

Someone reminds you

Use an alarm clock

Synchronized with certain events e.g. after meals

Others.....

16. Do you experience any problems when administering the drugs?

Yes No

If yes, what problems?

.....

How do you deal with the problem?

.....

17. Do you get to privately speak to the health care provider at the clinic?

Yes ☐ No ☐

18. Do you wait for long before you are attended to?

Yes ☐ No ☐

19. Are the TB drugs always available when you go to pick them from the clinic?

Yes ☐ No ☐

20. Are the days of operation of the clinic suitable for you?

Yes ☐ No ☐

If no, comment.....

21. What time do you usually attend the clinic?

Early morning ☐

Late morning ☐

Afternoon ☐

22. Are you comfortable with that timing?

Yes ☐ No ☐

If no, what is your preference.....

23. Is the amount of time that you spend with the health care provider enough?

Yes ☐ No ☐

If no, explain.....

.....

24. When you have a problem, does your health care provider assist you in sorting it out?

Yes ☐ No ☐

25. How does your health care provider respond when you fail to follow certain instructions e.g. default medication?

Scolds me ☐

Does not address the matter ☐

Explains the importance and consequences of not following the instruction ☐

26. Does your health care provider give you all the necessary information on the disease and drugs that the child is taking e.g. side-effects? ☐ ☐

Yes No

27. What is your level of education?

Primary education ☐

Secondary education ☐

Tertiary education ☐

Other.....

28. What is your marital status.....

29. What is your occupation.....

30. What is your spouse's occupation.....

31. What is the family's average monthly income?.....

32. How would you describe the cost of all the services provided for TB treatment?

Unaffordable ☐ Fair ☐

Expensive ☐ Easily affordable ☐

33. Do you incur any transport costs when coming for TB medication?

Yes ☐ No ☐

If yes, is it affordable? .....

34. Does the child receive at least three meals a day?

Yes ☐ No ☐

If no, why?.....

35. Where do you live?.....

36. Do you have any questions or concerns which you would like to be addressed?

.....

.....

37. Taxo-INH urine test results: Positive ☐ Negative ☐

THANK YOU FOR PARTICIPATING IN THIS STUDY.

APPENDIX II

CONSENT AND CONSENT INFORMATION

Dear respondent,

My name is Marion N. Ong'ayo a Pharmacist by profession. I am currently pursuing a Masters of Pharmacy Degree in Clinical Pharmacy at the school of pharmacy at the University of Nairobi. The Masters programme involves course work, practical work and clinical research in one's area of interest.

RESEARCH

My area of interest is adherence to TB treatment in children and am carrying out a study among patients aged 1-15 years who are attending the TB clinic. In this study I intend to determine the rate of adherence to anti-TB treatment and to determine the factors that contribute to non-adherence to the treatment. The results of the study will be used to address the factors that hinder adherence to treatment for TB and to enhance overall adherence to treatment.

METHODOLOGY

There is a set of questions which I will ask the caregivers of all the children between the age of 1 to 15 years who will be selected to take part in the study. A specimen of urine will also be required.

THE INTERVIEW

A simple questionnaire will be administered and all the questions will be read and interpreted in the simplest and comprehensible manner that you can understand and answer. You will be expected to answer the questions freely to the best of your knowledge. The answers you give will not in any way jeopardize the child's treatment and they will be kept under strict confidence. Your responses will be written down for further analysis, discussions, conclusions and recommendations where possible.

CONFIDENTIALITY

All the information you give will be treated in strict confidence without sharing with a third party unless your consent is sought first. This are the ethics normally held by any healthcare provider. The filled questionnaire will be securely locked and only I, the researcher will have access to them.

BENEFITS

There will be no immediate benefits to you. However any needs or concerns that may arise during the interview will be addressed promptly. The results obtained from this study will be used to make recommendations aimed at improving the adherence of children to TB treatment hence improving the overall treatment outcome of children on TB treatment.

RISKS

This study will involve interviewing you and collecting a urine sample from the patient. The only specimen required from the patient is a urine sample therefore it is a minimal or no risk study.

PARTICIPATION

Your participation in the study is purely voluntary and one can withdraw anytime at his or her own will and this will not affect the patient's receiving of medical care. You are encouraged to ask any questions regarding the study. You are also encouraged to ask any question for clarity, incase the questions are unclear to you.

DECLARATION BY THE RESEARCHER

I Marion N. Ong'ayo have clearly explained the purpose and the benefits of the interview to the participant. I have also explained that this is purely voluntary and the research will not jeopardize the patient's treatment in any way.

CONTACT NAME: Marion N. Ong'ayo

ID NUMBER: 21925354

ADDRESS: Department of Pharmaceutics and Pharmacy practice

School of pharmacy, University of Nairobi

P.O. BOX 19676, Nairobi.

Telephone number: 0721-579188

SIGNATURE: DATE:

DECLARATION BY PARTICIPANT

I.....do voluntarily agree to take part in this research study of adherence of paediatric patients to anti-TB treatment. The nature and the purpose of this study have been explained to me. Additionally I am clearly aware of the procedures required. I also clearly understand the benefits involved and that my participation is purely voluntary. I also understand that there are no risks involved because the study is purely by interview. I understand that my failure to participate will not jeopardize my patient's treatment. Dr. Marion N. Ong'ayo has explained all the above information to me.
I have been adequately briefed on objectives and methodology of the research and I hereby agree to participate in the interview.

NAME:

SIGNATURE: DATE:

WITNESSED BY: **DATE:**

APPENDIX III: KNH-ERC APPROVAL LETTER

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi.
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP", Nairobi.
Email: KNHplan@Ken.Healthnet.org

13th May 2010

Ref: KNH-ERC/ A/479

Dr. Marion N. Ong'ayo
Dept. of Pharmacology and pharmacognosy
School of Pharmacy
University of Nairobi

Dear Dr. Ong'ayo

RESEARCH PROPOSAL: "ADHERENCE TO ANTI-TUBERCULOSIS TREATMENT AMONG PAEDIATRIC PATIENTS AT KENYATTA N. HOSPITAL" (P8/01/2010)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and **approved** your above revised research proposal for the period 13th May, 2010 to 12th May 2011.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH/UON-ERC

c.c. Prof. K. M. Bhatt, Chairperson, KNH/UON-ERC
The Deputy Director CS, KNH
The Dean, School of Pharmacy, UON
The Chairman, Dept. of Pharmacology & Pharmacognosy, UON
The HOD, Records, KNH
Supervisors: Dr. George O. Osanjo,Dept.of Pharmacology & Pharmacognosy, UON
Dr. Margaret Oluka, Dept. of Pharmacology & Pharmacognosy, UON