ADHERENCE TO ISONAZID PREVENTIVE THERAPY AMONG HUMAN IMMUNODEFICIENCY VIRUS INFECTED CHILDREN AT COMPREHENSIVE CARE CLINIC IN MOI TEACHING AND REFERRAL HOSPITAL, ELDORET

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS OF MMED (CHILD HEALTH AND PEDIATRICS) OF SCHOOL OF MEDICINE, MOI UNIVERSITY.

DECLARATION

STUDENT'S DECLARATION

This dissertation is my original work done during Masters of Medicine in Child Health and Pediatrics degree course of Moi University.

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DEDICATION

I would like to dedicate this dissertation to God without whom it would not have been possible. To my family for their unconditional support, tremendous encouragement and motivation.

I am truly grateful.

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ABSTRACT

Background: Isoniazid preventive therapy (IPT) is recommended for six months to reduce active tuberculosis burden among children living with human immunodeficiency virus infection. This study sought to determine the level of adherence, completion rate and factors associated with adherence to isoniazid preventive therapy hence inform the program on the effectiveness.

Objectives: To determine the level of adherence, completion rate and describe factors associated with adherence to isoniazid preventive therapy among children living with human immunodeficiency virus infection at Moi Teaching and Referral Hospital.

Methods: Prospective study conducted between October 2018 to October 2019 at the Academic Model Providing Access to Health care of Moi Teaching and Referral Hospital among children living with human immunodeficiency virus infection aged 1-14 years initiated on Isoniazid preventive therapy. Two hundred and fifty one children were consecutively sampled. Data on child clinical characteristic, caregiver characteristics, completion and adherence to isoniazid were collected using structured questionnaire. Continuous variables summarized using median and corresponding interquartile range. Categorical variables summarized using frequencies and percentages. Factors associated with adherence included viral load suppression, follow up time and caregiver level of education were assessed using logistic regression and the odds ratios and corresponding 95% confidence interval reported.

Results: Among the 251 participants recruited the median age was 11.0 (IQR: 8.0, 13.0) years, 129(51.4%) were female, 229(92%) were virally suppressed. Caregivers median age was 40years (IQR 35.0, 44.0), 215 (87.7%) were female, 135 (53.8%) had primary level of education and 212 (84.5%) were aware of isoniazid preventive therapy. Two hundred and thirty six (94%) completed 6 months of isoniazid preventive therapy, 5 (2%) were lost to follow up and 10(4 %) were discontinued. Good viral suppression AOR 6.23 (1.48, 26.10), and caregiver secondary level of education AOR 0.29 (0.08, 0.96) were associated with completion. Adherence to isoniazid preventive therapy was 80.8%. Good viral suppression AOR 25.68 (95%CI: 6.22, 105.96) and follow up time with AOR: 4.42 (95% CI: 2.01, 9.70) for month 3 and AOR 30.86 (95% CI: 8.57, 111.07) for month 6 were associated with good adherence while participants whose caregiver had secondary/tertiary level of education were likely to be non-adherent with AOR: 0.36 (95% CI: 0.14, 0.95).

Conclusion: Adherence and completion of isoniazid preventive therapy was good with 8 in 10 being adherent while 9 in 10 completing. Good viral suppression and regular follow up were associated with good adherence while participants whose caregiver had secondary/tertiary level of education were likely to be non-adherent and less likely to complete IPT.

Recommendation: Provision of isoniazid preventive therapy should be continued. Further studies are needed to explore reasons why HIV infected children whose caregivers with secondary/tertiary level of education were non-adherent.

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ABBREVIATIONS

AMPATH	Academic Model Providing Access to Healthcare
GTB	WHO Global TB Programme
HIV	Human Immunodeficiency Virus
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
IREC	Institutional Research and Ethics Committee
MTRH	Moi Teaching and Referral Hospital
NTP	National Tuberculosis Control Programme
PLHIV	Persons Living with HIV
TB	Tuberculosis
TB/HIV	HIV Related Tuberculosis
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Adherence: It is the extent to which a person behavior in taking medication corresponds with agreed recommendation from health care provider.

Adherence assessment: It was done based on AMPATH validated adherence score tool. (Rachel C Vreeman et al., 2014)

AMPATH validated adherence score tool: It consists of four questions to determine the level of adherence i.e.

I. Caregiver has a problem getting the child to take medication,

II. Missing at least a dose in the last 7 days,

III. Giving a dose more than 1 hour late in the last 7 days

IV. Caregiver factors; Not being around to give medicines, Not wanting to give medicine around others or forgetting to give medicines.

Good adherence: A total score of 0 out of 4.

Fair adherence: A total score of 1 or 2 out of 4.

Poor adherence: A total score of 3 or 4 out of 4.

Adherent: A participant with a total score of 0/4 according to AMPATH validated adherence score tool during the six month period of isoniazid preventive therapy.

Adverse events: Any unfavorable symptom, sign or disease associated with the use of Isoniazid during the period of administration.

Completion: Documentation of use of isoniazid for a period six months duration as prescribed by the health care provider with no indication of stopping medication during the 6 months period.

Children: refers to a child aged 1 to 14 years.

IPT: Provision of Isoniazid to prevent development of active TB disease in case one has latent tuberculosis infection.

Severely ill: Any child who is critically ill with altered mental status and/or organ dysfunction and requires emergency care or admission.

TB infection: Person carries mycobacterium infection in the body hence has inactive form.

TB disease: Occurs when bacteria multiply and become numerous to damage organs and hence develop active disease.

CHAPTER ONE

1.1 INTRODUCTION

Tuberculosis is a multisystem disease with multiple presentations and manifestation. It is the most common cause of infectious disease related mortality worldwide. Mycobacterium tuberculosis is the causative agent; other causes include M. africanum and M. bovis. Humans are the only reservoir. Mycobacterium tuberculosis results from inhalation of infected droplets produced by a patient with pulmonary tuberculosis. TB may develop in certain instances as of age or defects in cell mediated immune response for instance HIV infection, malnutrition, prolonged steroid use and administration of chemotherapy. HIV infected children have a lifelong risk of developing tuberculosis (TB). The overall risk of developing TB is more than 20 times greater among PLHIV than those without HIV infection(W.H.O., 2012). HIV infection causes an increase in the risk of progression of tuberculosis infection and reactivation of latent tuberculosis infection by 5-15% annually.(Final-TB-Prevalence-Survey-Report.).Tuberculosis is one of the major causes of morbidity and mortality among people living with Human Immunodeficiency Virus. WHO estimates TB was associated with 251,000 deaths these accounted for 13% of total TB associated deaths in HIV infected persons.(WHO, 2019) Tuberculosis progress more rapidly to severe disease with high mortality while TB/HIV coinfection causes more rapid progression of HIV disease.

Isoniazid preventive therapy is a key public health intervention for prevention of tuberculosis among people living with Human Immunodeficiency Virus and has been recommended by World Health Organization as part of comprehensive HIV/AIDS care strategy. In Kenya, the ministry of health recommends Isoniazid preventive therapy for six months for all eligible people living with Human Immunodeficiency

Virus. However IPT implementation in Kenya has been slow since its official roll out in March 2015.(IPT_for_PLHIV_Operational_Guidelines_Sept_2015)

Isoniazid preventive therapy is provided using intensified case findings (ICF) tool for high risk children who have no signs and symptoms of tuberculosis disease. The categories who receive isoniazid preventive therapy includes all HIV infected children and all children under 5 years with contact with persons with sputum positive for tuberculosis. Isoniazid preventive therapy should be given at a dose of 10mg/kg for duration of six months. Isoniazid drug are available in form of 50mg/5 ml syrup, 100 mg tablet and 300mg tablet. They should be followed up monthly to check on adherence, adverse drug toxicity, screen for TB disease and to maintain contact register. Isoniazid preventive therapy for children with HIV infection will greatly reduce the likelihood of developing tuberculosis during childhood.

1.2 ADHERENCE TO MEDICATION

1.2.1 Adherence to all the medications

Adherence is defined as the extent to which the patient's history of therapeutic drug-taking coincides with the prescribed treatment. The level of adherence has two ways of measurement and it includes using outcome-oriented or process-oriented. Outcome-oriented use the end-result of treatment as an indicator of success. Process-oriented indicators make use of intermediate variables like appointment-keeping or pill counts. The sum of the patients who are cured and those who have completed treatment under the directly observed therapy, short course strategy, is a pragmatic indicator of treatment adherence. The significance of adherence to treatment is important in optimizing the patient’s response to treatment. Non-adherence may lead to treatment failure, waste of medications, disease progression, increase use of medical resources and development of drug resistance(Jimmy & Jose, 2011). The

World Health Organization proposes that adherence may be affected by the following factors, health care system or provider-patient relationship factors, disease and treatment factors, patient related factors, Socio-economic factors.(Alsaddig, Pharm, & Pharm, 2014). Children with social support from the care giver, family members in terms of giving assistance have better adherence to medications. Unstable living environment are associated with decreased level of adherence. Long term drugs administration of medication and adherence to treatment regimen often declines significantly overtime.

1.2.2 Adherence to isoniazid preventive therapy

Adherence is the primary determinant of treatment success. Children need the support of the parents and caretakers in taking their medications. Isoniazid preventive therapy is not any different, though the duration is longer and in some cases the children are perfectly well. This may pose a challenge to adherence among these children taking isoniazid preventive therapy. Therapy related factors for instance number of daily doses, duration of therapy and side effects have been associated with decreased level of adherence. In this study adherence was assessed using the AMPATH validated adherence score tool which consists of 4 questions i.e. Caregiver has a problem getting the child to take medication, Missing at least a dose in the last 7 days, Giving a dose more than 1 hour late in the last 7 days Caregiver factors; Not being around to give medicines, Not wanting to give medicine around others or forgetting to give medicines. (Rachel C Vreeman et al., 2014). Other studies have used recall methods like pill counts and patient self-reports to assess adherence to isoniazid preventive therapy. The AMPATH validated adherence score tool in cooperates the methods of assessing adherence used in other studies on adherence to isoniazid preventive therapy.

In a qualitative study looking at the barriers to the treatment of childhood tuberculosis and tuberculosis infection in Peru, there were some main barriers found. These included poor adherence to isoniazid preventive therapy, dosing errors and provider concern that isoniazid preventive therapy generates isoniazid resistance. This study emphasized the need to formulate strategies that encourage adherence to isoniazid preventive therapy (Chiang et al., 2017) . Mwangi et al in a hospital based study in Kenya reported adherence level to isoniazid preventive therapy of 82.4% and the good adherence to isoniazid preventive therapy was because most patients were acting in accordance to the directive by the health care provider to take isoniazid daily. Adherence was assessed by a patient having taken > 90% of doses in the preceding 2 weeks. The same study reported completion rate of isoniazid preventive therapy to be 88% and the reason cited for non-completion of isoniazid were pill burden and health care provider instigating because of poor adherence to isoniazid preventive therapy (Mwangi, 2016).A study done in Kenya on challenges affecting Isoniazid preventive therapy effectiveness in informal settlement reported that implementation of isoniazid preventive therapy was hampered by low acceptability and suboptimal adherence. The same study by Okwara et al reported adverse effects in 22.2% contacts leading was skin rash then GI disturbance 9.5%, neurological symptoms 5.4%.Rise in liver enzymes was also documented in 3 patients (Fn, Jp, & Were, n.d.). Previous studies done in Tanzania on acceptability and adherence to isoniazid preventive therapy in Human immunodeficiency virus infected patients clinically screened for latent TB reported the overall mean adherence among children to be 92.2%. The level of adherence to isoniazid preventive therapy was defined as consumption of 90% or more of the monthly prescribed isoniazid. (Shayo, Moshiro, Aboud, Bakari, & Mugusi, 2015)

1.3 Prevalence of tuberculosis in Kenya

Kenya is one of 30 high burden TB countries in the world and is among the 14 high burdens for TB, TB/HIV, MDR TB. According to WHO at least 1 million children suffer from tuberculosis every year and 140,000 children die of preventable, treatable and curable disease. Tuberculosis is a major cause of morbidity and mortality among children. There is higher risk and rapid progression of active TB among children thus leading to higher mortality. The estimated number of people that fell ill with TB in Kenya as at 2018 was 426 per 100,000 populations with annual incidence of 156,000 per person and the trends were presumed to be similar for children. (FINAL NTLD ANNUAL REPORT_2018). TB/HIV co infection in the year 2018 was reported to be at 27% of patients with TB. The co infection rate in children who were 14 years and below was 15%. TB related deaths among people living with HIV have was reported to be 251,000 deaths in the year 2018. (GTB 2019 REPORT, n.d.)

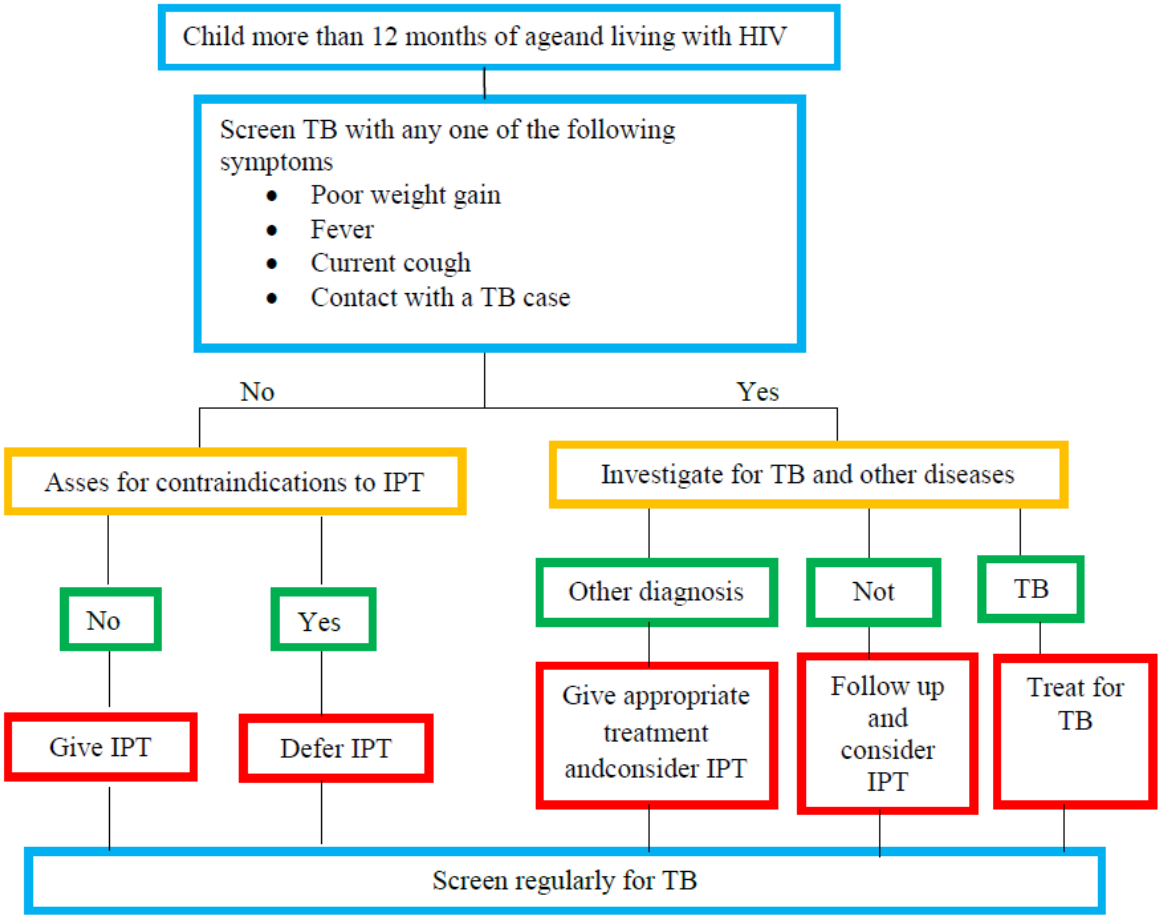
1.4 Description of Isoniazid preventive therapy .

Isoniazid is an effective drug used for prevention and treatment of tuberculosis. Human immunodeficiency virus infection triggered new approach to handling tuberculosis around the world and intervention started with world health organization which conducted global policy meeting to review evidence regarding intensified case finding (ICF) and Isoniazid Preventive Therapy (IPT) in 2010. It was found that Human immunodeficiency virus infection was the strongest risk factor for the development of TB with a probability ratio of between 20-37 times greater (Becker, 2015). TB was found to be responsible for quarter of deaths in People Living with Human Immunodeficiency Virus (PLHIV). Thus, WHO recommended 12 collaborative TB/HIV activities as part of TB –HIV prevention, care and treatment services. It included interventions that reduced morbidity and mortality from TB in

PLHIV such as provision of ART and the 3 I's –ICF, IPT, infection control. This was packaged as guidelines which were published and disseminated in Kenya in 2011. Intensified case finding of TB in HIV patients was started in May 2011 while provision of isoniazid preventive therapy commenced in September 2011. The health care providers have routinely screened all the children living with human immunodeficiency virus infection enrolled in the HIV care clinic during monthly visit using the standardized TB screening tool that inquires about presence of cough, duration, household contact with confirmed case of TB disease, hotness of body and weight loss. Child without the symptoms and signs is initiated on isoniazid preventive therapy at 10mg/kg once daily for duration of six months. The program was rolled out in pre-determined pilot treatment across the country which gave the basis for development of health system to ensure that isoniazid preventive therapy is optimally provided. Information from isoniazid preventive therapy pilot sites led to publishing of Kenya's first isoniazid preventive therapy standard operating procedure document launched in March 2015 in Siaya County. In September 2015, IPT for PLHIV was launched for implementation countrywide. In the year 2018, a total of 76% of PLHIV in care were reported to have ever been initiated on isoniazid preventive therapy. (FINAL NTLD ANNUAL REPORT_2018A, n.d.)

1.5 Isoniazid Preventive Therapy Protocol

Isoniazid preventive therapy is provided for children without evidence of active tuberculosis based on symptoms and signs. All HIV infected children above one year of age, all HIV infected below 12 months of age with recent contact with tuberculosis case, all children below five years with recent exposure to an adult with pulmonary Tuberculosis irrespective of their HIV status.



(Mwangi, 2016)

Figure 1: IPT Protocol.

Isoniazid is given at a dose of 10mg/kg/day with maximum dose of 300mg/day with pyridoxine 1-2 mg/kg/day for 6 months. The patient initiated on isoniazid preventive therapy should be reviewed every month unless those who develop symptoms and signs of isoniazid toxicity then clinical reviews are done in 2 weeks. The most serious adverse events associated with INH are drug induced liver injury, peripheral neuropathy and rash. Management include prompt discontinuation of the drug if symptomatic with liver enzymes >3 times the upper limit of normal or if asymptomatic with liver enzymes >5 times the upper limit. In case of peripheral neuropathy, increase the dose of pyridoxine to double the standard weight based dose but if symptoms do not improve then discontinue the INH.(Kenya ARV Guidelines 2018.pdf.part, n.d.)

During the clinical appointments done on monthly reviews, screening is done for active tuberculosis using intensified case finding tool (appendix 2). Patients are also evaluated clinically to rule out signs of toxicity including hepatitis and peripheral neuropathy. They are also assessed for level adherence.

The pediatric intensified case finding /Isoniazid preventive therapy card (appendix 2) was introduced by ministry of health and public health of Kenya in 2013. It contains four parts; first part has patients' data and demographic data. The second part enquires on the history of cough, the duration, history of hotness of body, weight loss and any contact with tuberculosis case. The third part enquires on action taken. The final part includes examination for signs of hepatitis, review of liver function tests and date of isoniazid preventive therapy and the outcome.

1.6 Problem Statement

It's estimated that one third of the world population is infected with mycobacterium tuberculosis. Approximately 10-15% occurs in children. Globally in 2018 it was estimated TB mortality among HIV positive to be 251,000 deaths. (GTB 2019 report). In the same year of 2018 Kenya reported an estimate of TB/HIV co-infection rate of 15% among children (FINALNTLDANNUALREPORT_2018.). Human immunodeficiency virus infection increases the risk of progression of latent tuberculosis to active disease by 20 to 37 fold (Becker, 2015). Isoniazid preventive therapy has been shown to be effective and safe for TB prevention strategy. Isoniazid preventive therapy has been shown to reduce the overall risk of developing TB by 33% (Becker, 2015). The World Health Organization recommends use of isoniazid preventive therapy as a strategy to decrease tuberculosis burden among people living with HIV infection. However, the uptake is lower in countries with high Tuberculosis burden. (Strategy et al., 2015)

Despite WHO rolling out isoniazid preventive therapy in 1998 among all countries in WHO region, adoption in Kenya was in 2015. IPT uptake in Kenya remains low at 33-40% with various reasons for slow roll out. In a retrospective study done in 30 counties on outcome of IPT among PLHIV in Kenya reported some of the challenges to be IPT stock out, poor adherence, drug reactions and development of active TB among others (Karanja et al., 2020). There is paucity of published data in our setting on adherence to isoniazid preventive therapy. Various studies in Kenya have shown variable adherence to isoniazid preventive therapy. Mwangi et al in a study done in Nairobi, Kenya reported adherence level of 82.4% and the good adherence was because most patients were acting in accordance to the directive to take isoniazid daily. Adherence was assessed by a patient having taken > 90% of doses in the preceding 2 weeks. The same study reported completion rate to be 88% and the reason cited for non-completion were pill burden and health care provider instigating due to poor adherence (Mwangi, 2016). Previous studies done in Eastern province of Kenya on outcome of IPT showed 91.7 successful completion rate 0.7% loss to follow up and 0.3% developed adverse reactions while 3% developed TB. (Masini, Sitienei, & Weyeinga, 2013). They were unable to determine the level of adherence but by the fact that isoniazid preventive therapy was dispensed as part of ART they believed that drugs were taken accordingly.

The fact that isoniazid preventive therapy is new we need to study the level of adherence, completion rates and factors associated with adherence to isoniazid preventive therapy among HIV infected children at AMPATH in MTRH. Adherence to treatment is important in optimizing the patient's response to therapy. Non adherence may lead to treatment failure, development of drug resistance to isoniazid.

1.7 Justification

TB prevalence is high due to poor ventilation, overcrowding and human immunodeficiency virus infection. Household contacts especially adults with tuberculosis infection poses a higher risk of transmission to children. TB/HIV co-infection rate in children in Kenya as at 2018 was 15%. (FINAL NTLD ANNUAL REPORT_2018). Use of isoniazid preventive therapy among HIV infected children has been shown to reduce the overall risk of tuberculosis by 33%(Becker, 2015). Isoniazid preventive therapy was implemented in Kenya in September 2015. Isoniazid preventive therapy is taken daily for a duration of 6 months. This period is long and may pose a challenge for children who are otherwise well without any illness. This study aimed to determine the level of adherence, completion rate and describe the factors associated with adherence and completion of isoniazid preventive therapy among HIV infected children at AMPATH clinic in MTRH. AMPATH clinic serves a large population of >6000 children infected with HIV. It also serves as a referral for the other satellite facilities in the region hence this population may be a representative of western Kenya. In addition, the gaps and drawbacks to isoniazid preventive therapy adherence will be identified and this will inform the program, the health care providers and policy makers on ways of mitigating the gaps. This study will also bring forth information on effectiveness of isoniazid preventive therapy among HIV infected children at AMPATH in MTRH. Once the gaps and drawbacks are mitigated it will contribute towards achieving End TB strategy for tuberculosis by the year 2025.The End TB strategy aims to end the global tuberculosis epidemic by reducing TB deaths by 75% and reduce TB incidence rate by 50% between 2015 and 2025 and to ensure that no family is burdened with catastrophic expenses due to tuberculosis(Strategy, For, & Prevention, 2015).

If this study is not conducted then the level of adherence, completion rate and the factors associated with adherence and completion of isoniazid preventive therapy locally will remain unknown. Lack of adherence to isoniazid preventive therapy may result in isoniazid resistance and treatment failure which will lead to an increase in tuberculosis disease which has been associated with increased mortality among people living with HIV. This will strain available resources and increasing the cost of treating TB which was estimated to be US $ 6.8 billion in 2019 up from 6.4 billion in 2018.(GTB 2019 REPORT , n.d.)

1.8 Research Questions

1. What is the level of adherence and completion rate of isoniazid preventive therapy among HIV infected children at AMPATH clinic in Moi Teaching and Referral Hospital?

2. What are the factors associated with adherence and completion of isoniazid preventive therapy among HIV infected children at AMPATH clinic in Moi Teaching and Referral Hospital?

1.9 Objectives

1.9.1 Broad Objective

To determine the level of adherence, completion rate and describe factors associated with adherence and completion rate of isoniazid preventive therapy among HIV infected children at AMPATH in Moi Teaching and Referral Hospital.

1.9.2 Specific Objectives

1. To determine the level of adherence and completion rate of Isoniazid preventive therapy among HIV infected children at AMPATH in Moi Teaching and Referral Hospital.
2. To describe factors associated with adherence and completion of Isoniazid preventive therapy among HIV infected children at AMPATH in Moi Teaching and Referral Hospital.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Tuberculosis

Tuberculosis is a multisystem disease with myriad presentations and manifestations, occurs when signs and symptoms or radiographic changes are apparent. LTBI occurs after inhalation of infective droplet nuclei containing M. tuberculosis. A reactive TST and absence of clinical and radiographic manifestations are the hallmark. The various forms of TB are pulmonary TB and extra pulmonary TB. Treatment of TB is use of anti-TB for a period of 6 months. The initiation phase is 2 months of RHZE and the continuation phase is 4 months of RH. Prevention of TB include BCG vaccination, use of IPT and infection prevention control.(For & Disease, 2021).

Human immunodeficiency Virus is a viral infection caused by virus HIV-1 and HIV-2 of retroviridae family. The mode of transmission is through sexual contacts, parenteral exposure to blood or vertical transmission from mother to child. The common clinical presentation is recurrent or chronic diarrhea, failure to thrive, recurrent respiratory infections, lymphadenopathy and oral thrush among others. HIV is classified into 4 stages depending on the clinical presentation of the patients. Treatment of HIV is use of ART i.e. first line regime of 2 NRTI + PI or intergrase inhibitor depending on the weight of the patient. In case of treatment failure a patient is started on second line treatment regimen. Treatment response is monitored using viral load levels which done 3 monthly for unsuppressed patients and 6 monthly for those with good viral suppression.(Kenya ARV Guidelines 2018.pdf.part, n.d.)

2.2 Effectiveness of IPT

Isoniazid preventive therapy (IPT) has been shown to be effective in preventing TB among children. In a meta-analysis on the efficacy of IPT in preventing TB in children, the study found that the risk of developing TB was reduced by 59% among children aged 15 years or younger except for those initiated earlier in infancy or for primary prophylaxis (Ayieko et al., 2014).

In children infected with HIV in a high TB incidence setting, one study, a prospective cohort analysis done in SA found that giving IPT to them reduced the incidence of TB by 23 % (Frigati et al., 2011) A pilot randomized control trial study looking at the efficacy of tolerability and safety of IPT among HIV infected children on ART showed that it's safe and well tolerated among HIV infected children. In this study, 4 out 85 who received IPT developed TB while 7 out 82 in the placebo group developed TB. It further showed that the severe adverse effects were rare at 2%. (Gray et al., 2014)

2.3 Completion rate and factors associated with completion of IPT

The duration of isoniazid preventive therapy is expected to be 6 months of daily drug intake of isoniazid. This requires that the caretaker or the parent assists the child to make sure that they take the drugs as required and as prescribed by the health care provider for the ideal duration. The longer duration may pose a challenge in terms of adherence and the completion of the isoniazid preventive therapy. A few studies have shown high completion rate of isoniazid preventive therapy among children living with human immunodeficiency virus infection.

In a prospective study done in Dar Dar pediatrics program clinic in Dar es salaam, Tanzania the completion rate was at 74% and some of the reasons cited for non-completion were due to side effects like vomiting and others reasons were lack of

documentation on whether the participants completed or did not complete. (Hunter et al., 2020)

In a retrospective study done in Congo on assessing Isoniazid preventive therapy completion rate and predictors of completion among HIV infected children in June 2013, found out that 86.6 % of children completed IPT. (YOTEBIENG et al., 2015).

In a retrospective study done in September 2011 in Eastern province of Kenya on the outcomes of IPT among HIV infected children, the completion rate of isoniazid preventive therapy was 91.7 %. This study also reported a low loss to follow up and few adverse drug reactions of isoniazid. This supports the idea of isoniazid preventive therapy provision in children. (Masini et al., 2013)

In a prospective multi centered cohort study on challenges of IPT among children in high TB burden areas in Kenya, the compliance rate was 93 % at the first one month and 85% at the sixth month. Challenges reported included, side effects (22%), programmatic concerns (86%) and drug related issues (70%). (Fn et al., n.d.)

In a study evaluating the IPT program in Shurungwi district in Zimbabwe in 2014, the IPT program faced challenges including inadequate formally trained staff and non-availability of INH drugs (Makoni et al., 2015).

In a retrospective mixed method study on factors affecting uptake and completion among HIV infected at national referral hospital in Kenya, they reported that participants who were virally suppressed were more likely to complete the six month period of isoniazid preventive therapy as prescribed by the health care provider. (Ngugi, Muiruri, Odero, & Gachuno, 2020). A retrospective study on outcomes of IPT among PLHIV in Kenya reported that participants characteristic were not statistically significant associated with completion of IPT but the level of facility and the type of facility were associated with IPT completion (Muthoni, 2020).A cross

sectional study in Ethiopia on IPT uptake and completion among HIV infected children did not find any participant factors to be associated with IPT completion. What was significant was health care worker explanation about IPT and disclosure of participants HIV status was associated with high completion of isoniazid preventive therapy. (Taye & Tigabu, 2018).

2.4 Adherence and factors associated with isoniazid preventive therapy.

Children need the support of the parents and caretakers in taking their medications. Isoniazid preventive therapy is not any different, though the duration of six months is longer and in some cases the children are perfectly well. This may pose a challenge to adherence among these children taking IPT. Measurement of adherence among HIV infected children in this study was done using the adherence validated tool(Rachel C Vreeman et al., 2014). The adherence tool consists of caregiver factors, participant factors, medication related and duration related factors. The adherence tool consist of four questions to determine the level of adherence i.e. Caregiver has a problem getting the child to take medication, Missing at least a dose in the last 7 days, Giving a dose more than 1 hour late in the last 7 days, Caregiver factors; Not being around to give medicines, Not wanting to give medicine around others or forgetting to give medicines.Adherence was dependent on the total score whereby score 0 out of 4 is good adherence, score of 1 and 2 out of 4 is fair and a score of 3 and 4 out of 4 will be poor adherence.

A number of studies have been done looking at adherence to Isoniazid preventive therapy in HIV infected children.

In a prospective study done in Tanzania on successful implementation of Isoniazid Preventive Therapy at pediatric HIV clinic reported an average monthly adherence of 98% among the participants who completed the Isoniazid preventive therapy. Adherence in this study was done using pill counts (Hunter et al., 2020)

In a qualitative study looking at the barriers to the treatment of childhood tuberculosis and tuberculosis infection in Peru, there were some main barriers found. These included poor adherence to IPT, dosing errors and provider concern that IPT

generates isoniazid resistance. This study emphasized the need to formulate strategies that encourage adherence to IPT.(Chiang et al., 2017)

In a prospective study looking at adherence of IPT among children (0-5 years) in Indonesia, the reported adherence rate was 49.5 % among children initiated on isoniazid preventive therapy. Some of the barriers and facilitators of adherence identified included regimen related, caregiver related factors, social support and access. (Triasih et al., 2016)

In a study done in Nairobi on implementation of Isoniazid preventive Therapy among HIV infected children using mixed method research, they defined the adherence to IPT as consumption of >90% of doses in preceding 2 weeks .They found good adherence to isoniazid preventive therapy at 82.4% this were participants who did not miss doses for the entire period. Those with poor adherence to isoniazid preventive therapy were at 17.6%.The reasons for non-completion showed that care giver initiated cessation of treatment due to immense pill burden (Mwangi, 2016).

In a study by Skinner et al where they were looking at the challenges of adherence among children on IPT, in-depth interviews were done among parents of children who adhered well as well as staff from three primary health care centers with high TB prevalence. The barriers to adherence identified included long duration of treatment, stigma about TB and the perceived association between TB and HIV. (Skinner, Hesseling, Francis, & Mandalakas, 2013).

Mohamed et al in Egypt in a descriptive cross sectional study looked at the outcomes of unsupervised adherence of IPT among children under five years with exposure to adults with PTB. Out of 217 patients receiving IPT, only 36 completed. (16.6%) This study had a very low adherence rate. (Mohamed, 2012)

Adherence rate in a study on the implementation of IPT among children in Benin was 86% of the children were adherent to IPT for at least 6 months. The rate of adherence in this study was high. (Adjobimey et al., 2016). This study was done in a country with moderately high TB incidence but with a functioning nation regional TB control program which could explain the high adherence to isoniazid preventive therapy.

Garie et al in the southern region of Ethiopia, in a prospective cohort study of children less than 15 years, they looked at the compliance of IPT and its effectiveness. Out of 82 children put on IPT, 27 took it for 4 months while only 10 completed the 6 months. The main reason for non-compliance was the perception that the drugs were not necessary in a child who is healthy. (Garie, Yassin, & Cuevas, 2011)

Adherence to medication of isoniazid preventive therapy must be optimized for its treatment to be effective. In a randomized control trial done in cape town south Africa, on adherence based on daily pill count compared two groups one on daily IPT and the other on three times weekly IPT. The overall adherence to IPT was excellent with mean adherence of 94.7% the respective group adherence was 93.8% for those on daily IPT and 95.5% for the group taking three times a week. The age was determinant factor for the adherence to isoniazid preventive therapy and better adherence was noted in children who were four years and above.(le Roux et al., 2009).

A study done in Indonesia on isoniazid preventive therapy among children documented adherence rate of 74.4% and they found high transport costs and medication costs were significantly associated with poor adherence. Access, medication barriers, disease and health service experience and caregiver TB and IPT knowledge and beliefs were found to be important determinants of adherence to isoniazid preventive therapy. (Rutherford et al., 2012).

2.5 Uptake of IPT

The World Health Organization recommends use of isoniazid preventive therapy as a strategy to decrease tuberculosis burden among people living with HIV infection. However, the uptake is lower in countries with high Tuberculosis burden. (Strategy et al., 2015)

A study done in Nairobi Kenya on implementation of isoniazid preventive therapy, using mixed method research combining cross sectional survey with structured Questionnaire, demonstrated poor uptake 53.2%. The reasons associated with uptake were due to revised World Health Organization guidelines on IPT. Previously before initiation of Isoniazid preventive therapy, chest x-ray and mantoux had to be done. Factors associated with good uptake included high CD4 count and caregivers had previously received IPT themselves (Mwangi, 2016). A mixed method study on IPT among children living with TB patients found out that child contacts (<6 years) of 129 index patients, 51 were contacted. Among them, 19 of 51 (37%) were screened for TB and one had TB. Only 11 of 50 (22%) children were started and 10 of 50 (20%) completed IPT.in this study lack of awareness, risk perception among parents, cumbersome screening process, isoniazid stock-outs, inadequate knowledge among healthcare providers and poor programmatic monitoring as main barriers to IPT implementation.(Singh et al., 2017). A study on isoniazid preventive therapy in two districts in India found that there was poor IPT uptake and implementation and the reasons being no home visit by the field staff (19%) and no education about Isoniazid preventive therapy (61%). Reasons for non-completion included isoniazid not provided (52%) and long duration of treatment (28%). (Shivaramakrishna et al., 2015)

CONCEPTUAL FRAMEWORK ON FACTORS ASSOCIATED WITH ADHERENCE TO ISONIAZID PREVENTIVE THERAPY.

Modified from (Makanjuola, Taddese, & Booth, 2014)

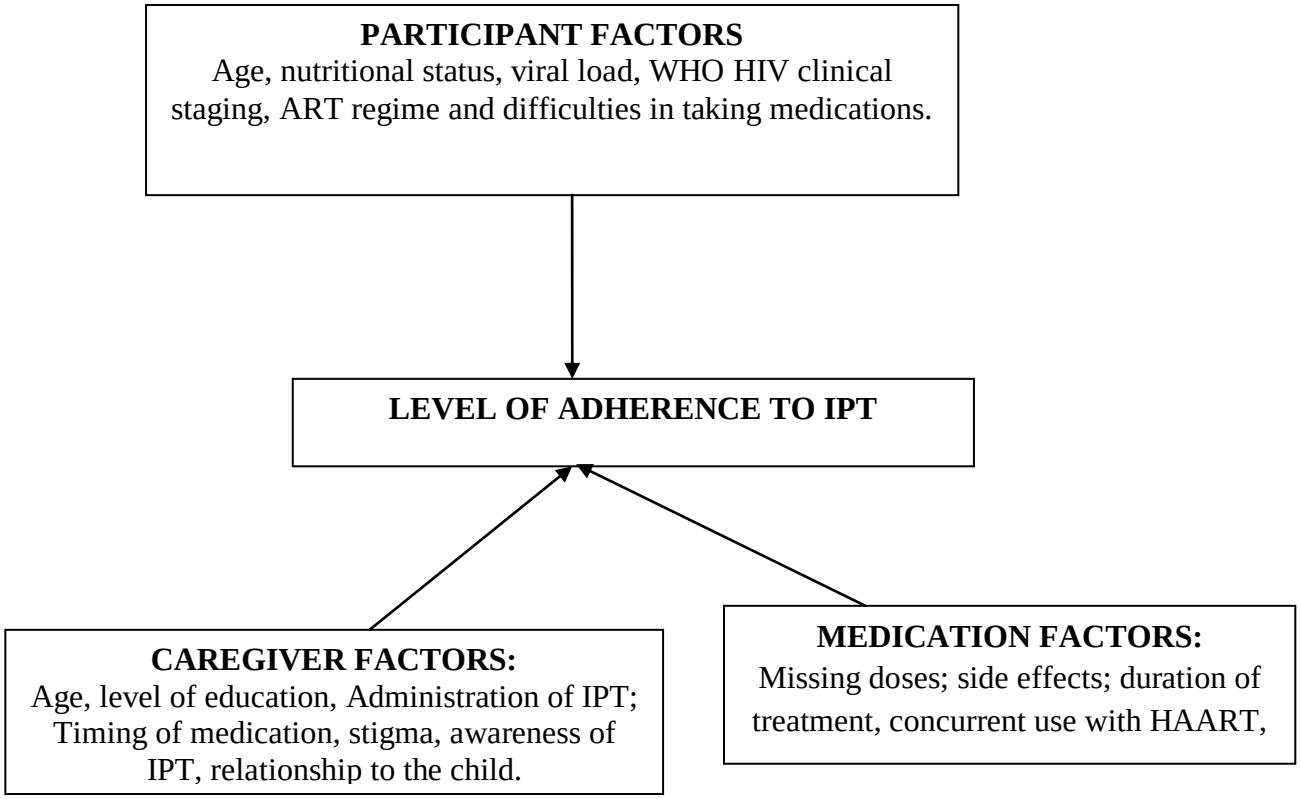


Figure 2: Conceptual framework.

2.6 Adverse Effects.

Isoniazid preventive therapy is associated with various adverse effects. It is either acute toxicity presenting as neurological deficit or chronic toxicity presenting as hepatoxicity. Studies have been done on the adverse effects and showed that most were low grade. A prospective cohort study done in royal Melbourne in 2014, where it looked at 100 patients of whom 86 reported at least one adverse effect and 6 patients experienced grade 3 or 4 adverse effects. The established potential adverse effects were hepatitis, peripheral neuropathy and allergic reactions. In this study the adverse effects were low grade and transient. The study also demonstrated high adherence and completion rate of isoniazid preventive therapy.(Denholm et al., 2014)

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

The study design was prospective cohort hospital based study.

3.2 Study Area

The study was conducted at the module four pediatric HIV clinics and Adolescent Rafiki Centre in the AMPATH clinic at Moi Teaching and Referral Hospital (MTRH). The MTRH Hospital is located in Eldoret town, which is 350 Kilometers North West of the Capital Nairobi. MTRH is a tertiary health facility serving as a teaching hospital for Moi University School of Medicine, Nursing, Public health and Dentistry. It is the referral hospital for the Western part of Kenya and North rift regions and has a catchment population of approximately 21 million people. AMPATH is a partnership between Moi University School of Medicine, MTRH and a consortium of North American academic medical centers led by Indiana University School of Medicine. AMPATH cares for more than 6,000 children who are living with HIV, and their comprehensive care goes far beyond treatment. AMPATH module 4 clinic serves as a referral Centre for the other satellite AMPATH clinics including Kapsoya clinic, Huruma centre and Langas among others. AMPATH provides free ART, septrin and isoniazid for isoniazid preventive therapy to all the children on follow up at the clinic. Other services provided are; primary care services, psychosocial and nutritional support for children and adults. All the services are provided to the clients daily.

The module four AMPATH clinic serve children aged 14 years and below who are HIV infected. Rafiki Centre in AMPATH also serves adolescents and children 10-14 years. The children in Rafiki Centre are transitioned from Module four once full

disclosure of HIV status has been done. The AMPATH module 4 clinic has specific scheduled days and specific bookings for the children on follow up as follows; Mondays is for children aged 5 years and below, Tuesday for children 6 to 9 years, Wednesday for children 10 to 14 years, Thursday is viremia clinic while Friday is for multidisciplinary team meeting. During the visits, children are registered then are sent to the outreach department then to social work office. They are triaged at the nursing station and vital signs are taken and referred to the clinician who sees the children and decided on plan for management. The patient is either referred to special clinics, nutrition counseling, or laboratory or to the pharmacy depending on the need of care. At the pharmacy the medication prescribed by the clinician is dispensed and also medication refill is done. The patient is free to exist. This site was ideal for my study as it serves as a referral facility for the other AMPATH satellite centers. The AMPATH also serves a large population of >6000 children living with human immunodeficiency virus infection initiated on isoniazid preventive therapy in western Kenya.

3.3 Target Population

The target population was all HIV infected Children aged 1 to 14 years enrolled to the AMPATH clinics in MTRH.

3.4 Study Population

The study population was HIV infected children aged 1 to 14 years initiated on Isoniazid preventive therapy at AMPATH clinics in MTRH.

3.5 Sample Size

Fisher's formula was used to calculate the sample size

$$N_0 = \left(\frac{Z^2 p(1-p)}{e^2} \right)$$
$$= \frac{(1.96)^2 \times 0.82 \times 0.18}{(0.05)^2}$$
$$= 226$$

- $Z^2 = 1.96$ the quintile of the standard normal distribution.

  p = 0.82 proportion adherent to IPT, e = 0.05 is the margin of error.

- P is 82.4% proportion of patients who were adherent to IPT in 6 months. (Mwangi, 2016)

We anticipate a drop out of 10 % so in order to cushion against insufficient sample size we adjusted for loss to follow up as follows;

$$\frac{\mathbf{N_o}}{\mathbf{1-r}} = \frac{\mathbf{226}}{\mathbf{0.90}} = 251,$$

Where r is the dropout rate.

3.6 Sampling Technique

Consecutive sampling technique was used whereby every child meeting the inclusion criteria was selected during the study period. The reason for doing consecutive sampling was because of the size of the study population. During the proposal development 445 HIV infected children had received Isoniazid preventive therapy out of 752 who were active in the program hence our study population was 307 of the HIV infected children who had not been initiated on isoniazid preventive therapy. The other reason for using consecutive sampling technique was because the participants had specific scheduled clinic dates for their routine care and for refilling medications.

3.7 Eligibility Criteria

3.7.1 Inclusion Criteria

HIV infected children aged 1 to 14 years initiated on IPT during the study period.

3.7.2 Exclusion criteria

Severely ill patients initiated on IPT during the study period. The reason for excluding the severely ill patients was because they needed emergency care and admission to the ward.

3.8 Execution of Study

The Principal Investigator recruited a research assistant with qualifications in clinical medicine on the basis of background knowledge, commitment and reliability. He was trained on the main purpose of the study, the recruitment procedure of the study participants and sensitized on professional conduct during the study period. The staff at Module four and Rafiki Centre at AMPATH clinics in MTRH were sensitized on the study. The Principle Investigator with assistance of research assistant recruited participants who met the inclusion criteria after completing their regular visits. This was done in a room that afforded everyone privacy. Informed consent was sought from all caregivers, and assent obtained for any child 8 years and older then participants enrolled into the study. A semi-structured questionnaire was administered by the principal investigator after the child had been seen by their regular health care provider and further information gotten from patient records. The participants were interviewed in a private consultation room where privacy and confidentiality was maintained throughout the study. The study visits were scheduled on the same day as the child's routine clinic visit where they are supposed to pick their medication. Monthly follow up was done on all participants initiated on isoniazid preventive therapy at 10mg/kg dose daily treatment. Monthly visit review of the participants was

done after the participants had been seen by the regular health care provider. At the time of each visit a standardized reporting form was completed by PI with the help of research assistant. Data collected monthly included clinical characteristics of the participant i.e. (age, gender, weight, height, WHO-HIV stage, and viral load levels), challenges on drug administration, and assessment of the adherence. Data on IPT outcome i.e. completed or loss to follow up or discontinued. It included reasons for discontinuation of Isoniazid preventive therapy and assessing for presence and severity of any adverse effects during the preceding period of treatment. Treatment adherence was being assessed using AMPATH validated adherence score tool which consist of caregiver factors, participant factors, medication related factors and duration related factors. The adherence score tool consist of four questions to determine the level of adherence i.e. Caregiver has a problem getting the child to take medication, Missing at least a dose in the last 7 days, Giving a dose more than 1 hour late in the last 7 days, Caregiver factors; Not being around to give medicines, Not wanting to give medicine around others or forgetting to give medicines. Participant was to answer either yes or no, if the answer is yes the participant scores 1 and if it's no the score is 0. Adherence was dependent on the total score whereby score 0 out of 4 was good adherence, score of 1 and 2 out of 4 was fair and a score of 3 and 4 out of 4 was poor adherence. Completion was defined as a participant's ability of taking Isoniazid preventive therapy for the recommended period of six months by the health care provider without missing any dose or stopping to take medication. Data on caregiver characteristic was collected and it included age, level of education, gender, relationship to the child and awareness of Isoniazid Preventive therapy. The study started in October 2018 and each participant was followed up monthly for six months from when they were initiated on IPT. We consecutively recruited participants for

first seven months beginning October 2018. The last participant recruited in April 2019 was followed up monthly for six months until October 2019.

3.9 Data Collection

Data was collected between October 2018 and October 2019 using an interview administered structured questionnaire. The gathered data was entered into an electronic database.

The database was encrypted to ensure confidentiality of the data, Back-up of the data was done to cushion against loss. Once the data was completely converted into the electronic database, the questionnaires were kept in a safe cabinet and accessible to the principal investigator.

3.10 Data Management

3.10.1 Data Entry, Cleaning and Storage

Data was entered into an electronic database in preparation for analysis. The Microsoft access database was used. Double data entry was done to check for any errors. During entry the data was de-identified to ensure confidentiality of the information and protect the participants. Completeness and consistencies was checked regularly. After entry and cleaning was completed, the questionnaires were kept in a safe cabinet by the investigator. The database was encrypted to prevent any unauthorized access. A backup for the database was created in remote disks and flash drives that was kept in different safe locations to guard against loss of information.

3.10.2 Data Analysis

Descriptive statistics were used to summarize continuous and categorical variables. Continuous variables (age, viral load, weight and height) were assessed for Gaussian assumptions using histograms and Shapiro-Wilk test for normality. These variables

violated the Gaussian assumptions thus they were summarized using the median and the corresponding interquartile range (IQR). Categorical variables such as sex, level of education, marital status, WHO HIV clinical stage, INH dose levels among others were summarized using frequencies and the corresponding percentages.

Factors associated with child adherence were assessed using logistic regression model. The model was implemented using Generalized estimating Equations (GEE) in STATA version 13.1 SE (College Station, 77845 Texas USA). This model account for the multiple measurements (repeated measures) within an individual. Robust standard errors assuming Gaussian distribution were calculated as an alternative against misspecification of the model covariance structure. The odds ratios (OR) and the corresponding 95% confidence intervals (95% CI) were reported.

The results presented using tables, pie chart and graphs.

3.11 Ethical Consideration

Approval to carry out the study was sought from the MTRH and Moi University Institutional Research and Ethics Committee (IREC). Approval was also sought from the AMPATH.

Parents or guardians to the study participants were informed about the study. Consent and assent was sought prior to recruitment to the study. No incentives were used to convince the guardians for consent to participate in the study. The data collection tool did not contain the names of the participants. Confidentiality was maintained throughout the study. Medical attention was given as necessary irrespective of their consenting to participate in the study. The raw data collected was stored in a locked cabinet throughout the study period while the data in the computer was in a password protected file.

3.12 Dissemination of Results

The findings from the study were made known to AMPATH program in Moi teaching and referral hospital and the staff in AMPATH clinics both module four and Rafiki clinic. The results were presented in the university oral thesis defense and the written thesis book be availed for reference at the College of Science Resource Centre. This research work was published in October 2020 issue of East Africa medical journal vol.97 No.10. The findings are available for access and use by the scientific and general population in the improvement of patient management.

3.12 Study execution diagram

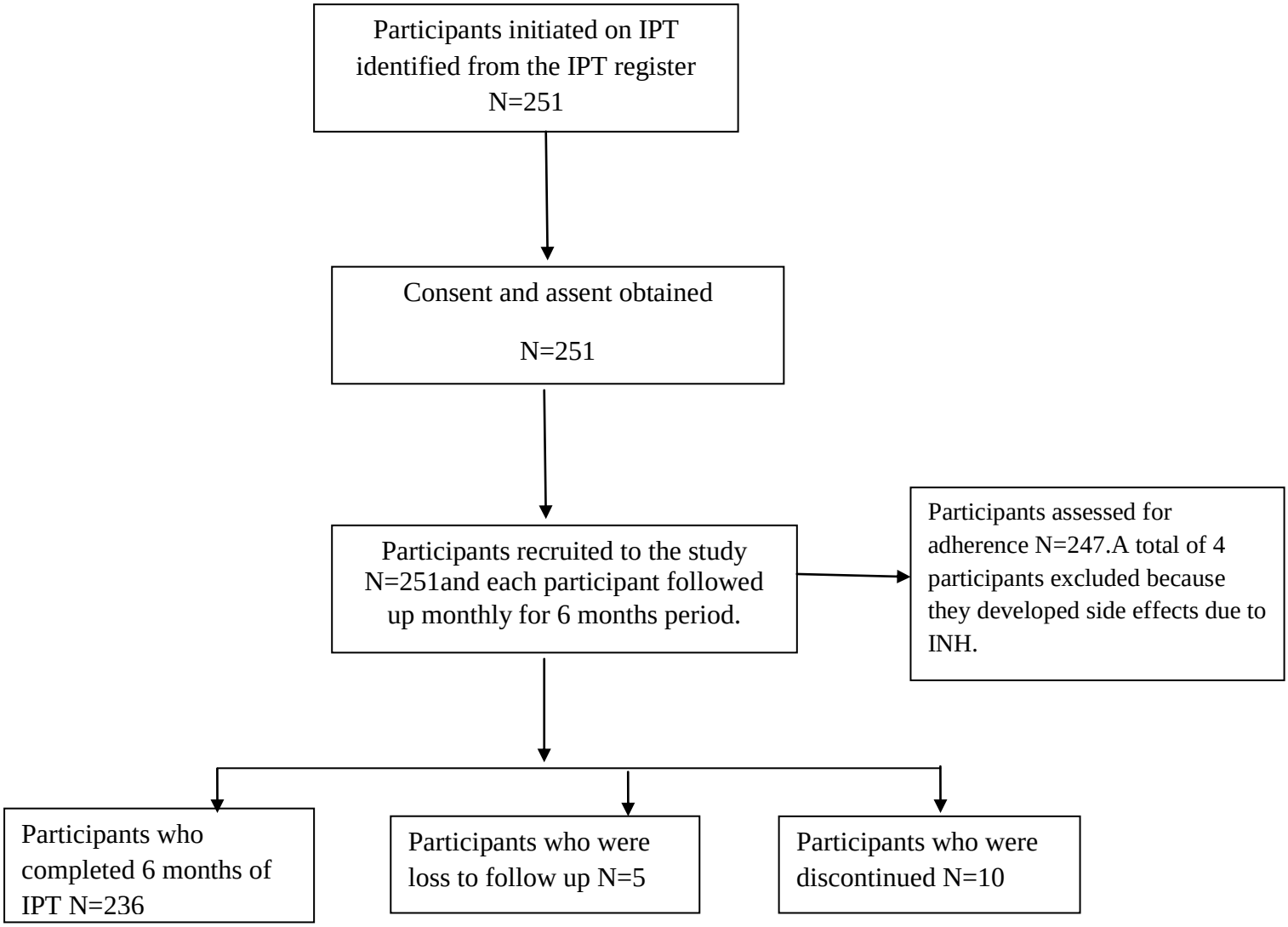


Figure 3: Study execution diagram

CHAPTER FOUR

4.0 RESULTS

There were 251 caregiver-children dyads recruited.

4.1 Child demographic and clinical characteristics.

Table 1 shows the demographic and clinical characteristics of the participants initiated on Isoniazid preventive therapy**.** The median age of the children was 11.0 (IQR: 8.0, 13.0) years with the youngest and the oldest children being 2.0 and 14.0 years respectively. Children below 5 years were 37(14.7%). Half the children were female.

Pyridoxine was administered for 231(92.0%) of the children who received it according to the age/weight requirements.

One third 84 (33.5%) of the children were in WHO HIV clinical stage III or IV, and the median viral load (measured in log base 10 scale) was 0.0 (IQR: 0.0, 2.1) copies per mL. The data shows that 229 (92.0%) of the children were virally suppressed (viral load < 1000 copies).

Table 1: Child's demographic characteristics at enrollment.

Characteristic	N	Median (IQR) or n (%)
Age (years), Median (IQR)	251	11.0 (8.0, 13.0)
Range (Min. – Max.)		2.0 – 14.0
≤ 5 Years		37 (14.7%)
6-10 Years		85 (33.9%)
> 11 Years		129 (51.4%)
Sex, n (%)		
Female	251	129 (51.4%)
Male		122 (48.6%)
INH dose (mg), n (%)		
100 mg		4 (1.6%)
200 mg	251	43 (17.1%)
300 mg		204 (81.3%)
Pyridoxine administered, n (%)		
No	251	20 (8.0%)
Yes		231 (92.0%)
Pyridoxine administration appropriate for age/weight, n (%)		
No	231	0 (0.0%)
Yes		231 (100.0%)
WHO clinical stage, n (%)		
I		103 (41.0%)
II	251	64 (25.5%)
III		72 (28.7%)
IV		12 (4.8%)
Viral load (log base 10)	251	
Range (Min. – Max.)		22(8.0%)
VLS (VL<1000)	251	229 (92.0%)
ART regimen, n (%)		
First line	251	201(80.0%)
Second line		50 (20.0%)

IQR – Inter quartile range, N – Number of children with characteristic measured and analyzed, VL – Viral load, VLS – Viral load suppression (VL<1000 copies per mL), ART – Antiretroviral therapy

4.2 Caregiver characteristics

Table 2 shows the caregiver characteristics of the participant initiated on isoniazid preventive therapy.

The median age of the caregivers was 40.0 (IQR: 35.0, 44.0) years with a minimum and a maximum of 19.0 and 74.0 years respectively. A total of 215 (85.7%) of the caregivers were female.

A total 197 (78.5%) of the caregivers were married and 43 (17.2%) were either single or separated. The rest were either a widow or widower.

Table 2: Caregiver characteristics.

Characteristic	N	Median (IQR) or n (%)
Age (years), Median (IQR)	251	40.0 (35.0, 44.0)
Range (Min. – Max.)		19.0 – 74.0
Gender		
Female	251	215 (85.7%)
Male		36 (14.3%)
Marital status		
Single		34 (13.6%)
Separated		9 (3.6%)
Married	251	197 (78.5%)
Widow		10 (4.0%)
Widower		1 (0.4%)
Level of Education		
None		12 (4.8%)
Primary		135 (53.8%)
Secondary	251	78 (31.1%)
Tertiary		26 (10.4%)
Caregiver-child relationship		
Mother		174 (69.3%)
Father		30 (12.0%)
Grandfather		2 (0.8%)
Grandmother		9 (3.6%)
Sibling	251	7 (2.8%)
Guardian		6 (2.4%)
Aunt		17 (6.8%)
Uncle		6 (2.4%)
Caregiver aware of IPT		
No		39 (15.5%)
Yes	251	212 (84.5%)

N – Number of caregivers who responded or with the characteristic measured and analyzed

One hundred and forty seven 147 (58.6%) of the caregivers did not have formal education nor had a primary level of education, and 104(41.5%) had a secondary or tertiary level of education.

A total of 204 (81.3%) of the caregivers were either the mothers or the fathers of the children with the mothers being 174(69.3%).

The caregivers comprised 7 (2.8%) siblings, 11(4.4%) grandparents and 29(11.6%) other relatives (Aunts & Uncles) or guardian.

Awareness of IPT by the caregiver was reported by 212(84.5%) of the caregivers.

4.3 IPT outcome

Figure 4 shows the outcome of isoniazid preventive therapy during the six month period. Two hundred and thirty six (94.0%) of the children managed to complete the IPT and 10(4.0%) discontinued. Of those who discontinued, 4(40.0%) had adverse drug reactions and 6(60.0%) had poor adherence to treatment (figure 3)

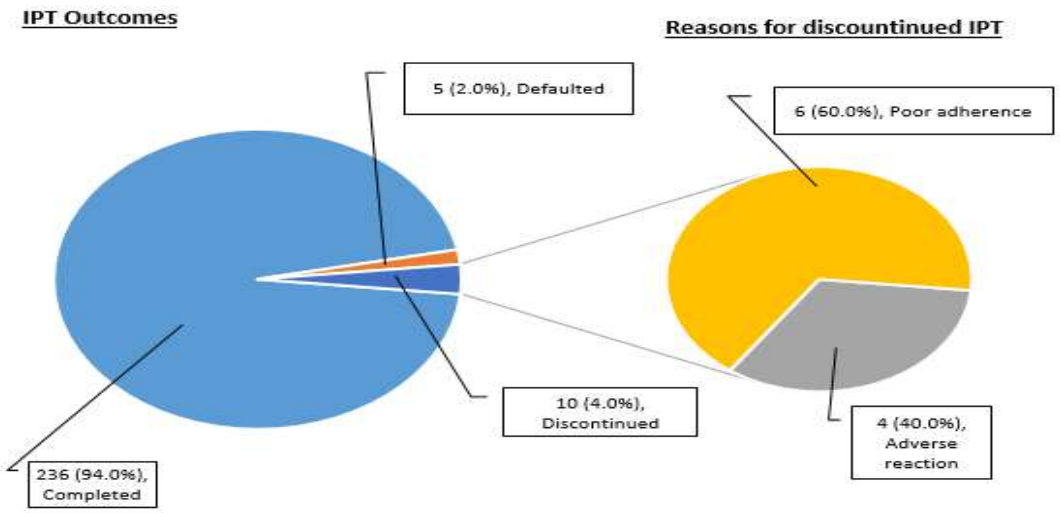


Figure 4: IPT outcome.

4.4 Challenges with the child in administering IPT

Figure 5 shows the challenges experienced by the participants during administration of isoniazid preventive therapy to the children.

During the first month visit following the baseline (or enrollment) the caregivers reported that 3 (1.2%) of the children complained of bad taste, 9(3.6%) were vomiting, 8(3.2%) were uncooperative and 6 (2.4%) reported high medicine burden.

During the second month visit the proportion reporting bad taste, vomiting, child being uncooperative and reports of high medicine burden had decline to 2 (0.8%),1 (0.4%), 3 (1.3%), and 1(0.4%) respectively. The decline was also observed in the subsequent months down to zero by month 5 except for reports of bad taste that was reported by 1 (0.4%) of the children at months 3, 4, 5, & 6.

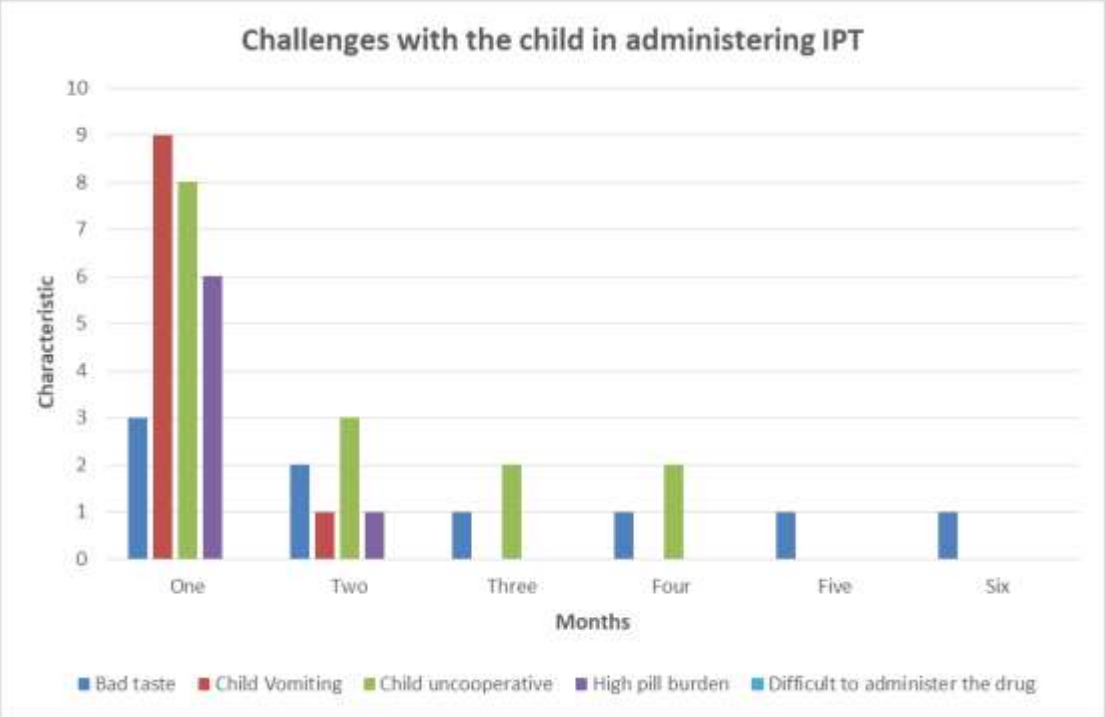


Figure 5: Challenges with the child in administering IPT

4.5 TB screening during the follow up.

Symptomatic TB screening during the follow up was conducted and the findings were that 1(0.4%) was positive for at least one symptom during the follow up; 1 (0.4%) reported cough at month 1 visit. The cough was not chronic and it was due to upper respiratory tract infection.

4.6 Side effects experienced by the children over the follow up time.

Table 3 shows the side effects experienced by the participants during the six months period of INH. At one month visit 12 (4.8%), 8 (3.2%), 4 (1.6%), 3 (1.2%) and 3 (1.2%) reported nausea, vomiting, abdominal pain, numbness and tingling respectively. At month 2 visit, 8 (3.4%) of the children reported nausea and by month 6 7 (3.0%) of the children were still reporting nausea. The side effects were no longer a problem to the children during the follow up time.

Table 3: Side effects experienced by the children over the follow up time

	Month					
	One	Two	Three	Four	Five	Six
Characteristic	N = 251	N = 239	N = 236	N = 236	N = 236	N = 236
Nausea	12 (4.8%)	8 (3.4%)	7 (3.0%)	6 (2.5%)	7 (3.0%)	7 (3.0%)
Irritability	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vomiting	8 (3.2%)	1 (0.4%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abdominal pain	4 (1.6%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RUQ pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Yellow eyes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Numbness	3 (1.2%)	1 (0.4%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)
Tingling	3 (1.2%)	2 (0.8%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	1 (0.4%)
Milestones	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

N – Number of children who responded or with the characteristic measured and analyzed

4.7 WHO HIV clinical stages

Figure 6 shows the WHO HIV clinical stage of the participants during the six months period of IPT. The data indicate a similar distribution of the children across all the clinical stages for the entire follow up time.

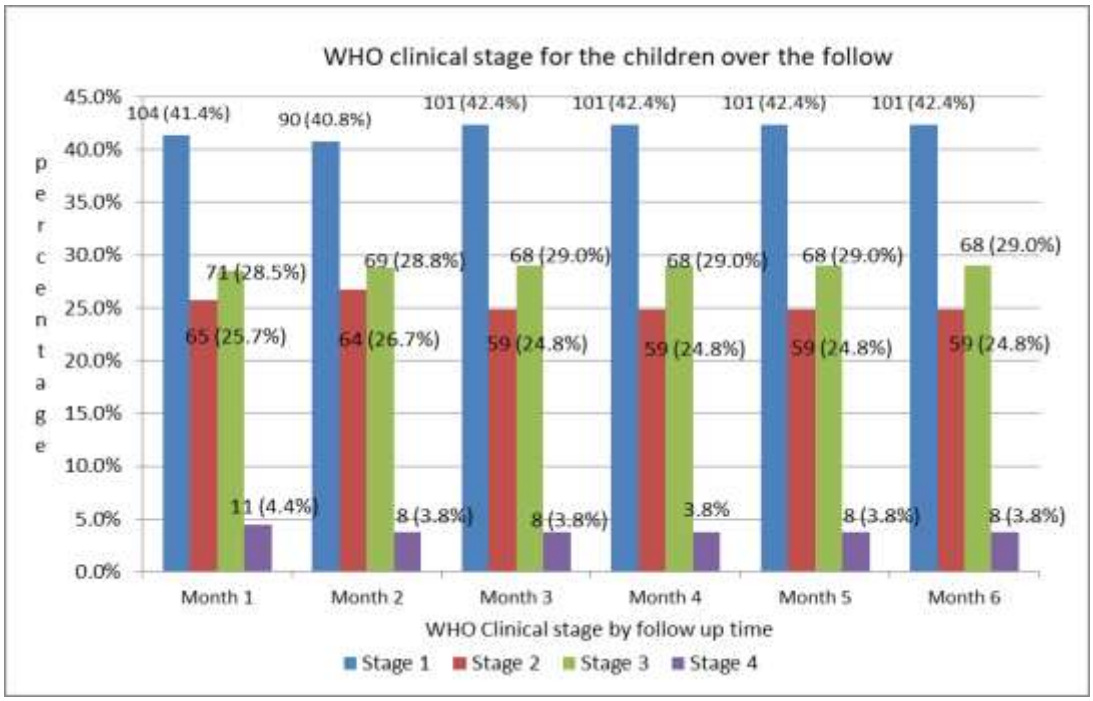


Figure 6: WHO clinical stage for the children over the follow up period.

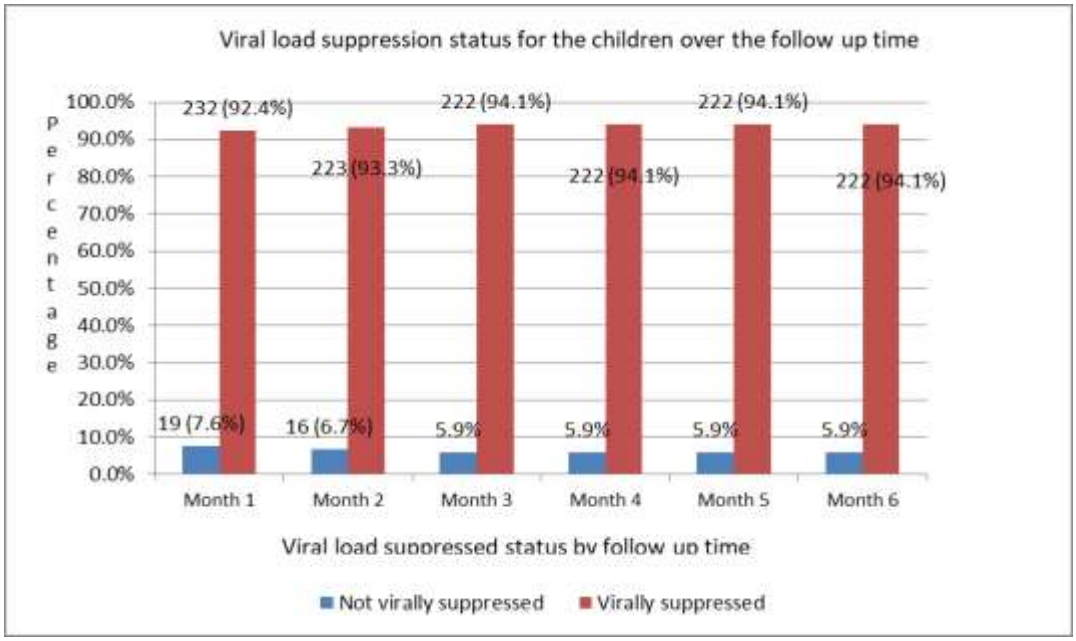


Figure 7: Viral load suppression status for the children over the follow up time.

4.8 viral load suppression

The data show that over 219(92%) of the children were virally suppressed across the follow up time.

4.9 ART regimen

Figure 8 shows the ART regimen for the children over the follow up time The proportions of the children on first line ART regimen were 201(80.4%) and those who were on second line ART regimen were 50(19.6%) of the participants. The ART regimen was relatively the same across the follow up time.

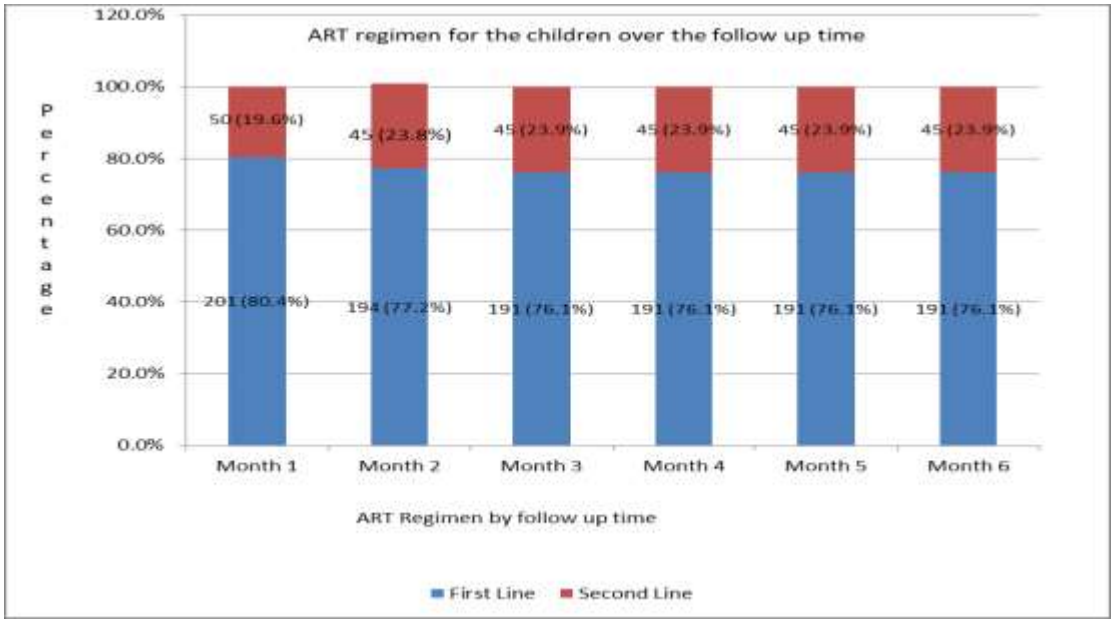


Figure 8: ART regimen for the children over the follow up time.

4.10 Adherence to isoniazid preventive therapy.

Table 4 shows the participants adherence to isoniazid preventive therapy during the month period of isoniazid. Adherence scoring (Appendix 3): Good adherence implies a score of 0 out of 4, fair adherence implies a score of 1 or 2 out of 4, and poor adherence implies a score of 3 or 4 out of 4. The participants who had fair or poor adherence in any month during the six month period of Isoniazid according to validated adherence score tool were classified non-adherent. A total of 247 participants were assessed for adherence to Isoniazid preventive therapy because we exclude participants 4 participants who were discontinued because they developed side effects hence adherence could not be assessed. The participants who were loss to follow up were lost from month 2 and 3 so we assessed adherence based on the prior month adherence score. The overall adherence rate to Isoniazid preventive therapy during the six month period was good at 80.2%. These were the participants who had a score of 0 out 4 during the six month period of Isoniazid preventive therapy.

Adherence rating of Isoniazid preventive therapy shows an increasing trend in the adherence level for the children over the follow up time.

Table 4: Adherence to Isoniazid preventive therapy.

	Non-Adherent	Adherent	P - value
	N=49(19.8%)	N=198(80.2%)	
Age			
<= 5 Years	11 (22.5%)	26 (13.1%)	0.119
6 - 10 Years	13 (26.5%)	74 (37.4%)	
> 11 Years	25 (51.0%)	98 (49.5%)	
Gender			
Male	23 (46.9%)	94 (47.5%)	1
Female	26 (53.1%)	104 (52.5%)	
WHO Clinical Stage			
Stage 1 or 2	28 (57.2%)	136 (68.7%)	0.35
Stage 3 or 4	21 (42.8%)	62(31.3%)	
Viral Load Suppression			
>= 1000	13 (26.5%)	9 (4.6%)	<0.001
< 1000	36 (73.4%)	189 (95.4%)	
ART Regimen			
First Line	36 (73.4%)	156(78.7%)	0.343
Second line	13(26.6%)	42(21.3%)	
Follow up time			
Month 1	42 (17.6%)	205(82.4%)	<0.001
Month 3	15(6.3%)	221(93.6%)	
Month 6	5(2.1%)	231(97.9%)	

4.11 Factors associated with adherence to IPT

Table 5 shows the association between the child characteristics and the child adherence to IPT. The results indicate that a higher proportion of children aged 5 – 10 years were adherent compared to children aged five years or less, OR: 4.68 (95% CI: 1.23, 17.76). The data also show that a higher proportion of children aged above ten

years were adherent compared to children aged five years or less though the difference was not statistically significant, OR: 1.79 (95% CI: 0.54, 5.92).

There was no evidence of a difference in the proportion of female children who were adherent compared to the male children, OR: 1.55 (95% CI: 0.59, 4.06). Similarly, the proportion of children who were adherent to IPT use among those who were using There was no evidence from the data to demonstrate that children who were in advanced WHO HIV clinical stage (WHO clinical stage 3 or 4) were less likely to be adherent compared to children who were in WHO HIV clinical stages 1 or 2, OR: 0.42 (95% CI: 0.16, 1.12). On the other hand there was evidence that children who were virally suppressed at baseline were more likely to be adherent to IPT use compared to those who were not virally suppressed, OR: 24.90 (95% CI: 7.36, 84.26).

Nutritional assessment indicator, height-for-age, shows that the proportion of children who were adherent among those who were stunted was similar to among those who had normal growth, OR: 0.43 (95% CI: 0.17, 1.13).

The proportion of children adherent to IPT use among those who were on second line was similar to those who were adherent among those who were on second line ART treatment, OR: 0.61 (95% CI: 0.21, 1.79).

Follow up time was strongly associated with adherence demonstrating an increasing proportion of children who were becoming adherent to IPT use over time, OR: 2.63 (95% CI: 1.35, 5.09) for month 2, 4.61 (95% CI: 2.11, 10.07) for month 3, 9.36 (95% CI: 3.77, 23.28) for month 4, 24.29 (95% CI: 7.33, 80.57) for month five and 32.21 (95% CI: 8.96, 115.75) compared to month 1.

Table 5: Association between child characteristics and child adherence to IPT.

Characteristic	N	UOR (95% CI)
Child characteristics		
Age (Years)		
≤ 5 years		Reference
6 – 10 years	251	4.68 (1.23, 17.76)
> 11 years		1.79 (0.54, 5.92)
Sex		
Male		Reference
Female	251	1.55 (0.59, 4.06)
INH dose (mg)		
100 or 200		Reference
300	251	1.58 (0.52, 4.82)
Pyridoxine administered		
No		Reference
Yes	251	3.37 (0.73, 15.54)
WHO clinical stage		
Stage 1 or 2		Reference
Stage 3 or 4	251	0.42 (0.16, 1.12)
VLS (VL<1000 cells per mL)		
No		Reference
Yes	251	24.90 (7.36, 84.26)
Height-for-age		
Normal		Reference
Stunted growth	251	0.43 (0.17, 1.13)
Regimen		
First line		Reference
Second line	251	0.61 (0.21, 1.79)
Follow up time		
Month 1		Reference
Month 2		2.63 (1.35, 5.09)
Month 3	251	4,61 (2.11, 10.07)
Month 4		9.36 (3.77, 23.28)
Month 5		24.29 (7.33, 80.57)
Month 6		32.21 (8.96, 115.75)

UOR – Unadjusted Odds Ratio, CI – Confidence interval, N – Number of children who responded or with the characteristic measured and analyzed

4.12 Caregiver factors associated with IPT adherence

Table 6 shows the association between caregiver characteristics and child adherence to IPT. The caregiver age, sex, and marital status were not associated with child adherence to IPT use.

The children of the caregivers who had secondary or tertiary level of education were less likely to be adherent to IPT use compared to children whose caregivers had no formal education or had primary level or education only, OR: 0.36 (95% CI: 0.14, 0.95).

The proportion of children adherent to IPT use among those whose caregivers were either the mother or the father was similar to the proportion adherent to ITP use among those who caregivers were either the grandparents, the uncle, the aunt or the sibling, OR: 0.41 (95% CI: 0.11, 1.60).

The caregiver age, gender, and marital status were not associated with child adherence to IPT use.

Table 6: Association between caregiver characteristics and child adherence to IPT.

Characteristic	N	P-Value	UOR (95% CI)
Caregiver characteristics			
Age (years)			
≤ 30		0.147	Reference
31 – 40	251		0.87 (0.21, 3.57)
> 41			1.53 (0.34, 6.92)
Sex			
Male	251	0.168	Reference
Female			2.13 (0.67, 6.81)
Married			
No (single, Separated, Widow, Widower)		0.459	Reference
Yes	251		1.08 (0.34, 3.39)
Education level			
None/Primary		0.063	Reference
Secondary/Tertiary	251		0.36 (0.14, 0.95)
Relationship with child			
*Other		0.682	Reference
Parent(Father/Mother)	251		0.41 (0.11, 1.60)

*Other = Grandfather, grandmother, Sibling, Aunt, Uncle, Neighbor, UOR – Unadjusted Odds Ratio, CI – Confidence interval, N – Number of caregivers who responded or with the characteristic measured and analyzed.

4.13 Factors associated with IPT adherence-Multivariate analysis

Table 7 shows the multivariate analysis of factors associated with child adherence to IPT. The results indicate that a higher proportion of children aged 5 – 10 years were adherent compared to children aged five years or less, OR: 4.68 (95% CI: 1.23, 17.76). The data also show that a higher proportion of children aged above ten years were adherent compared to children aged five years or less though the difference was not statistically significant, OR: 1.79 (95% CI: 0.54, 5.92).

There was no evidence of a difference in the proportion of female children who were adherent compared to the male children, OR: 1.55 (95% CI: 0.59, 4.06). There was no evidence from the data to demonstrate that children who were in advanced WHO-HIV clinical stage (WHO HIV clinical stage 2 3 or 4) were less likely to be adherent compared to children who were in WHO clinical stages 1 or 2, OR: 0.42 (95% CI: 0.16, 1.12). On the other hand there was evidence that children who were virally suppressed at baseline were more likely to be adherent to IPT use compared to those who were not virally suppressed, OR: 24.90 (95% CI: 7.36, 84.26).

Follow up time was strongly associated with adherence demonstrating an increasing proportion of children who were becoming adherent to IPT use over time, OR: 2.63 (95% CI: 1.35, 5.09) for month 2, 4.61 (95% CI: 2.11, 10.07) for month 3, 9.36 (95% CI: 3.77, 23.28) for month 4, 24.29 (95% CI: 7.33, 80.57) for month five and 32.21 (95% CI: 8.96, 115.75) compared to month 1.

Upon adjusting for the follow up time, caregiver level of education, child viral load suppression, and child’s gender and age were no longer associated with child adherence to IPT use.

Child's gender was also not associated with IPT use adherence after including it in the same model with child age, follow up time, caregiver level of education and viral load suppression, OR: 1.75 (95% CI: 0.65, 4.71).

The child baseline viral load suppression status was significantly associated with adherence to IPT use, OR: 25.68 (95% CI: 6.22, 105.96).

The caregiver level of education was significant in the model after including it with the child baseline characteristics, OR: 0.37 (95% CI: 0.14, 0.99).

Table 7: Multivariate analysis of factors associated with child adherence to IPT .

Characteristic	**UOR (95% CI)**	**AOR (95% CI)**
Child characteristics		
Age (Years)		
≤ 5 years	Reference	Reference
6 – 10 years	4.68 (1.23, 17.76)	3.68 (0.82, 16.46)
> 11 years	1.79 (0.54, 5.92)	1.31 (0.34, 5.00)
Gender		
Male	Reference	Reference
Female	1.55 (0.59, 4.06)	1.75 (0.65, 4.71)
VLS (VL<1000 cells per mL)		
No	Reference	Reference
Yes	24.90 (7.36, 84.26)	25.68 (6.22, 105.96)
Follow up time		
Month 1	Reference	Reference
Month 2	2.63 (1.35, 5.09)	2.54 (1.30, 4.97)
Month 3	4,61 (2.11, 10.07)	4.42 (2.01, 9.70)
Month 4	9.36 (3.77, 23.28)	8.99 (3.59, 22.51)
Month 5	24.29 (7.33, 80.57)	23.30 (7.05, 76.97)
Month 6	32.21 (8.96, 115.75)	30.86 (8.57, 111.07)
Caregiver education level		
None/Primary	Reference	Reference
Secondary/Tertiary	0.36 (0.14, 0.95)	0.37 (0.14, 0.99)

UOR – Unadjusted Odds Ratio, AOR: Adjusted Odds Ratio, CI – Confidence interval

4.14 Factors associated with IPT completion

Table 8 shows the association between child characteristics and child's completion rate of IPT**.** There was no evidence from the data to support the association between demographic characteristics of the child completion of the therapy. Except viral load suppression, there was no evidence of association between the clinical characteristics of the child and completion of the therapy. The children who were virally suppressed had increased odds of completing the therapy compared to those who were not virally suppressed, OR: 5.47 (95% CI: 1.54, 19.41).

Table 8: Association between child characteristics and child's completion rate of Isoniazid preventive therapy

		Completed IPT			
Characteristic	**N**	**No (n = 15)**	**Yes (n = 236)**	**P-Value**	**UOR (95% CI)**
Child characteristics					
Age (Years)					
≤ 5 years		1 (6.7%)	36 (15.3%)	0.43	Reference
6 – 10 years	251	2 (13.3%)	83 (35.2%)		1.15 (0.10, 13.12)
> 11 years		12 (80%)	117 (49.6%)		0.27 (0.03, 2.15)
Sex					
Male		11 (73.3%)	111 (47%)	0.062	Reference
Female	251	4 (26.7%)	125 (53%)		3.10 (0.96, 10.00)
INH dose (mg)					
100 or 200		1 (6.7%)	46 (19.5%)	0.623	Reference
300	251	14 (93.3%)	190 (80.5%)		0.30 (0.04, 2.30)
Pyridoxine administered					
No		3 (20%)	17 (7.2%)	0.054	Reference
Yes	251	12 (80%)	219 (92.8%)		3.22 (0.83, 12.52)
WHO clinical stage					
Stage 1 or 2		5 (28.6%)	220(93.2%)	0.32	Reference
Stage 3 or 4	251	10 (71.4%)	16 (6.8%)		0.74 (0.25, 2.15)
VLS (VL<1000 cells per mL)					
No		9 (60%)	158 (66.9%)	0.002	Reference
Yes	251	6 (40%)	78 (33.1%)		5.47 (1.54, 19.41) $^{\hbar}$
Height-for-age					
Normal		7 (46.7%)	138 (58.5%)	0.608	Reference
Stunted growth	251	8 (53.3%)	98 (41.5%)		0.62 (0.22, 1.77)
Regimen					
First line		11 (78.6%)	189 (80.1%)	1	Reference
Second line	251	3 (21.4%)	47 (19.9%)		0.91 (0.24, 3.40)

UOR – Unadjusted Odds Ratio, 95% CI – 95% Confidence Interval

$^{\hbar}$ 95% Confidence Interval is very wide, thus interpretation should be done with caution

4.15 Factors associated with IPT completion.

Table 9 shows **a**ssociation between caregiver's characteristics and child's completion rate of IPT**.** There was no evidence of association between the caregiver characteristics and the probability of completion of the therapy by the child. The education of the caregiver demonstrated some marginal association showing that the children of the caregivers who had a secondary or tertiary level of education were less likely to complete the therapy compared to the children of the caregivers who had no formal education or had a primary level of education, OR: 0.33 (95% CI: 0.11, 1.00).

Table 9: Association between caregiver's characteristics and child's completion rate of IPT

		Completed IPT			
Characteristic	**N**	**No (n = 15)**	**Yes (n = 236)**	**P-value**	**UOR (95% CI)**
Caregiver characteristics					
Age (years)					
≤ 30		2 (13.3%)	33 (14%)	0.225	Reference
31 – 40	251	5 (33.3%)	107 (45.3%)		1.30 (0.24, 7.00)
> 41		8 (53.3%)	96 (40.7%)		0.73 (0.15, 3.60)
Sex					
Male	251	2 (13.3%)	34 (14.4%)	0.257	Reference
Female		13 (86.7%)	202 (85.6%)		0.91 (0.20, 4.23)
Married					
No (single, Separated, Widow, Widower)		4 (26.7%)	50 (21.2%)	0.539	Reference
Yes	251	11 (73.3%)	186 (78.8%)		1.35 (0.41, 4.43)
Education level					
None/Primary		5 (33.3%)	142 (60.2%)	0.023	Reference
Secondary/Tertiary	251	10 (66.7%)	94 (39.8%)		0.33 (0.11, 1.00)
Relationship with child					
*Other		2 (13.3%)	45 (19.1%)	0.85	Reference
Parent(Father/Mother)	251	13 (86.7%)	191 (80.9%)		0.65 (0.14, 3.00)

UOR – Unadjusted Odds Ratio, 95% CI – 95% Confidence Interval

4.16 Multivariate analysis of factors associated with child's completion rate of IPT.

Table 10 shows multivariate analysis of factors associated with child's completion rate of Isoniazid preventive therapy. Female children and children who were virally suppressed had increased odds completing the six months period of isoniazid preventive therapy compared to the male children, AOR: 4.88 (95% CI: 1.23, 19.38) and 6.23 (95% CI: 1.48, 26.10) respectively.

Caregivers who had secondary or tertiary level of education were associated with reduced odds of completing the six months period of isoniazid preventive therapy, AOR: 0.29 (95% CI: 0.08, 0.96).

Table 10: Multivariate analysis of factors associated with child's completion rate of Isoniazid preventive therapy

Characteristic	UOR (95% CI)	AOR (95% CI) Final N = 251
Child characteristics		
Age (Years)		
≤ 5 years	Reference	Reference
6 – 10 years	1.15 (0.10, 13.12)	2.49 (0.13, 46.34)
> 11 years	0.27 (0.03, 2.15)	0.22 (0.02, 2.02)
Sex		
Male	Reference	Reference
Female	3.10 (0.96, 10.00)	4.88 (1.23, 19.38) ℏ
VLS (VL<1000 cells per mL)[1]		
No	Reference	Reference
Yes	5.47 (1.54, 19.41)	6.23 (1.48, 26.10) ℏ
Caregiver education level		
None/Primary	Reference	Reference
Secondary/Tertiary	0.33 (0.11, 1.00)	0.29 (0.08, 0.96) ℏ

UOR – Unadjusted Odds Ratio, AOR – Adjusted Odds Ratio, 95% CI – 95% Confidence Interval

ℏ 95% Confidence Interval is very wide, thus interpretation should be done with caution, [1]n = 251

CHAPTER FIVE: DISCUSSION.

5.0 Introduction

This study sought to determine the level of adherence, completion rate and factors associated with adherence and completion of isoniazid preventive therapy among HIV infected children at AMPATH clinic in Moi Teaching and Referral Hospital.

5.1 Completion rate of Isoniazid preventive therapy

Majority of the children managed to complete the IPT with 9 in 10 completing IPT for the six month period as recommended by the health care provider and only few were discontinued. The reasons for discontinuation were drug reactions and poor adherence to treatment. The high completion rate was because most of the participants were virally suppressed hence stable clinically with low risk of opportunistic infection with less medication and high chances of completing the six months period of isoniazid preventive therapy. Monthly regular visit which included counseling featuring encouragement and reinforcement from provider on importance of completing the 6 month period of INH contributed to the high rate of completion of IPT. Caregiver awareness of IPT also contributed to high rate of completion due to knowledge and better understanding of reasons for IPT.

We also speculate that because provision of Isoniazid preventive therapy was integrated with the routine HIV care could have contributed to the high completion of Isoniazid preventive therapy. This may be due to the routine habitual of taking medications.

A study done in Nairobi County, Kenya on implementation of IPT among HIV infected children had 88% completion and 12% non-completion. The cited reasons for

non-completion were caregiver initiation of cessation of treatment due to immense pill burden and also health care provider stopping medication due to poor adherence (Mwangi, 2016). The similar findings could be because of similar study population of HIV infected children between the age of 1-15 years and also similar study setting where they did their study in Kenyatta National Hospital which is a tertiary facility like our setting.

A prospective study done on successful implementation of Isoniazid preventive therapy at peadiatric HIV clinic in Tanzania reported a completion rate of 74%(Hunter et al., 2020).This was comparable to our study because of similar study design and similar study population in terms of age group and also all the study participants were HIV infected and hence the services were integrated. This study by hunter et al reported that some participants were discontinued by the health care provider due to side effects.

Masini et al in eastern province of Kenya reported high completion rate of 91.7 % among HIV infected children on isoniazid preventive therapy. The reason for the high completion rate was due to integration in HIV clinics with pre-existing patient retention mechanism. (Masini et al., 2013)

Similar to a study on implementation of WHO 2011 recommendation for IPT in children with HIV in Uganda where they reported 92.5% completion rate (Costenaro et al., 2016). The reason for high completion rate in this study was that most participants were more than 10 years of age and they had been informed of their HIV status and had better understanding of the reasons for medication. The similar findings could be explained by that most of their participants were in WHO HIV

clinical stage 1or 2 which were similar to our study where most of the study participants were in WHO HIV clinical stage 1 or 2.

A facility based cross-sectional study on IPT uptake and completion rates among HIV infected children in Ethiopia reported a completion rate of 67.9%. The study found different findings from our study and we speculate the reason could be that the study was done in multicenter where it was done in a referral hospital and other six satellite health facilities in Ethiopia. Also their study sample size was larger than in our study. (Taye & Tigabu, 2018)

None of the participants developed TB symptoms while on Isoniazid preventive therapy. In this study, the primary healthcare provider screened for signs and symptoms of TB prior to initiation of IPT and during our follow up we routinely check for features suggestive of TB. In addition, most of the participants had an undetectable viral load which implies most had good immune status with fewer chances of opportunistic infections. Similar to a study done in Ethiopia on uptake of Isoniazid preventive therapy among children, none of the children initiated on INH developed active TB symptoms (Tadesse et al., 2016). This was because of the monthly screening that they performed on the children. In contrast, in another study, (Mwayuma, Id, Graham, Uwimana, & Wyk, 2019), only one (1.2%) of the 84 child contacts who started IPT developed TB six months after completing the full 6-month IPT despite being asymptomatic while on IPT.

A prospective cohort study on implementation of WHO 2011 recommendation for IPT in children living with HIV reported 1.4% of the participants were discontinued due to active TB diagnosis (Costenaro et al., 2016). The low rate of TB diagnosis was due to exclusion of participants who had signs and symptoms of TB. Screening for

TB using the WHO recommendations (Program, 2017) prior to initiation of IPT is recommended to reduce the incidence of TB during the period of IPT therapy.

5.2 Child adherence to isoniazid preventive therapy

The adherence rating showed an increasing trend in the adherence level for the children over the follow up time. The overall adherence rate over the 6 month period of IPT was good with 8 in 10 being adherent to IPT. This study used AMPATH validated adherence tool and it has been shown to be working well in assessing ART adherence among HIV infected children. (Rachel C Vreeman et al., 2014). The AMPATH adherence tool method puts into account several factors in assessing the overall adherence. This tool is currently being used by the AMPATH clinic to measure the level of adherence to ART medication. The good adherence rate was due to monthly visits which constituted guidance, education and counseling session on importance of adherence and reasons for the medications by the counselor, the nurse and the clinicians who attended to the patients during their routine follow up clinics. The sessions featured encouragement and reinforcement of adherence to all medications from the health care provider. The good level of adherence in this study could be explained by the fact that most participants were virally suppressed which means most of these children were stable clinically and have lower risk of opportunistic infection hence low pill burden. Those with good viral suppression reflects good adherence to ART hence we think their behavior habits of being adherent and taking medications could explain the reason for the good adherence. Provision of Isoniazid preventive therapy was integrated with the routine care of ART refills hence there were no additional visits to the study participants. Maintaining routine care pattern may have contributed to the good level of adherence. A study done in Nairobi county on implementation of IPT among HIV infected children where

adherence for participants was defined as consumption of >90% of doses in preceding two weeks documented adherence rate at 82.4%. They found out that the adherence could be attributed to participants following the instructions by healthcare worker on daily intake of intake of isoniazid. These findings were similar to ours because of similar study population which was HIV infected children between age 1-15 years and also similar study setting which were both tertiary and referral facilities. (Mwangi, 2016).

Previous studies have reported high adherence amongst HIV infected children and one study done in Tanzania on successful implementation of IPT at pediatric HIV clinic reported an average monthly adherence rate of 98% (Hunter et al., 2020). The similar findings could be because of similar study population where the study participants were HIV infected and had routine care integrated with provision of Isoniazid preventive therapy. This finding is comparable to our study because it was facility based where the participants preferred facility based model because of fear community based model which would inadvertently disclose their HIV status to the neighbors.

Similarly, a pilot study on Isoniazid preventive therapy in HIV-infected children on antiretroviral therapy whereby adherence was assessed through pill count of returned tablets reported a mean adherence of 97%. (Gray et al., 2014). The reason for high adherence rate was reported that most of the HIV infected children taking IPT already had excellent adherence to ART medication.

A multicenter observational study done in Tanzania on acceptability and adherence to IPT in HIV infected patients reported 92.2 % mean adherence and the adherence was defined as consumption of 90% or more of monthly prescribed tablets of INH (Shayo

et al., 2015).The good adherence was as a result of patients acting in accordance to directive to take isoniazid daily by the health care provider. The similar findings on good adherence could be due to similar settings whereby the study was done in a national referral hospital which was similar to our study setting. A prospective descriptive study on adherence to IPT among children in close contact adult PTB patients, reported low adherence rate of 49.6%. (Paul & Gabriel-Job, 2019).The difference in the low adherence rate could be because of they had a sample size of 63 while in our study we recruited 251 study participants. The other reason could be, in this study 20% of their participants were HIV infected unlike in our population all were HIV infected. In this study by Paul et al, their study participants were aged 5 years and below.

5. 3 Factors associated with child adherence to Isoniazid preventive therapy.

5.3.1 Participants with good viral suppression.

There was evidence that children who were virally suppressed were more likely to be adherent to IPT use compared to those who were not virally suppressed, OR: 24.90 (95% CI: 7.36, 84.26). Most participants were virally suppressed which means most of these children were stable clinically and have lower risk of opportunistic infection hence less medication. Those with good viral suppression reflects good adherence to ART hence we think their behavior habits of being adherent to ART could explain the reason for the likelihood of being adherent to isoniazid preventive therapy. In contrast to our study, Shayo et al in a multicenter observational study done in Tanzania on acceptability and adherence to IPT in HIV infected patients found that children characteristics were not associated with adherence to isoniazid preventive therapy. The difference could be that in the study Shayo et al, they excluded participants who were non-adherent to ART and those who were on WHO HIV clinical stage 4. Also in

this study their study population included all HIV infected adults and children. (Shayo et al., 2015)

5.3.2 Regular follow up.

Follow up was strongly associated with adherence demonstrating an increasing proportion of children who were becoming adherent to isoniazid preventive therapy use over time. The increasing monthly adherence rate could be due to monthly adherence counseling session by the health care providers who would encourage and educate the participants on importance and benefits of good adherence to medications. A good relationship between the patient and health care provider which features encouragement and reinforcement of adherence has positive impact on adherence. In a prospective study on validation of a Short Adherence Questionnaire for Children Living with HIV on Antiretroviral Therapy in Kenya, they found that the adherence increased significantly over the duration of study.(Rachel Christine Vreeman et al., 2018).The similar findings could be because of similar study setting and similar target population that was HIV infected children aged 1-14 years.

In a prospective study by Mwayuma et al in Rwanda, there were no factors (individual characteristics of index cases, households and or health facility characteristics) found to be significantly associated with IPT adherence in the bivariate and multivariate analysis. The difference could be because 5% of their study participants were HIV infected unlike in our study all the study participants were HIV infected children. In the qualitative analysis, identified factors relating to parents/caregivers, disease, household and health-care providers as major themes determining IPT adherence (Mwayuma et al., 2019)

The caregiver age and gender were not associated with child adherence to IPT use. These findings were similar to a study done in Nairobi on implementation of IPT among HIV infected children where the age of the caregiver was not statistically significant. (Mwangi, 2016).The similarities in these findings could have been because of the similar study setting where the study was done in tertiary hospital similar to our study. The other speculation is that the study participants were similar to ours which were HIV infected children aged 1-15 years.

5.3.3 Caregiver secondary/tertiary level of education

Children under the caregivers who had secondary or tertiary level of education were less likely to be adherent, OR: 0.36 (95% CI: 0.14, 0.95). The higher level of education contributed to less likelihood of adherence because we speculate that the caregivers with higher level of education could seek different opinion prior to giving medication unlike those with primary level of education whom we think could follow the instructions from the health care provider on isoniazid preventive therapy. These findings were similar to a study done in Nairobi on implementation of IPT among HIV infected children where education was partially associated with IPT uptake and adherence. Children whose caregiver had attained secondary school level of education were less likely to have and adhere to IPT compared to those who had lower level of education. (Mwangi, 2016). The reason for better adherence among less educated care giver was cited by the health care provider that the less educated followed the health care provider instructions. The similar findings could be due to the similar study setting which were both referral facility. In contrast in a prospective study by Mwayuma et al in Rwanda, in the qualitative analysis, identified factors relating to parents/caregivers, disease, household and health-care providers as major themes determining IPT adherence. In the in-depth interviews they noted that caregiver

knowledge on the benefits of isoniazid preventive therapy and the threat of tuberculosis disease was associated with good adherence to isoniazid preventive therapy (Mwayuma et al., 2019). The difference could be because they did qualitative study while our study was quantitative.

5.4 Factors associated with completion of Isoniazid preventive therapy

5.4.1 Good viral suppression.

Participants who had good viral suppression were more likely to complete the six months period of Isoniazid preventive therapy. The reason could be that participants with good viral suppression reflects good level of adherence to ART hence their behavior habits of taking medication as recommended by the health care provider could explain the likelihood of completing medications. This finding was similar to a retrospective mixed method study on factors affecting uptake and completion among HIV infected at national referral hospital in Kenya where they found that participants who were virally suppressed were more likely to complete isoniazid preventive therapy (Ngugi et al., 2020). We speculate the similarities could be because of similar study setting where both are tertiary facilities and also similar study participants who were HIV infected children in WHO HIV clinical stage 1 or 2. A retrospective study on outcomes of IPT among PLHIV in Kenya reported that participants viral load level was not statistically significant (Muthoni, 2020).The reason for the different findings could be because they did their study in multicenter and also their study population were both adults and children with a large sample size compared to our study. A cross sectional study in Ethiopia on IPT uptake and completion among HIV infected children did not find any participant factors to be associated with IPT completion. (Taye & Tigabu, 2018). The reason for the different findings could be because they

did their study in multicenter in Gondar referral hospital and other six satellite facilities. Also in this study they had a large sample size compared to our study.

5.4.2 Female gender

Female gender was associated with completion of isoniazid preventive therapy whereby they were more likely to complete IPT compared to the male gender. We speculate the reason could have been that the female gender is at home in time to take medication unlike the male gender who may be preoccupied with outdoor activities hence likely to forget to take their medication. This finding was in contrast to a retrospective mixed method study on factors affecting uptake and completion among HIV infected at national referral hospital in Kenya where they found that participants gender was not statistically significant to completion of isoniazid preventive therapy (Ngugi et al., 2020). A retrospective study on outcomes of IPT among PLHIV in Kenya reported that participants' gender was also not statistically significant to completion of isoniazid preventive therapy. (Muthoni, 2020). The reason for the different findings could be because they did their study in multicenter and also their study population was both adults and children with a large sample size compared to our study

5.4.3 Caregiver secondary/tertiary level of education.

The education of the caregiver demonstrated some marginal association showing that the children of the caregivers who had a secondary or tertiary level of education were less likely to complete the therapy compared to the children of the caregivers who had no formal education or had a primary level of education. We speculate the reason for this finding could be the caregivers with primary level of education were more likely to follow the instructions from the health care provider unlike those with higher level education who might seek other opinion in regards the medication. We speculate also

that those caregivers with secondary/tertiary level of education may have had to attend to their work hence being unavailable to administer medications. In contrast a study on IPT uptake and completion among children in two referral hospital northwest Ethiopia found that isoniazid completion was associated with explanation of the reasons to take isoniazid pills. (Taye & Tigabu, 2018). The difference could be explained by the difference in the study setting whereby Taye et al did their study in multicenter while we did our study in one setting. Also their sample size was large than in our study.

5.5 Child demographic Characteristics

A total of 251 children participated in this study. Out of these, majority were females.

The median age of the children was 11.0 (IQR: 8.0, 13.0) years with the youngest and the oldest children being 2.0 and 14.0 years respectively. The children aged 5 years and below comprised 14.7%. These findings were similar to a study done in Nairobi County on implementation of IPT among HIV infected children where median age was 8 years and majority being female 58.9%. (Mwangi, 2016). In this study they included children between the ages of 1 and 15 years. A retrospective study in Zimbabwe on tolerability of Isoniazid preventive therapy among HIV infected children found that females were 46.1% and median age was 10yrs. (Mudzviti et al., 2019). This study was conducted among pediatric and adolescent population. This reflects the need for IPT among these populations.

In contrast, a pilot study done in cape town on Isoniazid preventive therapy in HIV infected children found that males were 48% and the median age was 32 months. (Gray et al., 2014). In this study the study population was younger with a range of 15 months to 76 months.

Two thirds (66.5%) of the children in our study were in WHO clinical stage I or II. Similar findings to a study on implementation of WHO 2011 recommendation for IPT in children living with HIV in Uganda where children were significantly more likely to have lower HIV WHO clinical stages (Costenaro et al., 2016). The reasons for low WHO staging was because prior to IPT initiation screening for TB was done, those with active TB and those previously treated for TB were excluded. Hence the excluded groups were of higher WHO stage. Contrast to a pilot study in cape town on Isoniazid preventive therapy in HIV-infected children on antiretroviral therapy reported 93% of the participants were in WHO stage III and IV.(Gray et al., 2014).

The data shows that 92.0% of the children were virally suppressed (viral load < 1000 copies). Most of the participants were virally suppressed because patients with high viral load levels are considered may have poor adherence to ART treatment. Poor ART adherence is considered to be a relative contraindication to initiation of isoniazid preventive therapy (Health, 2016). A pilot study in cape town on Isoniazid preventive therapy in HIV-infected children on antiretroviral therapy reported virally suppressed at 67.05%. (Gray et al., 2014)

5.6 Challenges during IPT use.

During the follow up, the challenges experienced by the caregivers during administration of the IPT to the children being 1.2% of the children complained of bad taste, 3.6% were vomiting, 3.2% were uncooperative and 2.4% reported high medicine-burden. In this study, the monthly adherence counseling sessions helped in terms of reducing the percentage of participants reporting challenges and helping them comply with their medication. Most of the challenges were related to the side effects of isoniazid. Those who reported high pill burden were mainly pupils in

boarding school where they reported that the medications were too many for them yet they had to do school activities at the same time.

However, the rate of challenges reported in this study was not as high as reported in the other studies. Previous studies have reported challenges with the administration of IPT. A qualitative study on factors affecting acceptability of IPT among health care providers in Nairobi reported challenges to be side effects and high pill burden. (Wambiya,Atela, Eboreime, & Ibisomi, 2018). Another study on correlation of IPT failure in children in high burden settings in Nairobi reported difficulties in administering the tablets among 44.3%, and 9.5% of the participants reported vomiting. (Fn et al., n.d.). In a qualitative study on implementation of WHO recommendation clinicians reported challenges to be pill burden, poor attendance to HIV follow ups and poor adherence to ART. (Costenaro et al., 2016)

5.7 Side effects reported.

At one month visit 12 (4.8%), 8 (3.2%), 4 (1.6%), 3 (1.2%) and 3 (1.2%) reported nausea, vomiting, abdominal pain, numbness and tingling respectively. At month 2 visit, 8 (3.4%) of the children reported nausea and by month 6 7 (3.0%) of the children were still reporting nausea. The findings were similar to a study done on correlation of IPT failure in children in high burden settings in Nairobi which reported GIT symptoms (nausea, anorexia and vomiting in 9.5% of the participants. Neurological symptoms (paraesthesia, weakness and irritability was reported in 5.4% of the participants.(Fn et al., n.d.).

A qualitative study on factors affecting acceptability of IPT among health care providers in Nairobi reported challenges to be side effects though not specified (Wambiya et al., 2018).

A pilot study in Cape Town on Isoniazid preventive therapy in HIV-infected children on antiretroviral therapy reported 6 events with transaminitis. Severe transaminitis was > 5.1 the upper limit. The transaminitis resolved on medication withdrawal.

The gastrointestinal symptoms reported in our study could have been due to hepatotoxicity effects of isoniazid medication though we were unable to assess the liver function tests to ascertain it due to financial constraints. Ten (3.98%) participants in our study developed gastrointestinal symptoms were stopped from continuing with isoniazid by the primary health care provider. The numbness and tingling sensation was mainly reported by participants whom pyridoxine had not been prescribed. The symptoms stopped once the pyridoxine was initiated.

5.8 Caregiver awareness to IPT.

Awareness of IPT was reported by 84.5% of the caregivers. The high rate of awareness of isoniazid preventive therapy was because most of the caregivers were either the father or the mother who had prior history of use of isoniazid as the primary caregiver. Similar to a mixed method study done in Rwanda on Adherence to isoniazid preventive therapy among child contacts where caregivers' knowledge about the benefit of Isoniazid preventive therapy and beliefs about the threat of TB disease were reported as a facilitator of Isoniazid preventive therapy adherence. (Mwayuma et al., 2019). Another study done in Nairobi on implementation of Isoniazid preventive therapy among HIV infected children where awareness of Isoniazid preventive therapy was reported to be 68%. The high level of awareness contributed to the good adherence rate by the participants (Mwangi, 2016).

5.9 Study limitations.

1. Adherence assessment was self-reported and may have been inaccurate indicator of adherence hence other direct methods of assessing adherence such as urine analysis to assess isoniazid metabolites might have been accurate.

2. Medication could be refilled and dispensed to the child or the primary caregiver hence sometimes the child was not present at follow up visits.

3. Selection bias in utilizing consecutive sampling technique and use of one AMPATH clinic center among other sites in the region.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusions

1. Adherence and completion of isoniazid preventive therapy among HIV infected children at AMPATH in MTRH was good with 8 in 10 being adherent and 9 in 10 completing six months period of taking IPT.

2. Participants with good viral suppression, regular follow up were associated with good adherence while participants whose caregiver had secondary level of education were likely to be non-adherent.

6.2 Recommendations

1. Provision of isoniazid preventive therapy should be continued.
2. Further qualitative studies to explore on reasons why HIV infected children whose caregivers with secondary/tertiary level of education were non-adherent are needed.

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APPENDICES

APPENDIX I: CONSENT FORM

English Version

Investigator: My name is Dr. Joan Koech. I am a qualified doctor, registered with the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Master's degree in Child health and Paediatrics at Moi University. I would like to request you to participate in my research which is to study the level of adherence to isoniazid preventive therapy among HIV infected children in AMPATH at Moi teaching and referral hospital.

Purpose: This study will seek to describe the level of adherence and factors associated with adherence to IPT among HIV infected children at AMPATH in MTRH.

Procedure: HIV infected children initiated on IPT will be recruited into the study after consent is sought. They will undergo proper history taking and physical examination. Data collection will be done by interviewing and filing of questionnaires. Data collecting material will be kept in a locked cabinet in the office of the principal investigator during the study period.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded same quality of management as non-study subjects. This study is aimed at improving monitoring of HIV infected children on IPT.

Risks: There are no anticipated risks to the participants attributable to this study.

Confidentiality: All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person

You are allowed to ask questions and seek clarification at any given stage my Contacts are Joan Koech Phone Number 0726464448 Email address joankoech01@gmail.com.

Rights to Refuse: Participation in this study is voluntary, there is freedom to refuse to take part or withdraw at any time. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital. If you have any questions regarding your child's rights in participating in the study or any complaints or an issue you cannot discuss with the investigator, please contact: The chairman IREC Moi Teaching and Referral Hospital P.O Box 3 Eldoret Kenya Tel no 33471/2/2

Sign or make a mark if you agree to take part in the study

Patient: ……. Date……..

Investigator: …….. Date……

Swahili Version

Mpelelezi: Jina langu ni Dr. Joan Koech. Mimi ni daktari aliyehitimu na kusajiliwa na bodi ya Kenya ya madaktari na madaktari wa meno. Mimi sasa natafuta shahada ya uzamili katika mafunzo ya afya na magojwa ya watoto (Child Health and Paediatrics) katika chuo kikuu cha Moi. Ningependa kukusajili katika utafiti wangu ambao ni wa kujifunza jinsi dawa ya Isoniazid inatumika kwa watoto walio na ukimwi katika hospitali ya mafunzo na rufaa ya Moi.

Kusudi: Utafiti huu itajaribu kueleza uhusiano wa kutumika kwa dawa ya Isonizid na matatizo ambayo wagonjwa wanapitia wakiwa wanaitumia.

Utaratibu: Watoto walio na ukimwi na walioanzishwa Isoniazid wataelezwa na kuombwa kujiunga na utafiti. Historia ya ugojwa na ukaguzi wa kimwili pia utafanywa. Data itakusanywa kwa kuulizwa maswali na pia kujaza fomu zilizo na maswali. Hifadhi zitakazo tumika katika ukusanyaji wa data zitawekwa kwa kabati iliyofungwa katika nyumba ya mpelelezi mkuu wakati wote wa utafiti.

Faida: Hakuna faida ya moja kwa kushiriki kwenye utafiti huu. Wanaofanyiwa utafiti watakuwa na haki na kupewa ubora sawa na wale ambao hawatafanyiwa utafiti huu. Utafiti huu una lengo la kuboresha jinsi watoto wanatumia dawa ya Isoniazid kwa kuzuia ugonjwa wa kifua kikuu.

Hatari: Hakuna hatari kwa washiriki kutokana na utafiti huu.

Usiri: Habari zote zitakazopatikana katika utafiti huu zitatwekwa kwa usiri mkubwa na wala haita tolewa kwa mtu yeyote asiyehusika na utafiti. Iwapo utakuwa na maswali kuhusu utafiti huu unaweza kuwasiliana na mchunguzi mkuu Joan Koech kupitia namba ya simu 0726464448 ama kwa barua pepe joankoech01@gmail.com

Haki ya kukataa: Kushiriki katika utafiti huu ni hiari yako. Kuna uhuru wa kukataa kushiriki au kutoka wakati wowote. Utafiti huu imepitishwa na Taasisi ya utafiti na kamati ya maadili (IREC) ya chuo kikuu cha Moi na hospitali ya rufaa ya Moi. Julisha idara hii ukiwa na maswali kuhusu haki ya mtoto wako kuhusishwa katika utafiti ama ukiwa na malalamishi au jambo ambalo huwezi kujadiliana na mtafiti kupitia kwa anwani hii: Mwenyekiti kamati ya maadili ya utafiti (IREC) ya chuo kikuu cha Moi na hospitali ya mafunzo na rufaa ya Moi Eldoret. Sanduku la posta 3 Eldoret. Nambari ya simu 33471/2/2.

Kusaini au kuweka alama kama unakubali kushiriki katika utafiti

Mgonjwa: ..... Mpelelezi: .....

Tarehe: ..... Tarehe: ……

APPENDIX II A: ASSENT FORM: (For the participants aged less than eighteen years)

Study Title:
Adherence to isoniazid preventive therapy among HIV infected children at AMPATH in Moi Teaching and Referral Hospital

Introduction:
My name is Dr. Joan Koech. I am a post-graduate student in the department of Child Health and Paediatrics at Moi University. As part of my post-graduate studies, I am required to carry out a research project. My research study is aimed at determining the level of adherence to Isoniazid preventive therapy among HIV infected children at AMPATH in Moi Teaching and Referral Hospital.

Study Procedure:
If you agree to participate in this study you will be asked questions surrounding adherence to isoniazid preventive therapy using an interviewer-administered questionnaire during the routine clinical visit. Routine clinical follow up will progress as usual without interference by the study.

Benefits of the study:
There is no direct benefit to the participants but the study will contribute to evidence-base, to inform policy makers on strengths and weaknesses in the provision of isoniazid preventive therapy. No payments will be made for participating in the study.

Harm of the study:
There will be no harm to the participants.

Confidentiality:
All information obtained from you will be kept strictly confidential and used only for research purposes. Your name will not appear on the data collection tools. All papers and computer records will be kept under lock and key and security codes respectively. The questionnaires will be filled in a room/place deemed private by the researchers after being identified prior to the study with assistance from the staff in the facility.

Rights to refuse or withdraw from study:
Participation is entirely voluntary. You are free to withdraw from the study at any point

In case of any question regarding the study, you can contact Dr. Joan Koech on mobile phone 0726 464 448

Contact persons:

NAME:	TITLE:	CONTACT
Joan Koech	Principal Investigator	Tel: 0726464448 Email: joan.koech 01@gmail.com

Having read and been explained to the above:
I
……..
With knowledge that this study is voluntary, do hereby give my assent to participate in the study.
I understand that I can withdraw from the study at any time without any penalty or harm.
Participant's signature……. Date ……
Principal investigator's signature …… Date …….

APPENDIX II B: FOMU YA MAKUBALIANO YA KUSHIRIKI KATIKA UTAFITI HUU KWA WASHIRIKI WALIO CHINI YA UMRI WA MIAKA KUMI NA NANE:

Kichwa cha utafiti:

Utumizi wa dawa ya Isoniazid kati ya watoto wanaoishi na Virusi Vya ukimwi wanaoenda katika kliniki ya waadhiriwa wa Virusi Vya Ukimwi katika hospitali ya mafunzo na rufaa ya Moi.

Utangulizi:

Kwa majina ni Joan koech. Mimi ni mwanafunzi katika chuo kikuu cha Moi. Nasomea taaluma ya udaktari wa watoto. Katika masomo yangu, nahitajika kufanya utafiti. Utafiti huu itajaribu kueleza uhusiano wa kutumika kwa dawa ya Isoniazid kwa kuzuia ugonjwa wa kifua kikuu na matatizo ambayo wagonjwa wanapitia wakiwa wanaitumia.

Utaratibu wa utafiti:

Iwapo utakubali kushiriki katika utafiti huu, utapewa karatasi iliyo na maswali kuhusu utumizi wa dawa ya Isoniazid kati ya watoto waliona maambukizi ya virusi vya ukimwi. Maswali haya utapewa utakapokuja kwenye kliniki au mikutano ya vijana

Faida ya kushiriki:

Hakuna malipo yoyote yatakayotolewa kwa kushiriki katika utafiti huu. Walakini, matokeo ya utafiti huu yatatumiwa na washika dau kuimarisha huduma kwa watoto wanaoishi na Virusi Vya Ukimwi.

Madhara ya kushiriki: Hakuna hatari kwa washiriki kutokana na utafiti huu

Siri: Habari zote zitakazopatikana katika utafiti huu zitatwekwa kwa usiri mkubwa na wala haita tolewa kwa mtu yeyote asiyehusika na utafiti. Iwapo utakuwa na maswali kuhusu utafiti huu unaweza kuwasiliana na mchunguzi mkuu Joan Koech kupitia namba ya simu 0726464448 ama kwa barua pepe joankoech01@gmail.com

Uhuru:

Kushiriki katika utafiti huu ni kwa hiari. Unaruhusiwa kutoka katika utafiti wakati wowote bila madhara yoyote.

Iwapo una swali lolote kuhusu utafiti huu, unaweza kuwasiliana na Joan Koech kupitia numbari ya simu ya rununu 0726 464448

Pia, waweza kuwasiliana na wafuatao:

JINA	CHEO	KUWASILIANA
Dr. Joan Koech	Mtafiti mkuu	Nambari ya simu: 0726 464448 Barua pepe: joan.koech01@gmail.com

Baada ya kusoma na kuelezwa kwa kina mambo yanayohusiana na utafiti huu;

Mimi……

……..natoa idhini yangu kushiriki katika utafiti huu. Nafahamu kuwa naweza kusitisha kushiriki kwangu katika utafiti huu wakati wowote bila madhara yoyote.

Sahihi ya mshiriki…… Tarehe……

Sahihi ya mtafiti mkuu …… Tarehe ……..

APPENDIX III: ICF TOOL

PEDIATRIC ICF / IPT CARD

(TB ICF FOR CHILDREN < 15 YEARS)

Patient unique No..... **Name of Child** ..... **Name of parent/ guardian** ... .

Date of birth: ...../...../..... **Age:** ..... **Sex:** □ **Male** □ **Female** **Weight (Kgs)** .....

Physical Address ..... **Nearest landmark** ..... **Contact telephone** .....

Treatment supporters Name ..... **Treatment supporters cell phone number** .....

Details of TB of smear positive TB contact: Address ..... District TB No.....

Date	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-
1 **Cough** of any duration **Y/N**														
2 **Fever Y/N**														
3 **Weight loss** or **Poor weight gain Y/N**														
4 **Contact** with a TB case **Y/N**														

(Key: Y-Yes; N – No)

If "Yes" to any of the above questions, suspect TB, examine the child and use the pediatric TB diagnostic algorithm to evaluate for active disease. Rule out other underlying conditions, refer if necessary. **Record** your action in the table below.

If "No" to all questions, Initiate workup for IPT and repeat screening at subsequent visits.

Indicate the Action taken

Action taken/Date	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-
Sputum smear /Gene Xpert (Pos /Neg)													
Chest x-ray (Normal N /Suggestive S)													
Referral (Y/N)													
Start anti-TB (Y/N)													
Invitation of contacts (Y/N)													
Evaluated for IPT (Y/N)													

Isoniazid Preventive Therapy client work up

Ask for the following		
1. Yellow coloured urine Y/N		
2. Numbness or tingling sensation, regression in motor milestones refusal to crawl, walk, or run Y/N		
Examination findings		
1.Yellowness of eyes Y/N		
2Tenderness in the upper right quadrant of the abdomen Y/N		
3 Liver function test results (if available)	*ALT*	
	AST	

If the client has any of the above history or examination findings, defer IPT: manage the underlying condition and re-evaluate on next visit

If no to all the above, initiate IPT and repeat evaluation on subsequent visit

Date started on IPT		__/___/___
Indication for IPT (Tick √)		
1	Child under 5 years exposed to active SM +ve PTB	
2	PLHIV (Y/N)	
3	Prisoner	

IPT Outcome (Tick√)	
Event	*Date*
Completed	
Defaulted	
Discontinued*	
Died	
Transferred out	

***Reason for discontinuation**	**(Tick√)**
Adverse drug reaction	
Poor adherence	
Active TB disease	
others	

IPT due date	**Date collected IPT**	Wt (kg) & INH dose	**Hepatotoxicity** (Signs & symptoms) vomiting, persistent irritability, abdominal, RUQ pain, yellow urine or eyes)		**Peripheral Neuropathy** (Signs & symptoms) (Older child – numbness, tingling, regression in motor milestones refusal to crawl, walk, run)		Does the patient have a **Rash?**		**Adherence Measurement** Good = missed < 3 doses / month Fair = missed 4 – 8 doses / month Bad = missed 9 doses / month	
			Yes (state action taken)	No	Yes (state action taken)	No	Yes (state action taken)	No	Good or Fair	Bad (state action taken)

Patients Intensified Case Finding/ Isoniazid Preventive Therapy charts
(Ministry of Medical Services, Ministry of Public Health and Sanitation)

APPENDIX IV: QUESTIONNAIRE ON ADHERENCE TO IPT AMONG HIV INFECTED CHILDREN AT AMPATH MTRH

PTID: IPT: 001/2018

1. DEMOGRAPHIC CHARACTERSISTICS

Age: _____

Gender: _____

Ethnicity: _____

2. CLINICAL DATA

Date of IPT initiation_____

Pyridoxine administration; YES ____NO____ appropriate dose for age/ weight_____

Table on ART initiation and follow up

Parameter	Baseline	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
WHO staging							
Initial viral load							
Latest viral load							
Date of ART initiation							
Current ART regimen							
Remarks							

3. NUTRITIONAL STATUS

	Baseline	Month 1	Month2	Month 3	Month 4	Month 5	Month 6
Weight							
Height							
LMUAC							
Presence of Oedema							

4: **CLINICAL CHARACTERISTICS**

Parameter		**Baseline**	**Month 1**	**Month 2**	**Month 3**	**Month 4**	**Month 5**	**Month 6**
Cough	**Yes**							
	No							
Night Sweats	**Yes**							
	No							
Hotness of Body	**Yes**							
	No							
Weight loss	**Yes**							
	No							
History of Contact	**Yes**							
	No							
Remarks								

5. SIDE EFFECTS REPORTED

		Month1	Month2	Month3	Month4	Month5	Month6
None	Yes						
	No						
	N/A						
Nausea	Yes						
	No						
	N/A						
Irritability	Yes						
	No						
	N/A						
Vomiting	Yes						
	No						
	N/A						
Abdominal pain	Yes						
	No						
RUQ pain	Yes						
	No						
	N/A						
Yellow eyes	Yes						
	No						
	N/A						
Numbness	Yes						
	No						
	N/A						
Tingling	Yes						
	No						
	N/A						
Milestones Regression	Yes						
	No						
	N/A						
Rash	Yes						
	No						
	N/A						
LFTS	AST						
	ALT						
Others							

6. Have you experienced any challenges administering the medication?

Yes ☐ No ☐

If yes, what challenges?

		Month1	Month2	Month3	Month4	Month5	Month6
Bad taste	Yes						
	No						
Child vomits	Yes						
	No						
Child uncooperative	Yes						
	No						
High pill burden	Yes						
	No						
Difficult administering	Yes						
	No						
Others							

7. ADHERENCE MEASUREMENT AS PER DOSES MISSED- ACCORDING TO ICF TOOL

Good: Missed 3 doses per month

Fair; missed 4-8 doses per month

Bad; missed 9 doses per month

Doses missed monthly.

Month 1_____

Month 2_____

Month 3_____

Month 4_____

Month 5_____

Month 6_____

8. ASSESSMENT OF ADHERENCE IN CHILDREN AGED 1-14YRS

According to AMPATH adherence validated tool.(Rachel C Vreeman et al., 2014)

	No	Yes
1. Caregiver has a problem getting the child to take medication	0	1
2. Missing at least a dose in the last 7 days	0	1
3. Giving a dose more than 1 hr late in the last 7 days	0	1
4. Caregiver factors; i. Not being around to give medicines ii Not wanting to give medicine around others. iii. Forgetting to give medicines		

Interpretation

Total score 0/4 good adherence

Total score 1/4 fair adherence

Total score 2/4 fair adherence

Total score 3/4 and 4/4 poor adherence

Monthly adherence scores.

Month 1_____

Month 2_____

Month 3_____

Month 4_____

Month 5_____

Month 6_____

9. IPT OUTCOME

Event	**Date**
Completed	_____
Defaulted	_____
Discontinued	_____
Died	_____
Transferred out	_____

10. REASONS FOR DISCONTINUATION

Adverse drug reaction ☐

Poor adherence ☐

Active TB disease ☐

Others _____

11. CAREGIVER CHARACTERISTICS

i) Age _____

ii) Gender:

Male ☐ Female ☐

iii) Marital status:

Single ☐ Separated ☐

Married ☐ Divorced ☐

iv) Level of education:

None ☐

Primary ☐

Secondary ☐

Tertiary ☐

v) Relationship to the child

Mother ☐

Father ☐

Grandfather ☐

Grandmother ☐

Sibling ☐

Guardian ☐

vi) Awareness of IPT

Yes ☐

No ☐

vii) Reasons for IPT.

Prevention of TB ☐

Treatment of TB ☐

Others (specify) _____

APPENDIX V: IREC APPROVAL

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2017/117
Approval Number: 0001972

9th November, 2017

Dr. Joan Koech
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr .Koech,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Adherence to Isoniazid Preventive Therapy among HIV Infected Children at AMPATH Clinic of Moi Teaching and Referral Hospital."

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1972*** on 9th November, 2017. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 8th November, 2018. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF.E.O.WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Principal - CHS Chairman - COBES

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2017/117
Approval Number: 0001972

9th November, 2018

Dr. Joan Koech,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Koech,

RE: CONTINUING APPROVAL

The Institutional Research and Ethics Committee has reviewed your request for continuing approval to your study titled:-

"Adherence to Isoniazid Preventive Therapy among HIV Infected Children at AMPATH Clinic of Moi Teaching and Referral Hospital"

Your proposal has been granted a Continuing Approval with effect from 9th November, 2018. You are therefore permitted to continue with your study.

Note that this approval is for 1 year; it will thus expire on 8th November, 2019. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH
Principal - CHS
Dean - SOM
Dean - SPH
Dean - SOD