UPTAKE AND FACTORS ASSOCIATED WITH ISONIAZID PREVENTIVE THERAPY USE AMONG HIV POSITIVE CHILDREN IN DAR-ES-SALAAM.

Emilia Ludovick Karugaba, MD

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By

Emilia L Karugaba

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: **"Uptake and factors associated with IPT use in HIV positive Children in Dar es Salaam, Tanzania**, in partial fulfillment of the requirements for the degree of Master of Medicine in Paediatrics and Child Health of Muhimbili University of Health and Allied Sciences.

_____

Dr. Theodora Kazimoto
(Supervisor)

_____

(Date)

_____

Dr. Helga Naburi
(Co-Supervisor)

_____

(Date)

_____

Dr. Livin Mumburi
(Co-Supervisor)

_____

(Date)

DECLARATION AND COPYRIGHT

I **Emilia L. Karugaba**, declare the content of this dissertation to be the result of the work carried out since the date of approval of the research and it does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any other university and it does not contain any material previously published or written by another author except where due reference have been made in the text.

_____

(Signature of candidate)

_____

(Date)

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DEDICATION

I dedicate this work to my very dearest parents whom have always been there for me; Mr. and Mrs. Ludovick A. Karugaba, I love them so much, to my lovely family of Karugaba for their love and support, to my darling husband my number one support system, Dr Mandela C. Makakala for standing by my side through it all, for his constant encouragement and overall support which made me reach this point and last but not least, to my lovely newborn son, Xavion-Zion.

ABSTRACT

Background: TB is the leading infectious cause of death worldwide ranking above HIV. Having HIV infection is one of the major risk factors for the development of TB infection. Isoniazid preventive therapy (IPT) introduced since 1993 and revised in 1998 has been recommended by WHO to be used for all people living with HIV infection including children in areas with a high prevalence of TB exceeding 30%. The role of IPT is to prevent the progression of latent TB to active TB, prevents re-infection with TB upon exposure to an open case of TB. In Tanzania, IPT started to scale up in 2011, of which to date it is still the treatment of choice for latent TB infection (LTBI). There is limited data on IPT use especially in pediatric age group in Tanzania.

Objective: To determine the level of IPT uptake and the factors associated with IPT use among HIV infected children attending CTC clinics in Dar-es-Salaam.

Methodology

A hospital-based cross-sectional study was conducted in four HIV care and treatment clinics in Dar es Salaam, Muhimbili National Hospital (MNH), Mwananyamala, Temeke and Amana hospitals. The study was carried during the months of October 2019 to January 2020 on 320 HIV positive children aged 1 to 14 years. Standardized structured questionnaire was used to collect data on IPT uptake and other clinical data, and parents/caregivers were interviewed for socio-demographic factors. TB screening was done according to WHO, anthropometric measurements were recorded from the participants' cards. Data was analyzed using SPSS version 25. Continuous variables were analyzed using mean, median, range and interquartile range while categorical variables using frequencies and proportions. Differences in proportion were tested using the Chi-square test or Fisher's exact test. A p-value < 0.05 was considered significant. Logistic regression was used to assess independent factors associated with IPT use.

Results: A total of 320 children with a mean age of 9 years (SD=3.6) in four HIV clinics in Dar es Salaam were enrolled in this study. The overall level of IPT uptake was 224/320 (70%), this included 72/320 (22.5%) of those who were currently using IPT and 152/320

(47.5%) who ever used IPT previously. Excellent adherence was found in 57/72 (79.2%). Participants' age, viral load and caregivers' education on IPT use showed a significant association with IPT use.

Conclusion: Level of IPT uptake in HIV positive children attending four CTC in Dar-es-Salaam is low (70%), which is below the global target of ≥90% for End TB strategy in people living with HIV. Level of adherence of IPT in children is also relatively low 79.2%. Older age 10-14years, a higher HIV viral above 1000 copies/ml and having a care giver who had received education on IPT were predictors of IPT use. To improve the IPT uptake the health care workers in CTC should use these factors to identify children and support children who are likely to have poor uptake.

MUHTASARI

Utangulizi: Kifua kikuu ni moja wapo ya ugonjwa unaoongoza vifo ulimwenguni baada yavirusi vya ukimwi (VVU). Kuwa na maambukizi ya VVU ni moja wapo ya hatari kubwa ya maambukizo ya Kifua Kikuu. Tiba ya kuzuia kifua kikuu Isoniazid (IPT) iliyoletwa tangu mwaka 1993 na kukaguliwa mnamo 1998 imependekezwa na Shirika la afya duniani (WHO) kutumiwa kwa watu wote wanaoishi na maambukizo ya VVU ikiwa ni pamoja na watoto waliopo katika maeneo yenye kiwango kikubwa cha ugonjwa wa Kifua kikuu kinachozidi 30%. Jukumu la Isoniazidi ni kuzuia kuenea kwa Kifua kikuu. Nchini Tanzania, tiba ya kuzuia kifua kikuu isoniazidi ilianza kuongezeka mwaka 2011, ambayo hadi leo bado ni matibabu yaliyochaguliwa kukinga maambukizo ya kifua kikuu. Kuna data ndogo juu ya matumizi ya tiba ya kuzuia kifua kikuu ya isoniazidi, haswa katika kundi la umri wa watoto nchini Tanzania

Lengo:Kuangalia kiwango cha utumiwajiwa tiba ya kuzuia kifua kikuu ya isoniazidi na sababu zinazohusiana na utumiaji wa tiba ya kuzuia kifua kikuu isoniazidi kati ya watoto walioambukizwa VVU wanaohudhuria kliniki za VVU jijini Dar-es-salaam.

Mbinu: Utafiti wa hospitali ulifanywa katika kliniki nne za VVU Dar es salaam, Hospitali ya Kitaifa ya Muhimbili (MNH), Hospitali za mkoa za rufaa Mwananyamala, Temeke na Amana. Utafiti huo ulifanywa wakati wa miezi ya Oktoba 2019 hadi Januari 2020 kwa watoto 320 wenye VVU wenye umri kati ya miaka 1 hadi 14. Dodoso ilitumika kukusanya data juu ya utumiaji wa tiba ya kuzuia kifua kikuu ya isoniazidi na data zingine za kliniki, na wazazi / walezi walihojiwa kupata maelezo kwa ujumla. Uchunguzi wa kifua kikuu ulifanywa kulingana na shirika la afya duniani (WHO), vipimo vya anthropometri vilirekodiwa kutoka kwa kadi za washiriki. Takwimu zilichambuliwa kwa kutumia toleo la SPSS 25. Viwango vinavyoendelea vilichambuliwa kwa kutumia njia za wastani, anuwai na zenye kuhusika wakati data zilizo katika vitengo zilichambuliwa katika asilimia na idadi. Tofauti katika sehemu zilitathminiwa kwa kutumia kipimo cha Chi-mraba au Fisher. Thamani ya $p< 0.05$ ilizingatiwa kuwa muhimu. Logistic regression ilitumika kutathmini mambo huru yanayohusiana na matumizi ya tiba ya kuzuia kifua kikuu isoniazid.

Matokeo: Jumla ya watoto 320 walio na umri wa wastani wa miaka 10 (SD = 3.6) katika kliniki nne za VVU jijini Dar es salaam waliandikishwa kwenye utafiti huu. Kiwango cha jumla cha matumizi ya tiba ya kuzuia kifua kikuu isoniazidi kilikuwa 224/320 (70%), hii ni pamoja na 72/320 (22.5%) ya wale ambao kwa sasa walikuwa wakitumia IPT na 152/320 (47.5%) ambao waliwahi kutumia IPT hapo awali. Ufuatiliaji bora wa dawa ya tiba ya kuzuia kifua kikuu isoniazidi ulipatikana katika 57/72 (79.2%). Umri wa watoto, kiwango cha virusi na elimu ya walezi juu ya matumizi ya tiba ya kuzuia kifua kikuu isoniazidi ilionyesha ushirika muhimu na matumizi ya IPT.

Hitimisho: Kiwango cha utumiaji wa tiba ya kuzuia kifua kikuu isoniazidi kwa watoto wanaoishi na VVU wanaohudhuria kliniki za CTC Dar-es-salaam ni chini (70%), ambayo iko chini ya lengo la ulimwengu la ≥ 90% ya mkakati wa kumaliza Kifua kikuu kwa watu wanaoishi na VVU. Kiwango cha uzingatiaji wa tiba ya kuzuia kifua kikuu isoniazidi kwa watoto pia ni chini (79%). Watoto wa miaka 10-14,kiwango cha VVU zaidi ya nakala 1000 kwa mililita na mzazi/mlezi ambaye amepata elimu juu ya tiba ya kuzuia kifua kikuu isoniazidivilikuwa vitabiri vya matumizi ya tiba ya kuzuia kifua kikuu isoniazidi. Ili kuboresha utumiaji wa tiba ya kuzuia kifua kikuu isoniazidi wafanyikazi wa huduma ya afya katika kliniki za VVU wanapaswa kutumia mambo haya kubaini watoto na kuwasaidia watoto ambao wanaweza kuwa na utumiaji duni wa tiba ya kuzuia kifua kikuu isoniazidi.

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ACRONYMS

ALT	Alanine aminotransferases
ART	Antiretroviral Therapy
AST	Aspartate aminotransferases
BCG	Bacille Calmette Guerin
BMI	Body mass index
CD4	Cluster of Differentiation 4
CDC	Centre of Disease Control and prevention
CTC	Care and Treatment Clinic
CXR	Chest X-ray
DNA	Deoxyribonucleic Acid
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
IGRA	Interferon Gamma Release Assay
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
IQR	Interquantile Range
IRB	Institutional Review Board
LTBI	Latent TB infection
MAM	Moderate malnutrition

MDH	Management and Development of Health
MDR-TB	Multidrug Resistance Tuberculosis
MNH	Muhimbili National Hospital
M. tb	Mycobacterium tuberculosis
MUHAS	Muhimbili University of Health and Allied Sciences
PCR	Polymerase Chain Reaction
PEPFAR	President's Emergency Plan for AIDS Relief
PLWHIV	People Living With HIV
PMTCT	Prevention of Mother To Child Transmission
SAM	Severe Acute Malnutrition
SD	Standard Deviation
SPSS	Statistical Package for Social Sciences
TB	Tuberculosis
TST	Tuberculin Skin Test
UNAIDS	United Nations Programme on HIV/AIDS
VAS	Visual Analogue Scale
VVU	Virusi Vya Ukimwi
WHO	World Health Organization

OPERATIONAL DEFINITIONS:

IPT: Use of isoniazid at the dose of 10mg/kg (maximum 300mg) for the purpose of treating latent tuberculosis infection (LTBI) thus, prevention against active Tuberculosis (TB) (WHO).

IPT use: is a patient who is on Isoniazid Preventive Therapy or history of consumption of IPT for prevention of active TB.

IPT Uptake: is the proportion of patients who are using or who have used isoniazid preventive therapy to the number of total patients eligible for IPT.

IPT completion: consumption of isoniazid at 10mg/Kg to complete a full course of 6months or more in case of interrupted treatment(1).

IPT adherence: Good adherence consumption of ≥ 90% of the monthly prescribed dose less than 90% will be defined as poor adherence(2).

TB screen symptoms: chronic cough that is not improving for ≥ 2 weeks, fever ≥ 38°C for ≥ 2 weeks other common causes having been excluded and weight loss or weight faltering or failure to thrive(3).

Poor weight gain: is defined as self reported weight loss or according to WHO Z-scores, that is; very low weight-for-age (< –3 z-score), underweight (weight for-age < –2 z-score), confirmed weight loss (> 5%) since the last visit or growth curve flattening(4).

Active TB: Refers to illness that occurs in someone infected with *Mycobacterium tuberculosis* and is characterized by clinical signs and symptoms, with or without laboratory or radiographic evidence(3).

Latent tuberculosis infection (LTBI): A state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB. There is no gold standard test for direct identification of

Mycobacterium tuberculosis infection in humans. The vast majority of infected people have no signs or symptoms of TB but are at risk for active TB disease(4).

HIV Stage: Clinical staging system for HIV infection developed by WHO based on clinical parameters to guide decision making for management of HIV/AIDS patients(5).

Caregiver: Parents or close relative or guardian who is taking care of the child and able to provide written informed consent for the child.

1. INTRODUCTION

1.1 Background

Epidemiology of HIV and TB

Worldwide the number of HIV infected children of age 0 to 14 years is 1.8 million by the year 2017(6,7). Most of these infections are transmitted during perinatal period and majority of the cases are in sub-Saharan Africa. There is significant reduction in mortality after introduction of Highly Active Antiretroviral Therapy (HAART) era however in Tanzania in year 2017 it was estimated that only 48% of children aged 0 to 14 years living with HIV were on ARTs, and there were 6000 AIDS-related deaths in these children(8). AIDS-related deaths remains to be among the top five killers in Africa as it was estimated in year 2017(6).

Globally Tuberculosis (TB) is the major cause of death in people living with HIV contributing to about one-third of all HIV related cases(9). In the estimated 1 million of children who develop TB every year 136,000 of them will die from the disease of which 40,000 children are infected with HIV and 3% of deaths are due to multidrug-resistant tuberculosis (MDR-TB) which currently has become a challenge in the treatment of TB (12).

HIV infection is one of the major risk factors for the development of TB infection, either from a latent infection or a new infection(1). The risk of developing TB in people living with HIV (PLWHIV) is 5 to 10% every year(1) and its 20% to 37% higher in PLWHIV than those who do not have HIV infection (10). By 2015 WHO estimated that 10% of HIV infected had active TB and in 2017 estimates showed that 239,000 deaths in children less than 15 years of age due to TB, with 17% of them being having TB HIV co-infection(11).

There are a lot of challenges in diagnosis and treatment of Tuberculosis (TB) in pediatric population with HIV. Obtaining bacteriological confirmation in children has been a challenge as it can be achieved in only 30 to 40% of children and less than 75% of infants. Children mostly present with non-cavitary, paucibacillary pulmonary TB, thus the

diagnosis in this population is mostly based on clinical criteria (32, 33). Another challenge of TB diagnosis in children suspected to be have pulmonary disease is the difficulty in obtaining sputum samples due to lack of tussive force to expectorate adequate samples thus gastric aspiration is the procedure commonly used or sputum induction if feasible(34,35). Therefore prevention of TB in a patient living with HIV is invariably important.

IPT use in HIV

Several tuberculosis preventive strategies have been advocated by WHO such as intensified case finding, infection prevention and control, BCG vaccine and Isoniazid preventive therapy in high risk groups. Isoniazid is the most effective bactericidal drug currently available. Isoniazid preventive therapy (IPT) introduced since 1993 and revised in 1998 has been recommended by WHO to be used for all people living with HIV infection including children in areas with high prevalence of TB exceeding 30%(1). The role of IPT is to prevent the progression of latent TB to active TB and prevents re-infection with TB upon exposure to an open case of TB. IPT has been shown to prevent the risk of developing TB by 60% and recommended to be included in the package of care for all PLWHIV whom active TB has been excluded(1).

Increase in IPT coverage has been shown to reduce TB incidence in general HIV population, where increase in IPT coverage among adolescents reduce TB incidence by 5-34% and coverage of 90% reduced TB incidence by 9-40%(12). IPT use in HIV uninfected children doesn't have the same impact compared to HIV infected pediatric population(13). IPT use in HIV infected children has been shown to play a major role in reducing mortality in this population(14).

In Tanzania, IPT started to scale up from the year 2011, of which to date it is still the treatment of choice for latent TB infection (LTBI) prescribed at the dose of 10mg/kg (7mg to 15mg) maximum of 300mg daily for 6 months. IPT is indicated to all newborns with no symptoms of active TB born to mothers with active TB, to all HIV infected children younger than 12 months with known TB contact, to all HIV infected children 12 months or older with no symptoms of active TB and to all children younger than 5 years with no symptoms of TB but have a known TB contact. Treatment is given for 6 months only after

excluding active TB disease. This intervention is incorporated in the Tanzania HIV care, given free of charge (10, 11).

In Tanzania, HIV patients on IPT had 48% lower TB incidence rate compared to patients who were not on IPT, more efforts were recommended to increase provision and coverage of IPT(15).

Despite confirmed efficacy of IPT and recommendations that have been put for decades, its uptake remains limited. Some of the barriers being fear of creating isoniazid resistance, problem in patient acceptance and lack of commitment of health managers(16).

Most IPT uptake studies have been done in adult population and there is paucity of data in pediatric population. Given the challenges of TB diagnosis in pediatrics especially in excluding TB, it is important to assess IPT uptake and factors associated with IPT use in children living with HIV in Tanzania.

Hence this study aimed at assessing IPT uptake and factors associated with IPT use in HIV positive children attending CTC in Dar es Salaam, Tanzania.

1.2 Problem statement

Tanzania is among the countries with a high burden of TB infection and HIV. The high mortality in PLWHIV including those on antiretroviral therapy is contributed by opportunistic infections commonly being tuberculosis. IPT is required as part of a package of care to be delivered by the HIV and TB service providers to people living with HIV. The use of IPT for 6 months has been recommended by WHO for treating LTBI in high-risk groups including all HIV infected children above 12 months of age without TB disease(4).

However, according to the WHO 2005 report, less than 1 million people living with HIV received IPT worldwide even though data has shown IPT use reduces the mortality caused by TB among PLWHIV by 60%(1). Despite the abundant evidence for the efficacy of IPT and the availability of well-established national guidelines the level of IPT uptake has been low in adult population especially in developing countries with paucity of data in pediatrics population.

Not only the difficulties in diagnosis of TB in children but also children with HIV infection in resource limited settings are at increased risk of getting active TB infection and even worse, they are prone to develop disseminated TB contributed by factors such as immunodeficiency and poor nutritional status. Hence it is invariably important to determine the level of uptake and the factors associated with IPT use in this particular age group in Tanzania.

1.3 Rationale

Appropriate management of HIV among children depends highly on the prevention and treatment of opportunistic infection including tuberculosis. PLWHIV are 20 times more likely to develop active TB than those without HIV. IPT has been shown to reduce both the incidence and mortality related to Tuberculosis, and thus recommended by WHO as one of the TB prevention strategies among people living with HIV. Understanding the level of IPT uptake and factors associated with IPT use in Tanzania is expected help in designing public health interventions to increase IPT uptake among HIV infected children and subsequently reduce the incidence and mortality related to Tuberculosis to achieve the global target of reducing TB deaths among people living with HIV by 75% by the year 2020.The findings are expected to have the potential to improve quality of life among children living with HIV in Tanzania.

1.4 Research questions

1. What is the proportion of HIV infected children who are on IPT or have ever received IPT among those attending CTC at Dar-es-Salaam?
2. What is the level of adherence to IPT among HIV infected children attending CTC at Dar-es-Salaam?
3. What are the factors associated with IPT use among HIV infected children attending CTC at Dar-es-Salaam?

1.5 Objectives of the study

Broad objective:

To determine the level of IPT uptake and the factors associated with IPT use among HIV infected children attending CTC in Dar-es-Salaam.

Specific objectives:

1. To determine the proportion of HIV infected children who are on IPT or have ever received IPT among those attending CTC in Dar-es-Salaam.
2. To determine the level of adherence to IPT among HIV infected children attending CTC in Dar-es-Salaam.
3. To determine factors associated with IPT uptake among HIV infected children attending CTC in Dar-es-Salaam.

1.6 Conceptual framework

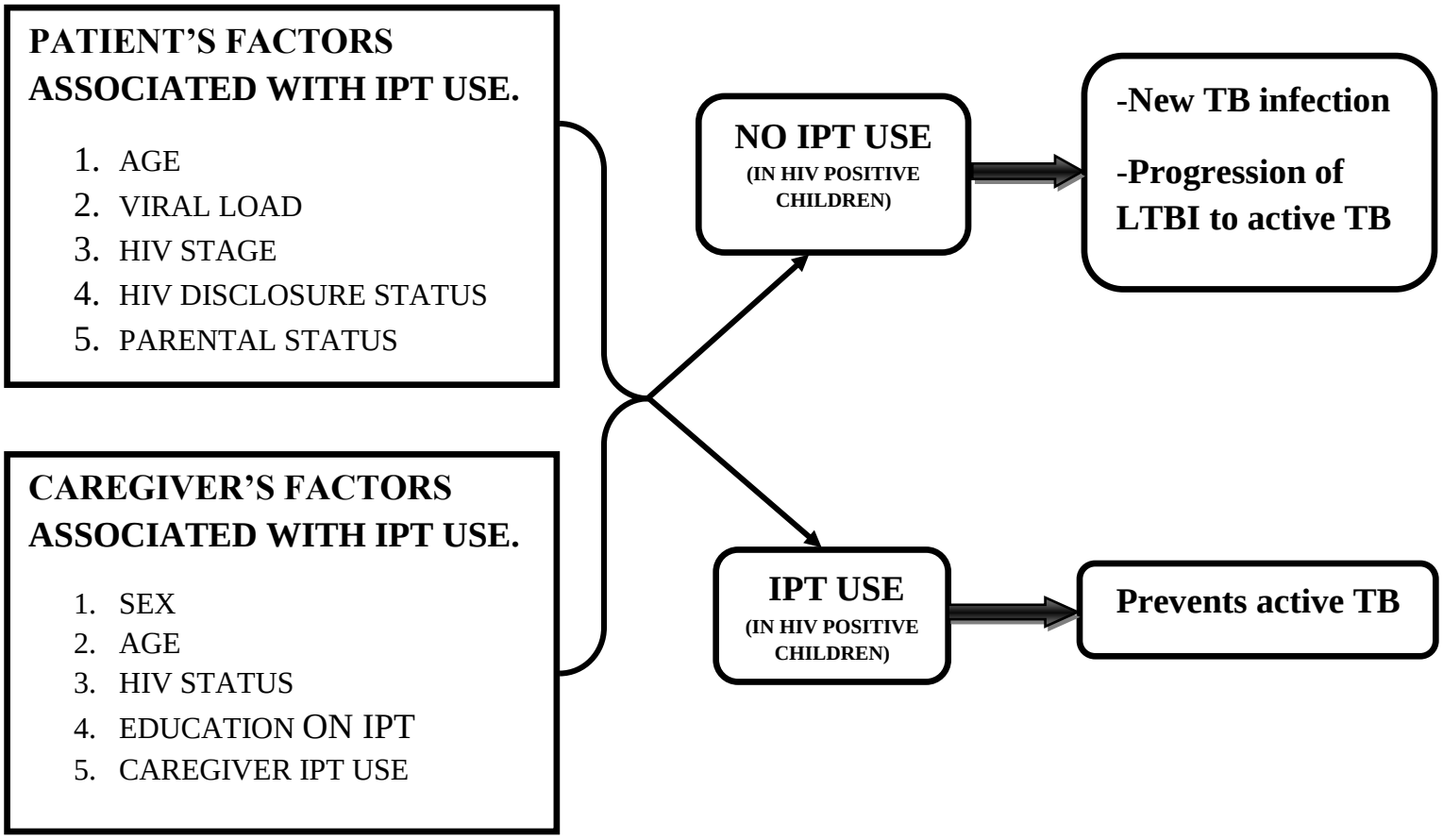


Fig 1: Conceptual Framework

This conceptual framework elaborates that having HIV infection is a risk factor of progression of LTBI to active TB thus it is important to use IPT to prevent new TB infection or progression of LTBI to active TB infection to HIV positive individuals (17,18). However, the use of IPT can be associated with several patients' and caregiver factors. This study will focus on determining the level of IPT uptake in HIV infected children and assessing the factors associated with IPT use. (The conceptual framework developed by principal investigator).

2 LITERATURE REVIEW

2.1 IPT use among HIV patients

Isoniazid safety in children has been studied in several areas such as in Greece 1977, In Brooklyn whereby the use of INH in the required dosage is associated with very few side effects. Mild and transient raise of alanine aminotransferases (ALT) and aspartate aminotransferases (AST) which would resolve spontaneously if uninterrupted thus, making it well tolerated and thus making Isoniazid safer than rifampicin and pyrazinamide containing regimens for prevention of latent TB infection. INH resistance is not significantly associated with IPT(19–21).

Several studies shows effectiveness of IPT in reducing the burden of TB example in Brazil data from a cohort study of 2003 to 2005 had shown that the use of IPT to patients on ARTs would decrease the incidence of TB by 76% which is greater than the use of ARTs alone, making IPT essential in controlling the burden of TB.(22) Similarly a study done in 2004 in HIV infected children in South Africa, IPT led to reduction of incidence of TB in HIV infected children by 70% and mortality by 50% (23).

In 2003-2007 a cohort study demonstrated effectiveness of INH on HIV infected children on ARTs with a 0.23 reduction in the risk of developing TB(24). While in 2007 to 2012 in Addis Ababa it found that IPT was effective in causing a significant reduction in TB incidence by 93.7% in PLWHIV than using ARTs alone and renders a 3 years TB protection(25).

Another cohort study done in Dar es Salaam, Tanzania from 2011 to 2014 in adult HIV patients showed that those using IPT have 48% lower TB incidence compared to those who are not in use (15). Therefore based on the evidence, which showed the safety and effectiveness of IPT, the WHO recommends the use of IPT to reduce the incidence of TB and related deaths. The first WHO recommendation was in 1993 for IPT to be used in PLWHIV, the same year when TB was declared to be a global emergency(26). IPT is recommended to be used daily for 6 months at a dose of 10mg/kg/day in children and has been packaged as one of the collaborative TB/HIV activities recommended by WHO(27).

Data on uptake of IPT in children is very scarce, however even the data available in the general population reveal under usage of IPT in PLWHIV. In a systematic review done between 2002 and 2009 globally showed only 1.3% of PLWHIV received IPT(28).
Despite early initiation of ARTs, being an effective strategy the best prevention of active TB infection in PLWHIV is IPT. However in 2013 only 21% of the countries globally had started to provide IPT in people living with HIV and among the 41 countries with the highest burden of tuberculosis, only 14 countries were providing IPT to the PLWHIV(29). In addition to that year in 2017 the global tuberculosis report showed that 958,559 of PLWHIV in the world had started IPT uptake(30).

In Ethiopia, the use of IPT in year 2012 to 2014 was 20% in the HIV clinics of 11 hospitals, though the IPT policy was adopted since 2005 and it's uptake started from around the year 2010 – 2012(16). Not only that but also Nigeria, the 5th country among the 22 countries with the highest global TB burden IPT uptake, in the general population of PLWIV, was found to be low in 2013 and 2015, with the IPT uptake being only 30% and 35% respectively(31,32).
Kenya which is ranked as the 15th country out of 22 countries with the highest burden of TB, IPT uptake started in September 2011 with uptake ranging from 33% to 40%(33). However, a study done in 2015, showed a marked improvement in the IPT uptake up to 77% which was higher than the national uptake, but lower than the national target of 90% in Kenya (34).

2.2 Adherence and completion of IPT

Adherence is important in the prevention of active TB. When IPT is used with excellent adherence in children, its effectiveness is close to 100%. In a study conducted in seven pilot sites in Zimbabwe which implements a course of 6 months of IPT in people living with HIV, IPT completion rate was found to be high; whereas 466 out of 578 patients(81%) completed IPT(35). In three HIV care clinics in eastern Kenya, more than 90% of the HIV-infected children aged between 1 and 14years who started on IPT completed successfully, The INH was prescribed from September 2011 for 6 months or more for those who had interrupted treatment(36).

In the Democratic Republic of Congo; Kinshasa, 86.6% of children living with HIV in the year 2013 aged 1-15 years had completed IPT at a minimum of 6 months(33). Similarly, high rates were reported in a randomized control trial done in HIV infected children on ART in South Africa in the year 2005 to 2009. Furthermore, IPT adherence in these children as assessed by pill counting was found to be excellent with no adverse reactions in 97% of the children(37).

In Tanzania, available data are on the adult population. A study done, in adults living with HIV who were participating in the DarDar study in a cohort of 2001 to 2005, In this cohort, among those offered IPT for 6 months 87%completed their IPT treatment(2). While in 2012 to 2014 IPT acceptance and adherence in HIV infected people from 10 years of age and above was studied. In this multicenter observational study that involved screening for TB and providing INH at 300mg dose for 6 months, the adherence rate was 92.2%(38). Although IPT adherence is not excellent, this should not hinder IPT uptake as suggested by the WHO, as the benefits outweigh the risks in PLWHIV.

2.3 Factors associated with IPT uptake

Few factors associated with IPT use have been studied these include lost to follow up, toxicity/adverse reaction, and drug stock-outs. Moreover, being on ART and receiving a more than 2 month supply of isoniazid at the beginning of the treatment were associated with a lower risk of not completing IPT(35).In Ethiopia, a mixed study done among fifty health providers, isoniazid stock-out was one of the barriers in the uptake of IPT for people living with HIV(16).

In Kenya where there is a high prevalence of HIV and TB/HIV co-infection, IPT also is recommended in all PLWHIV above 1 year of age. In a study done in a high volume primary health center in Nairobi, noted that having IPT related health education increases the likelihood of IPT uptake by 5 folds, and to the PLWHIV who have a fear of acquiring TB are more likely to use IPT, while having a good relationship with the healthcare-worker increases the likelihood of using IPT by 2 folds(34).

Furthermore in Kinshasa Congo, in a study which was done in both children and adults showed high IPT uptake and completion more in people on ARTs (89%) than those who

were not on ARTs(33). While in Tanzania, in a study which was done in adults in 2005, having fear of developing TB, understanding the importance of IPT and having received counseling were among the factors which enhanced the IPT uptake and completion(2).

This study will also try to determine patient-related factors associated with IPT uptake these are such as parents/care-takers age, sex, marital status, level of education, HIV status, previous TB diagnosis and IPT use as well as child's factors such as age, sex, CD4 count, viral load, HIV stage, and BMI.

3. MATERIALS AND METHODS

3.1 Study design

A descriptive, multi-centre, clinic based cross-section study. This research looked at the level of IPT uptake in HIV infected children attending CTC by determining how many children out of all eligible attendees were using or have used IPT and factors associated with IPT use.

3.2 Study area

Paediatric CTCs at MNH, Mwananyamala, Amana and Temeke Hospitals which are located in Dar es Salaam. All these HIV clinics are completely run by the Tanzania Ministry of Health, Community Development, Gender, Elderly and Children which directs and coordinates all the HIV-AIDS related treatment protocols and policies for Tanzania.

Muhimbili National hospital is a tertiary referral hospital also a teaching hospital for the Muhimbili University of Health and Allied Sciences (MUHAS). Mwananyamala, Temeke and Amana are Regional Referral hospitals. On average MNH CTC clinics attends 200registered pediatric HIV patients, Temeke has 500 registered patients, 400 in Amana and Mwananyamala has 300 registered HIV paediatric patients. These centres are being supported by Management and Development for health (MDH) under the United States President's Emergency Plan for AIDS Relief (PEPFAR) funding the supply of free ARVs, testing for HIV viral load and CD4 levels but additional laboratory tests are not catered for. Multiple sites were purposefully chosen to have adequate representation of Dar es Salaam since these specific centres carter for children from all the districts in the region and to facilitate the attainment of the minimum sample size within the short study period.

New patients are registered in specific clinics in which they receive treatment and monitoring. Demographic information, patient contacts, anthropometric measurements (weight and height), TB screening, CD4 cell count and viral load test are taken at the beginning of the treatment and in follow up. Follow up is done monthly to three monthly where several information is obtained from the patients or caretakers and filled in CTC 2 cards. In children less than 5 years of age, CD4 count is checked every 6 months while for those above 5 years of age and clinically stable with CD4 count of > 350cells/$mm^3$and viral suppression, CD4 cell count is not regularly monitored unless there is an indication

such as treatment failure. Viral load is being checked after 6 months of ARTs initiation then annually if viral copies are < 1000 copies/ml to monitor treatment(5).
Participants from four CTC clinics, all public institutions, were recruited in this study.

3.3 Study Population

All HIV positive children aged 1 to 14 years attending Paediatric CTC at MNH, Mwananyamala, Amana and Temeke Hospitals.

The age group of 1 to 14 years was chosen because according to WHO and national policy recommendation on LTBI treatment, IPT is recommended in all HIV children from 1 year and above regardless of a history TB contact. In paediatric HIV clinic at the age above 14 years, they get transitioned to adolescent clinic which most of them attend clinics independently and are not being accompanied by caregivers, not only that but also the uptake and factors associated with IPT use differ immensely among these two age categories, hence 1 to 14 years age group was chosen.

Inclusion criteria:

(i) All children aged 1 year to 14 years confirmed to be HIV positive by documented DNA/PCR or HIV serology results

Exclusion criteria:

(i) Children who had active TB infection.
(ii) Children who were on ongoing TB treatment.
(iii) Children with a prior diagnosis of TB and have received treatment within 2 years.
(iv) Children who had less than 6 months of HIV diagnosis and clinic attendance.
(v) Children who were not accompanied by caregiver.

3.4 Sample size determination and justification

A pilot study was done at MNH paediatric CTC clinic where 20 patients were assessed for IPT use. Five patients (25%) were found to have IPT use; hence this was used as proportion of IPT uptake to calculate sample size using the formula for estimating proportion as described below.

Due to lack of similar studies in this paediatric age group, a pilot study was conducted as an alternative to the use of a 50% for unknown proportion so as to estimate a closer value similar to the reality of our settings(39,40).

Aim of a cross-section study is to estimate the prevalence of unknown parameter from the target population using a random sample, therefore the Kish Leslie formula for calculating sample size in a prevalence study was used(40).

$$n = \frac{z^2 p\,(100-p)}{\varepsilon^2}$$

Where

z= level of confidence (1.96 for 95% confidence level)

p = expected proportion of HIV children with IPT uptake =25% this is the estimated proportion since the actual value is unknown.

ε= margin of error = 5%

n= (1.96 x 1.96 x 25 x 75)/25

n = 288

Addition of 10% non-response rate = 28

288 + 28 = 316

n = 320

3.5 Sampling procedure:

Study participants were enrolled consecutively until the required minimum sample size was attained in each study site. The excluded participants were identified.

Representative samples from each CTC clinic were obtained by probability proportional to size sampling(41).Total expected patients in all the four CTC clinics was 1400 that included (500 from Temeke, 200 from MNH, 400 from Amana and 300 from Mwananyamala).

Probability proportion = n/N

n= calculated study sample size

N= Total number of paediatric HIV patients from all the 4 CTC clinics

Probability proportion = $\frac{320}{1400}$ = 0.23

Probability proportion to size sample = n/N x number of total HIV paediatrics patients in each clinic.

Temeke 500 x 0.23= 114 participants

MNH 200 x 0.23 = 46 participants

Amana 400 x 0.23 = 91 participants

Mwananyamala 300 x 0.23 = 69 participants

} Total 320 participants

3.6 Study variables

Variables measured included;

Dependent variables: IPT use and IPT adherence

Independent variables: were age of the child, recent viral load of within 1 year, children's HIV disclosure status, age of the caregiver, gender of the caregiver, level of education of the caregiver, HIV status of the caregiver, caregiver's history of IPT use and caregiver's education on IPT.

3.7 Data collection tools, study procedure and measurements:

3.7.1 Data collection tools

Data was collected using a researcher administered standardized structured questionnaire which was developed by the principal investigator based on the Tanzania National guidelines for the management of HIV/AIDs sixth edition 2017 and Tanzania National guidelines for the management of TB in children 3rd edition 2017(5,42). The questionnaire was developed in English and translated into Kiswahili, Tanzanian national language. This enabled participant to respond in a language they fully comprehend.

The questionnaire was pre-tested amongst 20 participants to ensure clarity and that the questions were well understood by the participants. This helped to identify queries before actual data collection begins and it was solely used to modify the questionnaire. Data from the pre-test did not contribute to the final data set.

3.7.2 Data collection procedure

Data was collected by the principal investigator and two trained research assistants (intern doctors), who had a good understanding on the subject of the study. The research assistants underwent a three days training on how to conduct an interview before commencement of the study on how to use the structured questionnaire and how to extract clinical data from the CTC-1 and CTC-2 Cards. The principal investigator supervised and crosschecked the quality of data collected.

Screening to identify the candidates was conducted at the HIV CTC followed by investigator establishing a good rapport with a client. The interview was conducted after obtaining consent from the parent/caregiver of the participant and assent was sought from children 7 years and above. The questionnaire was simultaneously filled by the researcher during the interview process which took place in a private room with no interference.

Standardized questionnaire gathered data on the following: Social demographic factors of children and their parents/care-givers, clinical data such as weight, height, recent records of CD4 level, viral load, HIV stage, use of ART was extracted from their medical records (CTC cards, case notes, online system) whichever was being used in that facility. Screening for TB by WHO symptoms screen (if symptoms suggestive of TB patient were referred to responsible clinician for further investigation), history of previous TB infection, Use of IPT (if the child had never used IPT and had no symptoms of active TB, was referred to clinician to initiate IPT).

3.7.3Data measurements

Measures of adherence

Adherence of IPT for those currently on IPT was measured by four indirect methods: 4 days self recall report, a visual analogue scale which was a 1 month self recall report, counting the remained pills from pills provided in the last visit and the number of scheduled clinic appointments missed were assessed. Good adherence was defined as having a response of greater than 90% for each of these measures while less than that was poor adherence(2).

a) *For 4-day self-recall report:* participants(43) (patient/parent/caregiver) were asked to recall if they had missed any dose over the last 4 days, if reported more than one missed dose it was considered as poor adherence <90%. If they report one or no missed doses it was considered good adherence (>90%)

b) *For the 1 month-self recall report (Visual Analogue Scale*(44,45)*):*a calibrated line as a reflection of the way they took their medications over the last one month was used and participants were asked to mark on. The mark was measured using a 10 cm ruler scale on

the questionnaire which has been translated into percentages. If the mark is below 9cm (<90%) it was considered as poor adherence. If marked above 9cm (>90%) it was considered as good adherence.

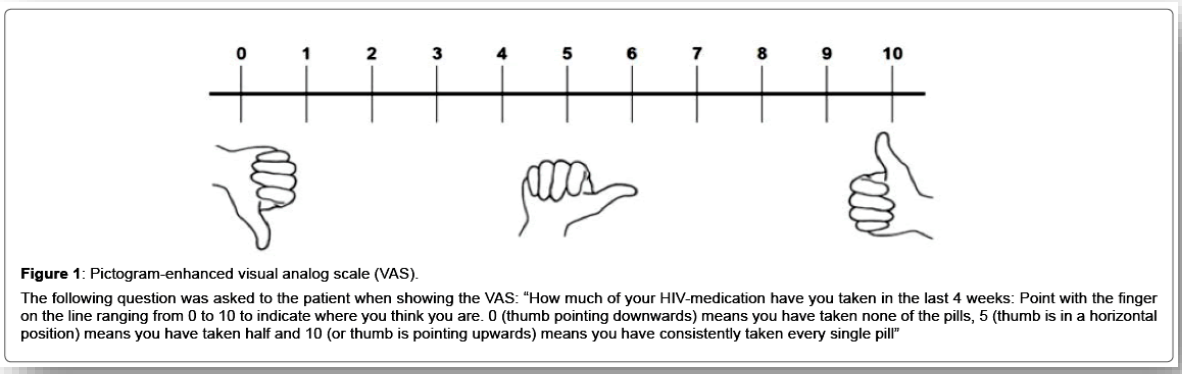


Figure 1: Pictogram-enhanced visual analog scale (VAS).

The following question was asked to the patient when showing the VAS: "How much of your HIV-medication have you taken in the last 4 weeks: Point with the finger on the line ranging from 0 to 10 to indicate where you think you are. 0 (thumb pointing downwards) means you have taken none of the pills, 5 (thumb is in a horizontal position) means you have taken half and 10 (or thumb is pointing upwards) means you have consistently taken every single pill"

Fig 2. Pictogram-enhanced visual analog scale (VAS) (44)**.**

c) *The number of clinic appointments missed:* records of visit schedules and missed appointments for the past 6 months was sought and counter checked with the pharmacy refill records to ensure drugs were picked up. If a patient missed one appointment and had not turned up for a scheduled visit/refill within the next two days of appointment, it was considered as poor adherence (<90%).

d) *Pill counting*. This was an additional measure which was carried out to those who brought their pill bottles. An office pill count was done to corroborate with actual recall findings and having consumed <90% of their dose, was considered poor adherence. The following formulae was used to calculate adherence(2).

$$\text{Adherence} = \frac{\text{No. of pills actually taken}}{\text{No. of pills supposed to have been taken}} \times 100$$

The overall good adherence was qualified when the participant did well in all four adherence measures. If he/she performed less than 90% in any one adherence measure, was qualified as having poor overall adherence.

Factors associated with IPT use

Factors associated with IPT use in this study were patients' factors and caregivers' factors. The social-demographic factors were obtained from interviewing the caregivers while clinical data such as weight, height, HIV stage, CD4 count, viral load count, IPT use was extracted from the CTC cards, clinical notes or online system if applicable in that facility.

Caregiver's education on IPT was measured by two questions, both being answered correctly: whether a caregiver had ever heard of IPT, and whether caregiver was aware of the required duration of IPT course.

Nutrition status: among the clinical data assessed was patients' nutrition status; the weight and height recorded in the CTC-2 card on date of interview were recorded, the WHO standard growth charts Z scores were used to interpret the nutritional status in terms of weight for length for children ≤ 5years and BMI (Kg/m^2) for those > 5 years. In this study, both Moderate Acute Malnutrition (MAM) and Severe Acute Malnutrition (SAM) were grouped together as Malnutrition.

3.8 Data management and analysis:

Data entry and cleaning was conducted by the principal investigator using statistical package for social science (SPSS) version 25. Consistent checks were performed to ensure quality of data entered. Categorical variables such as sex, level of education, marital status, HIV status of care-givers, status of IPT use were summarized in tables, frequencies, and proportion. For continuous variables like age, weight, height, CD4 count, viral load; mean, median and standard deviation or IQR were used. Difference in proportion was tested using the Chi-square test or Fisher's exact test. Respective 95% confidence intervals were determined and P-value of < 0.05 was considered statistically significant. Univariate and multivariate Logistic regression were used to determine odds ratios and p values for different factors associated with IPT use. Only those factors whose odds ratios had p values of < 0.2 on univariate analysis were further adjusted for in grouped manner on multivariate analysis. Adjusted odds ratios with p values of < 0.05 on multivariate analysis, were considered to be significant.

3.9 Ethical consideration

Ethical clearance was sought from MUHAS IRB and permission to conduct this study was obtained from Directorate of Research, Training and Consultancy ***(Ethical clearance approval reference number DA.287/298/01A/),*** to conduct the study. Individual permission was sought from the management of MNH, Temeke, Amana and Mwananyamala Regional hospitals. Parents or Caregivers were informed about the study, its importance and the steps which were to be followed; if they understood and agreed to participate they were requested to sign a written informed consent.

For older children above 7 years who were aware of their HIV status also signed an assent form before enrollment and the decision was completely autonomous, no one was forced to participate rather, they participated from their own free will. Confidentiality was maintained during the whole period of study by using a study identification number assigned to each participant to preserve anonymity.

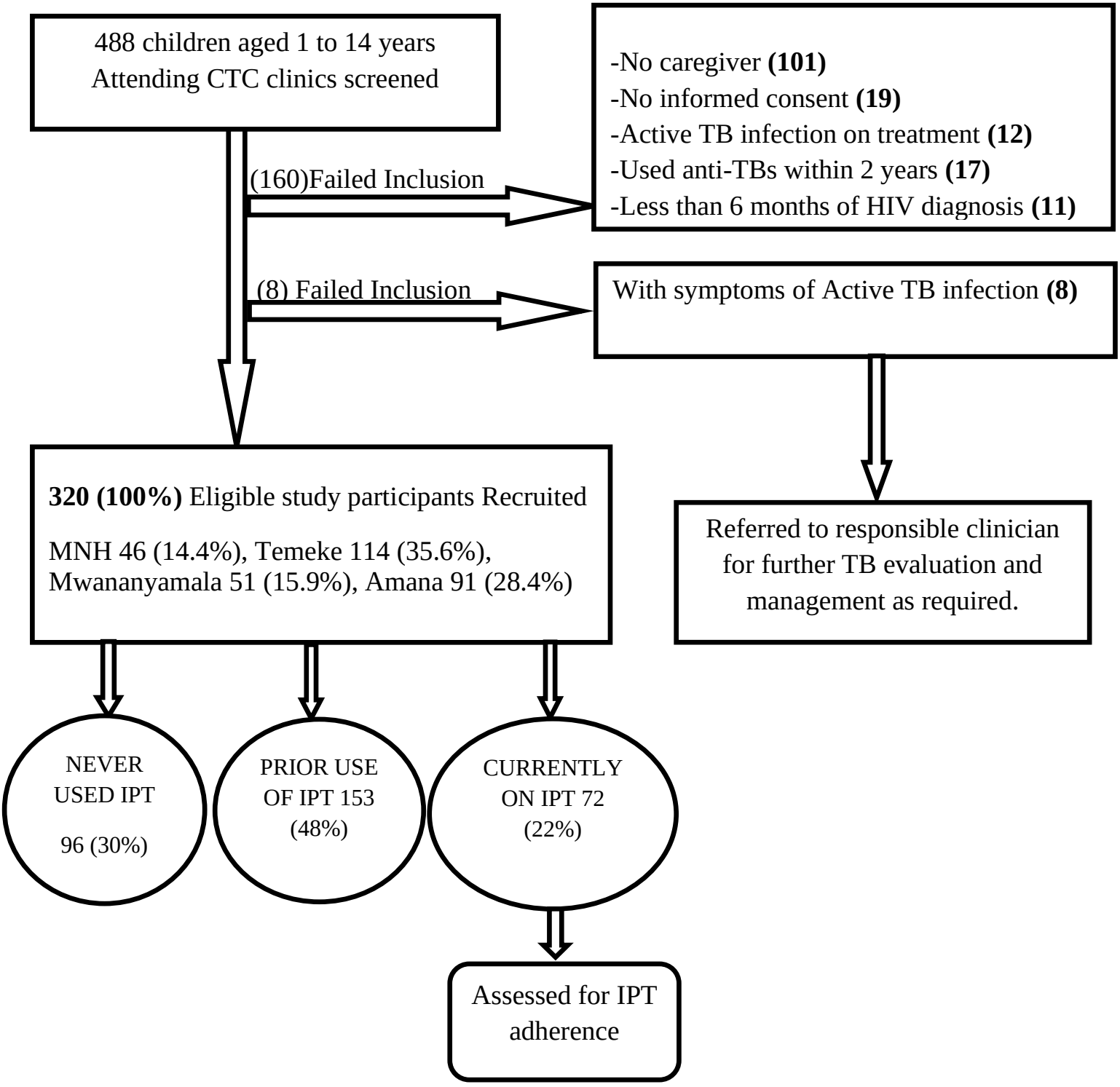
All children received the best standard of care offered as per hospital/national guidelines regardless of whether they accept to participate in the study or not. This study observed non-maleficence by not imposing any harm to the participants because there was no

intervention given to the participants and no invasive procedures were done. There was no unintended disclosure of HIV status to the children who were not aware of their HIV status during the interview so as not to inflict psychological pain. The study participants (the caregivers and older children who had their HIV status disclosed before the study) benefited because they became more aware of benefits of IPT in prevention of Tuberculosis in HIV population.

4.0 RESULTS

4.1 Recruitment and sampling of participants

A total of 488 children aged 1 to 14 years who attended CTC clinic during October 2019 to January 2020 were assessed for eligibility. A total of 168 children did not meet inclusion criteria because 101were not accompanied by caregivers, 19 did not provide consent, 17 had completed TB treatment within the last 2 years, 12 had confirmed active TB infection and were on anti-TB treatment, 11 were newly diagnosed and 8had clinical symptoms of active TB thus were referred for further evaluation. The remaining 320 participants who met the inclusion criteria were recruited in the study and their findings were included in the final analysis. (Figure 3)



**MNH: Muhimbili National Hospital*

Fig 3: Flow chart showing participants recruitment and study population.

4.2 Social demographic characteristics of the participants and their caregivers.

Out of 320 children who met the inclusion criteria mean age of the children was 9 (SD=3.6) years. Majority of the participants were school aged children (>7years) and of these 282/320 (88.1%) were attending school. Most of the children 295/320 (92.2%) had a normal nutritional status. Less than a half of participants 135/320 (42.2%) were under the care of both parents (Table 1a).

Table 1a: Social demographic characteristics of 320 HIV positive children aged 1–14 years attending CTC clinics in Dar es Salaam, Tanzania, 2019–2020.

Social demographic Characteristics	Category	N=320
Mean Age in years(SD)	9.1(3.6)	320 (100%)
Age Category (years)	1-5 6-9 10- 14	63 (19.7%) 100 (31.3%) 157 (49.1)
Sex	Female Male	163 (50.9%) 157 (49.1%)
Schooling status	Attending Not Attending Preschool[#]	282 (88.1%) 9 (2.8%) 29 (9.1%)
Mean Weight in Kg (SD)	26.4(10.4)	320 (100%)
Mean Height cm (SD)	127.2 (74.3)	320 (100%)
Nutrition Status[*]	Normal Malnourished	295(92.2%) 25(7.8%)
Parental Status	Both Parents Single Parent Non-Biological	135(42.2%) 115(35.9%) 70(21.9%)

**WHO Z-scores, normal nutritional status means weight for height ≥ - 2SD for children under five years or BMI for age ≥ 2SD for those above 5 years. Malnourished is; moderately wasted; weight for height < –2SD or severely wasted; weight for height < –3SD, or BMI for age < –2SD or < –3SD for those above five years. #Preschool age below 7 years*

4.3 Clinical characteristics of the participants and their caregivers.

In this study, all the 320 participants were on ARTs however two thirds of the participants 211/320 (66%) were in WHO HIV clinical disease stage III and IV at diagnosis. The mean CD4 count was 1078 (SD =767) cells/mm^3 and 142/188 (75.5%) had a CD4 count of more than 500 cells/mm^3. The median viral load was 20 (IQR=0- 607) copies/ml and more than two-thirds 240/309 (77.7%) of the participants had a viral load category of less than 1000 copies/ml. Among the participants 143/320 (45%) knew their HIV status (Table 1b)

Table 1b: Clinical parameters of 320 HIV positive children aged 1–14 years attending CTC clinics in Dar es Salaam, Tanzania, 2019–2020.

Clinical parameters	**Category**	**N=320**
HIV Clinical Stage	I & II	109 (34%)
	III & IV	211(66%)
Mean CD4 count in cells/mm^3(SD)	1078 (767)	188(58.8%)
CD4 Category*in cells/mm^3	>500	142 (75.5%)
	350-500	23 (12.2 %)
	<350	23 (12.2 %)
Median Viral Load in cp/ml (IQR)	20 (0, 607)	309(96.6%)
Viral Load Category**	<1000	240(77.7%)
	≥1000	69(23.3%)
HIV disclosure Status	Yes	143(44.7%)
	No	100(31.3%)
	Inappropriate age***	77(24.1%)

**CD4 count out of 188participants, **Viral load counts out of 309 participants, ***Inappropriate age was those preschool aged children, age less than 7 years.*

4.4 Social-demographic and clinical characteristics of caregivers.

Mean age was of the caregivers was 39 (SD =10) years with majority of them being females 253/320 (79.1%).Above a half 189/320 (59%) were in aged below 40 years, 168/320 (52.5%) were married and 205/320 (64.1%) were HIV positive. Among the caregivers, majority 216/320 (76.5%) had primary level of education. More than two thirds 255/320 (79.7%) had received education on IPT and 171/320 (53.4%) had used IPT (Table2).

Table 2: Social-demographic and clinical characteristics of 320 biological and non-biological caregivers.

Social demographic Characteristics	Category	N=320
Caregiver Mean age(SD) years	39 (10) years	320(100%)
Age category (years)	≤ 40	189 (59%)
	>40	131 (41%)
Caregiver's Sex	Female	253(79.1%)
	Male	67(20.9%)
Caregiver's Marital Status	Single	77(24.1%)
	Married	168(52.5%)
	Cohabiting	19(5.9%)
	Widow	29(9.1%)
	Divorced	27(8.4%)
Caregiver's Education Status	No formal Education	23(7.2%)
	Primary	216(76.5%)
	Secondary	62(19.4%)
	Beyond	19(5.9%)
Caregiver's HIV status	Positive	205(64.1%)
	Negative	100(31.3%)
	Unknown*	15(4.7%)
Caregiver's Education on IPT	Yes	255 (79.7%)
	No	65 (20.3%)
Caregiver's IPT use	Yes	171 (53.4%)
	No	149 (46.6%)

**Unknown HIV status means not checked, not applicable ART status was for the HIV negative caregivers.*

4.5 Level of IPT uptake in HIV children attending CTC

Among all the 320 participants, the level of IPT uptake was 224/320 (70%), the remaining 96/320 (30%) of the children had never used IPT. The 224/320 (70%) IPT use comprises of 72/320 (22.5%) of children who were using IPT during the study period and 152/320 (47.5%) had ever used IPT before the study period.

Time when IPT was used

Among the 224/320 (70%) children who had had a history of using IPT, 72/224 (32.0%) were using during the study period, 77/224 (34.2%) had used within the past six months, 58/224 (25.8%) had used it more than six months and a few 18/224 (8.0%) had used it more than 2 years ago prior to the study. (Figure 4)

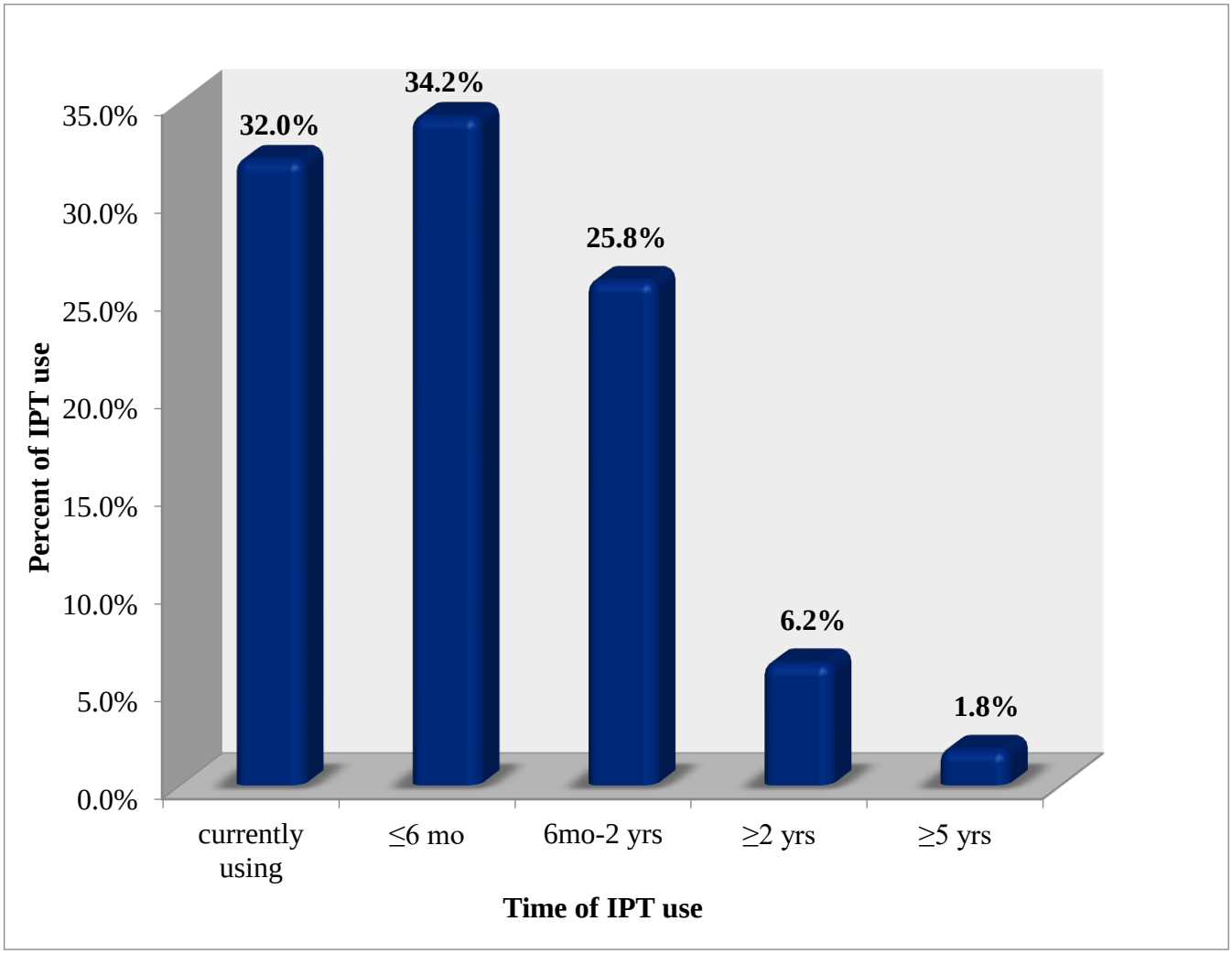


Fig 4: Distribution of HIV infected children according to time when IPT was used

4.6 Self reported adherence status

Based on the four indirect (self-reported) methods of assessment of adherence of IPT that is; four-days self-recall method, one month self-recall method, counting pills and missed clinic visits, of the 72 participants who were currently using IPT, more than two thirds of them 57/72 (79.2%) had excellent adherence to the IPT.

4.7 Factors associated with IPT use

4.7.1 Patients' and caregivers' factors associated with IPT use.

Among patients factors, older children of 10 to 14 years were noted to have higher IPT use131/157 (83%) compared to the younger ones (p-value of <0.001). Those who had a higher viral load of ≥1000 Cp/ml were found to have a higher IPT uptake 56/69 (81%) than those with a lower viral load (p-value =0.027). Higher IPT use was also noted in almost three quarters 209/282 (74%) of the children who were attending school (p-value <0.001) and most of the children whom their HIV status was disclosed had a higher IPT use 80/100 (80%) compared to those who were not aware of their HIV status (p-value <0.001). All other patient factors assessed did not have statistically significant difference. (Table 3a)

On the other hand, only caregivers who had received education on IPT had a higher IPT use 194/255 (76%) than those who had not (p-value <0.001). All other caregivers' factors had no statistical significant difference on the use of IPT. (Table 3b)

Table 3a: Patients' factors associated with IPT use.

Patients' factors (n=320)	IPT use		Chi-square
	No IPT use	**IPT use**	**P-value[#]**
Age (years)			
1-5	35 (56%)	28 (44%)	
6-9	35 (35%)	65 (65%)	<0.001
10- 14	26 (17%)	131 (83%)	
Sex			
Female	53 (33%)	110 (68%)	
Male	43 (27%)	114 (73%)	0.32
Parental status			
Non-biological	24(34%)	46(66%)	
Both parents	42(31%)	93(69%)	0.47
Single parent	30(26%)	85(74%)	
CD4 count* in cells/mm^3			
>500	46 (32%)	96 (68%)	
350-500	7 (30%)	16 (70%)	0.59
<350	5 (22%)	18 (78%)	
HIV viral load**			
<1000 Cp/ml	77 (32%)	163 (68%)	
≥1000 Cp/ml	13 (19%)	56 (81%)	0.027
Schooling status			
Attending	73 (26%)	209 (74%)	
Not attending	3 (33%)	6 (67%)	<0.001[##]
Disclosure status			
Disclosed	20(20%)	80(80%)	
Not Disclosed	33(23%)	110(77%)	<0.001

**CD4 count out a total of 188 participants, ** viral load out of a total of 309 participants, #p-value from Chi-square test, ##p-value from fisher's exact test*

Table 3b: Caregivers' (Biological/Non-biological) factors associated with IPT use.

Caregivers' factors (n=320)	IPT use		Chi-square (χ^2)
	No IPT use	IPT use	P-value[#]
Caregiver sex			
Female	79 (31%)	174 (69%)	
Male	17 (25%)	50 (75%)	0.35
Caregivers age			
≤40 years	63 (33%)	126 (67%)	
>40 years	33 (25%)	98 (75%)	0.12
Marital status			
Married	57 (34%)	111 (66%)	
Single	23 (30%)	54 (70%)	
Cohabiting	4 (21%)	15 (79%)	0.38[##]
Widow	5 (17%)	24 (83%)	
Divorced	7 (26%)	20 (74%)	
Education level			
None	6 (26%)	17 (74%)	
Primary	62 (29%)	154 (71%)	
Secondary	22 (36%)	40 (64%)	0.74
Beyond	6 (32%)	13(68%)	
HIV status			
Negative	31(31%)	69(69%)	
Positive	61(30%)	144(70%)	0.98[##]
Unknown	4(27%)	11(73%)	
Education on IPT			
No	35 (54%)	30 (46%)	
Yes	61 (24%)	194 (76%)	<0.001
Caregiver IPT use			
No	51 (34%)	98 (66%)	
Yes	45 (26%)	126 (74%)	0.12

#p-value from Chi-square test, ##p-value from fisher's exact test

4.7.2Univariate analysis of patients' and caregivers' factors associated with IPT use.

Among the patients factor studied, age and HIV viral load significantly associated with IPT use in a univariate analysis. Children aged 10 to 14 years were six fold (OR 6.30; 95% CI: 3.28-12.08, P <0.001) more likely to use IPT compared to age the younger age groups. In addition, participants who had viral load ≥ 1000 copies/ml were twice more likely (OR: 2.08:95% CI: 1.08-4.04, P = 0.029) to have used IPT than children with viral load <1000copies/ml (Table 4).

With regard to the caregivers factors children whose caregiver had received education on IPT were more likely (OR3.71; 95% CI: 2.11-6.54, P = <0.001) to have used IPT compared to those whose caregivers had not been given education on IPT (Table 4).

Table 4: Univariate analysis of patients' and caregivers' factors associated with IPT use.

Patients' factors (n=320)			Caregivers' factors (n=320)		
	cOR(95% CI)	**P-value#**		**cOR(95% CI)**	**P-value#**
Age (years)			**Caregiver sex**		
1-5	Ref		Female	Ref	
6-9	2.32 (1.22-4.42)	0.010	Male	0.75(0.41- 1.38)	0.35
10- 14	6.30 (3.28-12.08)	<0.001			
Sex			**Caregivers age**		
Female	Ref		≤40 years	Ref	
Male	0.78(0.48-1.27)	0.32	>40 years	1.49 (0.90-2.44)	0.12
Parental status			**Marital status**		
Non-biological	Ref		Married	Ref	
Both parents	1.16(0.63-2.13)	0.65	Single	0.82 (0.31 -2.21)	0.37
Single parent	1.48 (0.78-2.82)	0.24	Cohabiting	0.68(0.27-1.71)	0.41
			Widow	1.31 (0.32-5.32)	0.70
			Divorced	1.68(0.46- 6.12)	0.43
CD4 count			**Education level**		
>500	Ref		None	Ref	
350-500	1.10(0.42-2.85)	0.85	Primary	0.88(0.33- 2.33)	0.72
<350	1.73(0.60-4.94)	0.31	Secondary	0.64(0.22- 1.86)	0.42
			Beyond	0.77(0.20- 2.93)	0.70
HIV viral load**			**HIV status**		
<1000 Cp/ml	Ref		Negative	Ref	
≥1000 Cp/ml	2.08(1.08- 4.04)	0.029	Positive	1.06(0.63-1.78)	0.82
			Unknown	1.24(0.37-4.19)	0.73
Schooling status			**Education on IPT**		
Attending	Ref		No	Ref	
Not attending	0.70(0.17-2.87)	0.62	Yes	3.71(2.11-6.54)	<0.001
Disclosure status			**Caregiver IPT use**		
Not disclosed	Ref		No	Ref	
Disclosed	0.83(0.45-1.56)	0.57	Yes	1.46 (0.90-2.36)	0.12

**CD4 count out a total of 188 participants, viral load out of a total of 309participants.Cp/ml =copies/milliliter) # p-value from univariate analysis, CD4 count in (cells/mm^3)*

4.7.3 Multivariate analysis of factors associated with IPT use.

In the multivariate analysis factors with P-Value of <0.2 in univariate analysis which included participants' age, HIV viral load, caregivers' age, caregivers' education on IPT and the IPT use status of the caregivers were used in a final model. In the final adjusted model, participants' older age group, higher viral load and caregivers' education on IPT use were significant predictors of IPT use (OR: 5.39, 95% CI: 2.64-11.0, p < 0.001), (OR: 2.48, 95% CI: 1.20-5.13, p=0.014) and (OR: 3.62, 95% CI: 1.89-6.91, p< 0.001) respectively (Table 5).

Table 5: Multivariate analysis of patients' and caregivers' factors associated with IPT use.

Variables (n=320)	**Multivariate**	
	aOR (95% CI)	**P-value[#]**
Age (years)		
1-5	Ref	
6-9	2.39(1.17-4.89)	0.017
10- 14	5.39(2.64-11.0)	<0.001
HIV viral load[@]		
<1000 Cp/ml	Ref	
≥1000 Cp/ml	2.48(1.20-5.13)	0.014
Caregivers age		
≤40 years	Ref	
>40 years	1.10 (0.63-1.94)	0.74
Caregiver IPT Education		
No	Ref	
Yes	3.62 (1.89-6.91)	<0.001
Caregiver IPT use		
No	Ref	
Yes	1.23 (0.70-2.17)	0.45

*@Viral load out of a total of 309participants, *Cp/ml is HIV Viral copies per milliliter of blood.[#] p-value from multivariate analysis*

5. DISCUSSION

IPT use is among the indicators for performance in HIV Program. This is among the first studies to evaluate IPT uptake and factors associated with IPT use among children aged 1 to 14 years attending HIV Care and Treatment Clinics.

In Tanzania IPT is freely available and recommended in the National TB guidelines. In this study which involved three regional referral hospitals and a national hospital, the level of IPT uptake among these children was 70%. This falls short of the WHO End TB strategy of 2015 aiming at ≥90% uptake among people living with HIV for elimination of TB(46,47).

A trend was noted on the levels of IPT uptake increasing with time, whereby there was a rise of 33% in five years. This trend could possibly be due to increased awareness and emphasis on IPT to both health care workers and the clients, which has been taking place and readily availability of isoniazid in the centers. Therefore we may achieve a higher level of IPT uptake to reach the target of ≥90% set by End TB strategy by the year 2030, with emphasis on similar efforts.

In 2015 Kenya had a higher level of IPT uptake (77%) in people living with HIV compared to the finding in this study despite the fact that these two countries have similar IPT policy(5,48) since the year 2011; this disparity could mainly be due to differences in age groups studied, as they included participants from 18 years of age(34).Thus, the lower IPT uptake in our study could have been contributed by the challenges of excluding active TB in the paediatric age group.

Most African countries have adopted the IPT policy, however studies from some of these countries also experiencing a high TB burden, found a much lower IPT uptake in contrast to our study. Example Ethiopia had only 20% of IPT uptake among 11 hospitals which were studied in 2014 (16). Comparably, in Nigeria, the level of IPT uptake was 30% in 2013 and 35% in 2015, an increase of 5% in a period of 2 years(31,32). The large difference between these two studies done in Ethiopia and Nigeria, contrasted with this study done in Tanzania, could likely be due to the difference in the periods which studies were done. Emphasis and awareness of IPT to the doctors and patients/caregivers was still

low 5 years ago, despite that these countries also follow the same WHO recommendation released in 2011 for PLWHIV (49).

Older children (10 to 14 years) in this study were more likely to use IPT compared to younger ones. This could possibly be related to the challenges of prescribing appropriate dose of isoniazid, as the pediatric formulation is not readily available. At present, most clinicians estimate the dose from a 300mg tablet, which can be challenging and difficult for caregivers given the low weights of young children. However this strategy is cost effective and easy to supply.

In this study, a higher viral load of ≥ 1,000 copies/ml was among the strong predictors of IPT uptake. Higher viral load has been shown to be an important risk factor for TB, regardless of CD4 cell counts as reported in an adult study (50). Thus the observation in this study could probably be clinician's evidence informed decision making to focus on emphasizing more IPT intake in this group of patients to reduce the risk of morbidity and mortality and thus improving their quality of life.

In this study, the only caregiver factor which was independently associated with IPT uptake was caregivers' education on IPT. This is not unexpected observation since the mean age (9 years) for children in the current study are still within the age where most depend on their caregivers to support and supervise their treatment. Findings from this study was similar to a study done in adults in Kenya which found that those who received health education on IPT were more likely to be initiated on IPT than those who were not(34). Also similar findings in a study done in adults in Tanzania, where understanding the importance of IPT was one among the factors which was associated with uptake and completion of IPT (2). Findings from these studies, are in line with the fact that in chronic illnesses such as HIV where there is a risk of several opportunistic infections, TB being highest on the list; the opportunity to access preventive measures and information on the role of IPT, can influence both patients and the caregivers to make informed decision on the use of IPT for TB. This is because TB/HIV comorbidity is perceived to be a severe disease, which requires a long time treatment and increases pill burden in a addition to increased risk of morbidity and mortality.

Among 22.5% children who were on IPT during the time of this study, were evaluated for their level of adherence, using four different methods which include; a four days self-recall report, a one month self-recall report through a visual analogue scale, counting pills and assessing number of scheduled clinics appointments missed, of which excellent adherence was defined as having a response of greater than 90% for each of the method used. In this study, the adherence level was 79.2%. This adherence rate is less than expected taking in consideration that, all children were on ARTs and IPT refills done in the same clinic which could act as a motive to come to the clinic without extra need of travelling or additional time for IPT refill.

There are possibilities that multiple self-reported methods of assessment of adherence used in our study, which provides more objective estimates (51) could have affected the overall adherence. In a study done in South Africa the mean adherence was found to be very high 97%, a prospective randomized clinical trial where there was a close follow up of the few participants enrolled and a single method of assessing adherence (pill count) was used. Though studies on isoniazid started to be carried out early in South Africa (23,52), IPT implementation started officially in 2011 like most other African countries. The high level of adherence observed in their study can be explained by the fact that, the study design they used allows for close follow up and reinforcement of adherence, as compared to a real life setting where there is a little control over the study participants. Furthermore the use of one pill count though is easy to perform and it is not prone to recall bias, it can be manipulated by patients. The other reason for the difference can be attributed to the fact that; their cohort consisted of much younger children with a median age of 3.2 years, the group which more often receives treatment under strict supervision and assistance from the caregivers as compared to older children included in the current study (37).

In a prospective, multicentre observational study done in Dar es Salaam which included children from 10 years of age and adults, the level of good adherence was 92.2% among children aged 10 to 18 years. Despite the fact that the two studies were done in the same settings, the discrepancy in the rate of adherence can be explained by the fact that they used pill counting only as a method for assessment of adherence, which could have overestimated their results, also they studied adolescents, most of who are informed of

their HIV status and participate in peer support groups which makes them more prepared to comply with interventions that are said to improve their health (38).

Strengths of the study

- This was a multi- centered study involving four of the large CTCs in Dar es Salaam, thus providing adequate representation of the region.
- Multiple methods of assessing adherence of IPT were used thus minimizing systematic biases.
- This is among the first studies to provide data on IPT in paediatric HIV patients in Tanzania.

Study limitations:

- Recall bias and desirability bias in assessing adherence. This was minimized by including a question on missing clinic appointments which was confirmed from clinic records and also using more than one measure to assess adherence.

6. CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion.

Level of IPT uptake in HIV children attending four CTC in Dar-es-Salaam is low (70%) which is below the global target requirement of ≥90% of IPT use in people living with HIV for End TB strategy. Level of adherence of IPT in children is also low 79%, this invariably affects the effectiveness of IPT strategy, and therefore challenges that affect drug adherence in this special group of patients should be addressed. Having an older age 10-14 years, a higher HIV viral load ≥1000 copies/ml and having a care giver who had received education on IPT were the predictors of IPT use. This information is important so as to strengthen our IPT programmes in the region.

6.2 Recommendations

In order to improve IPT uptake in HIV infected children to meet the global target requirement for the End TB strategy by the year 2030, this study recommends the following

1. Emphasis on IPT use needs to be made in the younger age group children, below 10 years of age to improve on the level of IPT uptake in all HIV infected children.
2. IPT prescription should also be emphasized in children with viral load of < 1000 copies/ml since all HIV infected children are at risk of developing active TB.
3. Education on IPT should readily be provided to the caregivers since these children aged 1 to 14 years are under the supervision of their caregivers and needs ongoing supervision and assistance to ensure adherence to the IPT recommendations.
4. This study supports the need of further studies to assess institutional factors that might be associated with IPT use to further improve the IPT use as this assessed patients and caregivers factors.

7. SUPPLEMENTARY

7.1 Additional information on patients and caregivers.

In addition three (1%) of the participants had a history of TB contact within the last 3 months prior the study and 36 (11%) had a prior history of active TB of which 78% of them had completed TB treatment more than 2 years ago, 19% completed TB treatment within the past 2 years and 3% did not complete TB treatment. Among the caregivers 181/320 (56.6%) were self-employed, Less than a quarter 50/320 (15.6%) of care givers had a prior history of TB infection. (Table 6)

Table 6: Additional patients' and caregivers' general characteristics.

Social demographic Characteristics	Category	N=320
Patients' TB contact	No	317 (99.1%)
	Yes	3 (0.9%)
Patients' Prior history of TB	No	284 (88.8%)
	Yes	36 (11.3%)
Caregiver Occupation	Self-Employed	181(56.6%)
	Employed	71(22.2%)
	Unemployed	68(21.3%)
Caregiver on ARTs	Yes	204(63.7%)
	No	4(1.3%)
	Not applicable[#]	112(35.0%)
Caregiver prior TB diagnosis	Yes	50(15.6%)
	No	270(84.4%)

 # Not applicable for all non-HIV caregivers

7.2 IPT distribution per centre

Among the centers, MNH had the highest proportion of children who had used IPT 37/224 (80.4%), followed by Mwananyamala 52/224 (75.4%), while Amana had the least participant who had used IPT 52/224 (57.1%). (Figure 5). Comparing the four hospitals, level of IPT uptake was higher in the National hospital which was 80.4% compared to other hospitals, the discrepancy could have been observed due to differences in the size of the population from each centre, Muhimbili having a fewer number of clients and having majority of children with a higher viral load could be the reason of ranking the first in IPT uptake. Also being a national, tertiary and teaching hospital, more efforts and emphasis could be taking place in adherence of the HIV treatment and care guidelines including IPT. However from our findings, further studies on institution factors associated with IPT are recommended.

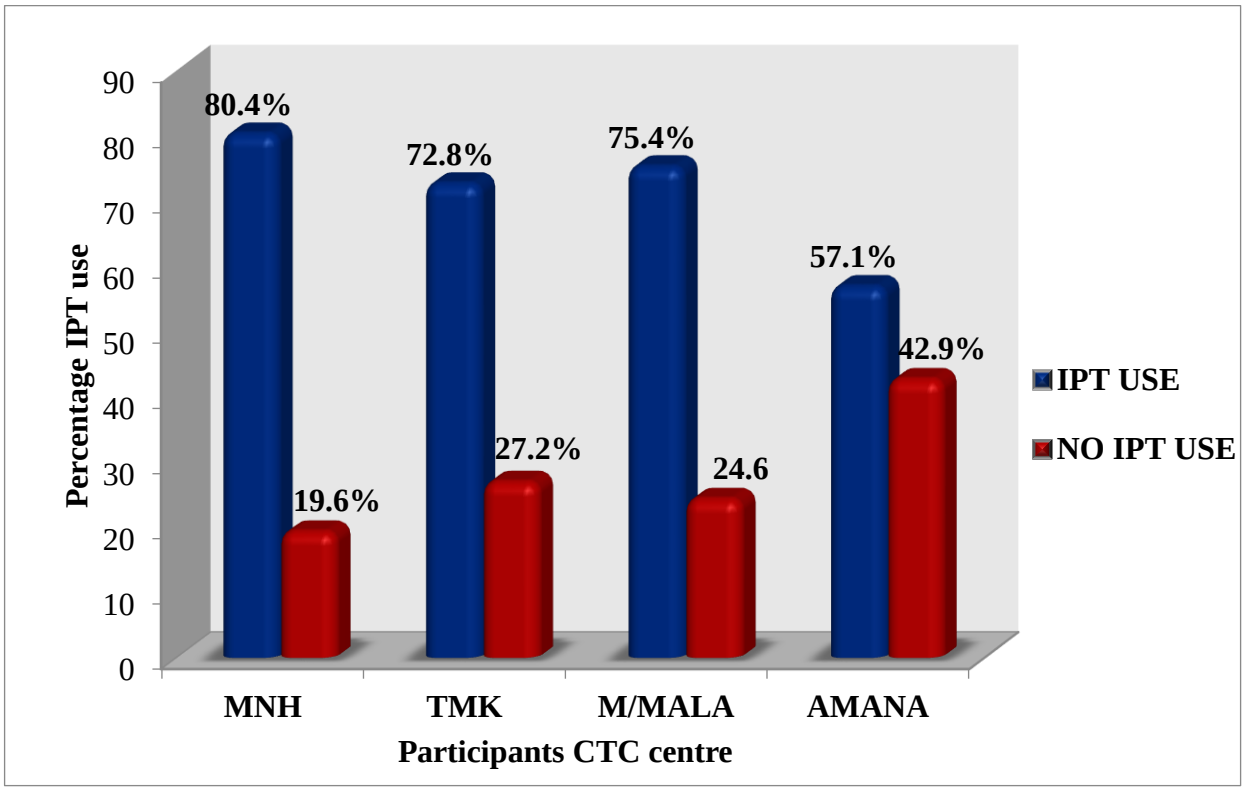


Fig 5: Distribution of HIV infected children according to IPT use status and CTC attended.

7.3 IPT completion

Among those children who had used IPT before the study period 131/152 (86.2%) of children were reported to had completed a six month course of IPT. Reasons mentioned for non-completion were such as isoniazid being out of stock in the centre, participants experiencing adverse reactions and some caregivers were not aware of the required duration of the course of IPT.

7.4 Additional information on patients' factors associated with IPT use on univariate analysis.

There was no statistical significance on patients' nutrition status, HIV stage, TB contact or history of prior TB infection with regards to IPT use as (Table 7) which is a continuation of table 3 elaborates.

Table 7: Other patients' factors associated with IPT use on univariate analysis.

	IPT use		**Univariate**	
	No IPT	**IPT use**	**cOR(95% CI)**	**P-value**
Nutrition status*				
Normal status	88(30%)	207(70%)	Ref	
Malnutrition	8(32%)	17(68%)	0.90(0.38-2.17)	0.82
HIV stage				
Stage 1 and 2	37(34%)	72(66%)	Ref	
Stage 3 and 4	59(28%)	152(72%)	0.76(0.46-1.24)	0.269
TB contact				
No	95 (30%)	222 (70%)	Ref	
Yes	1 (33%)	2 (67%)	1.17(0.11-13.0)	0.899
Prior TB diagnosis				
No	83 (29%)	201 (71%)	Ref	
Yes	13 (36%)	23 (64%)	1.37(0.66- 2.83)	0.390

As per WHO Z-scores, normal nutritional status means weight for height ≥ - 2SD for children under five years or BMI for age ≥ 2SD for those above 5 years. Malnourished is; moderately wasted; weight for height < –2SD or severely wasted; weight for height < –3SD, or BMI for age < –2SD or < –3SD for those above five years.

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9. APPENDICES

9.1 Questionnaire

UPTAKE AND FACTORS ASSOCIATED WITH IPT USE AMONG HIV POSITIVE CHILDREN IN DAR-ES-SALAAM.

DATE…… STUDY ID……

A: DEMOGRAPHIC CHARACTERISTICS

1. Age……..
2. Age category a) 1-5 yrs b) 6-9 yrs c) 10-14 yrs
3. Sex: (a)Female (b)Male
4. Schooling status of child a) Attending school b) Not attending school c) Not Applicable
5. Parental status a) Both parents b) Single parent c) non-parental caretaker

B: CLINICAL ASSESSMENT

6. Weight (Kg)……..
7. Height (cm)……..
8. Weight/Ht…….. a) SAM b) MAM c) Normal
9. BMI (Kg/m^2)……a) SAM b) MAM c) Normal
10. HIV Clinical staging a)I b) II c) III d) IV
11. CD4+ count … a) >500cells/mm^3b) 350 -500 cells/mm^3 c) <350 cells/mm^3 Date……..
12. Viral load…….. a) < 1000copies/ml b) > 1000 copies/ml Date:……...
13. Use of ARTs a)Yes b)No if Yes a) ≤ 6 months b) ≥ 6 months
14. Any history of positive TB contact a) Yes When……. b) No
15. Prior Diagnosis of TB a)Yes When…… b)No ……if NO go to section C
16. Completed TB treatment a) ≤ 2 years b) ≥ 2 years c) Not completed

C: TB SYMPTOMS SCREENING

17. Chronic cough ≥ 3 weeks a) Yes b) No
18. Fever ≥ 2 weeks a) Yes b) No
19. Weight loss/faltering/failure to thrive a) Yes b) No
20. Night sweats a) Yes b) No

D: IPT USE

21. Use of IPT a) Used b) Currently using c)Never used→ Go to Section F
22. When was IPT used a) ≤ 6 months b) ≥ 1 year c) ≥ 2 years d) ≥5 years
23. Did you complete 6 months course a) Yes b) No→ Reasons……...

E: IPT ADHERENCE

24. Many people find it hard to administer INH every single day. How often does the child take INH a) Daily b) Almost daily c) Occasionally
25. In the past 4 days how many days has the child missed taking all their doses
    a) None b) One day c) Two days d) Three days e) Four days
26. On the scale of 1 to 10, mark a line on this scale of how the child took their pills over the past one month, 0 meaning none pills were taken, 5 means half doses were taken and 10 means each and every pill was taken over the whole month.

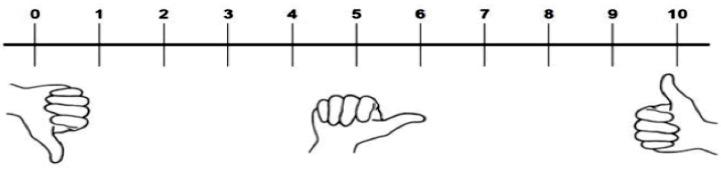

Figure 1: Pictogram-enhanced visual analog scale (VAS).
The following question was asked to the patient when showing the VAS: "How much of your HIV-medication have you taken in the last 4 weeks: Point with the finger on the line ranging from 0 to 10 to indicate where you think you are. 0 (thumb pointing downwards) means you have taken none of the pills, 5 (thumb is in a horizontal position) means you have taken half and 10 (or thumb is pointing upwards) means you have consistently taken every single pill"

27. How many appointments did the child have scheduled over the past 6 months?
    a) One b) two c) three d) Four e) Five f) Six***[the researcher to verify with the card as well]***
28. How many visits attended? a)1 b) 2 c) 3 d) 4 e) 5 f) 6 ***[researcher to verify with the card]***
29. Do you have the pill bottle with you? a) Yes b) No

30. If yes, No. of pills actually taken X 100 = _____%
    No. of pills supposed to have been taken
31. Adherence: a) Excellent (consumed ≥ 90% dose) b)Poor (consumed ≤ 90% dose)

F: CAREGIVER CHARACTERISTICS

32. Age of caregiver: ……
33. Relationship with care-taker a) Biological Parent b) Non- biological Parent
34. Sex: a)Female b)Male
35. Marital status: a) single b) Married c) Cohabiting d) Widow e) Divorced
36. Level of Education: a)No formal Education b) Primary c) Secondary d) Beyond
37. Occupation of care-taker: a) Self-employed b) Employed c) Unemployed
38. Serostatus a) Positive b) Negative c) Unknown →Go to question 40
39. On ARTs a) Yes b) No
40. Is the HIV status disclosed to the child? a) Yes b) No c) Not Applicable
41. Do you know about IPT? a) Yes b) No
42. Have you ever received education on IPT a) Yes, if able to respond to the following questions (For how long is the course of IPT? What is the role of IPT) b) No
43. Have you ever used IPT a) Yes b) No
44. Prior diagnosis of TB a) Yes b) No

9.2 Dodoso

TAREHE……

NAMBA YA DODOSO……

DODOSO JUU YA MATUMIZI YA DAWA YA ISONIAZID YA KUZUIA MASHAMBULIZI YA KIFUA KIKUU KWA WATOTO WENYE VVU DAR ES SALAAM.

A: TAARIFA ZA DEMOGRAPHIA

1. Umri……..
2. Kundi la Umri,miaka a) 1- 5 b) 6 – 9 c) 10 - 14
3. Jinsia: (a)Kike (b)Kiume
4. Hali ya shule ya mtoto a) Anaenda shule b) Haendi shule
5. Hali ya wazazi a) wazazi wote wawili b) mzazi mmoja c) walezi

B: TAARIFA ZA CTC

6. Uzito (Kg)…….
7. Urefu (sm)…….
8. Uzito/Urefu……
9. BMI……
10. Steji ya VVU a)I b) II c) III d) IV
11. CD4+ count…….. a) >500cells/mm^3 b) 350 -500 cells/mm^3 c) <350 cells/mm^3Tarehe……
12. Kiwango cha Virusi…….. a) 1000copies/ml b) > 1000 copies/ml Tarehe……..
13. Matumizi ya dawa za ARTs a)Ndio b)Hapana
14. Umewahi kuugua kifua kikuu? a) Ndio b)No
15. Lini ulimaliza matibabu ya Kifua kikuu?a) ≤ 2 years b) ≥ 2 years c) Hukumaliza
16. Umewahi kuwa karibu na mtu mwenye maambukizo ya kifua kikuu? a) Ndio b)Hapana

C: UCHUNGUZI WA DALILI ZA KIFUA KIKUU

17. Kikohozi ≥ 3 wikia) Ndio b)Hapana
18. Homa ≥ 2 wiki a) Ndio b)Hapana
19. Kupungua/kushindwa kuongezeka uzito a) Ndio b)Hapana
20. Anatoka sana jasho usiku? a) Ndio b)Hapana

D: MATUMIZI YA ISONIAZIDI DAWA YA KUZUIA KIFUA KIKUU

21. matumizi ya isoniazidi a) Umewahi kutumia b) Unatumia c) Hujawahi kutumia
22. Lini ulitumia isoniazidi a) ≤ 6 miezi b) ≥ 1 mwaka c) ≥ 2 miaka d) ≥5 miaka
23. Ulimaliza miezi 6 a) Ndio b) Hapana

E: UZINGATIAJI WA DAWA YA ISONIAZID

24. Watu wengi wanaona ugumu kutumia dawa kila siku. Je mtoto huwa anatumiaga dawa za kuzuia kifua kikuu mara ngapi? a) Kila siku b) Karibu kila siku c) Mara chache
25. Je ndani ya siku 4 zilizopita mtoto amekosa dawa ya kuzuia kifua kikuu kwa siku ngapi? a) hajakosa kabisa b) siku 1 c) siku 2 d) siku 3 e) siku 4
26. Kwa kiwango cha 1-10, weka alama ya kiwango ambacho mtoto ametumia dawa ya kuzuia kifua kikuu ndani ya mwezi mmoja uliopita, 0 ina maanisha hakuna dawa zilizochukuliwa, 5 ina maanisha nusu ya dozi ilichukuliwa na 10 ina maanisha kila kidonge kilichukuliwa

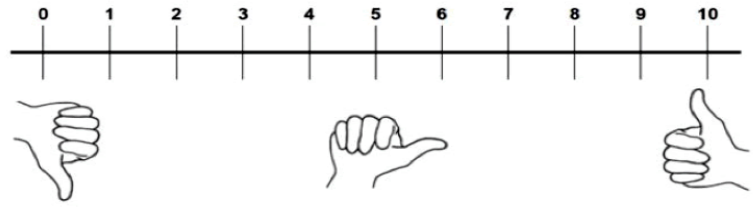

Figure 1: Pictogram-enhanced visual analog scale (VAS).
The following question was asked to the patient when showing the VAS: "How much of your HIV-medication have you taken in the last 4 weeks: Point with the finger on the line ranging from 0 to 10 to indicate where you think you are. 0 (thumb pointing downwards) means you have taken none of the pills, 5 (thumb is in a horizontal position) means you have taken half and 10 (or thumb is pointing upwards) means you have consistently taken every single pill"

27. Mtoto alipangiwa kuhudhuria kliniki mara ngapi ndani ya miezi 6 iliyopita? a) 1 b) 2 c) 3 d) 4 e) 5 f) 6[***mtafiti kuhakikisha kwa kuangalia na kwenye kadi pia***]
28. Alihudhuria mara ngapi? a) 1 b) 2 c) 3 d) 4 e) 5 f) 6[***mtafiti kuhakikisha kwenye kadi pia***]
29. Je, unacho kikopo chako cha vidonge? a) Ndio b) hapana
30. Kama ndio, Idadi ya vidonge vilivyotumika X 100 = _____ %
    Idadi ya vidonge vinavyotakiwa kutumika
31. Uzingatiaji: a) mzuri (matumizi ≥ 90%) b) Mbaya (matumizi ≤ 90%)

F: TAARIFA ZA WAZAZI/WALEZI

32. Umri: ……
33. Mahusiano na mtoto a) Mzazi b) Mlezi
34. Jinsia a) Kike b) Kiume
35. Hali ya ndoa: a) Sijaolewa b) Nimeolewa c) Kuishi pamoja d) Mjane e) Mtalaka
36. Kiwango cha elimu: a) Sijasoma b) shule ya msingi c) Sekondari d) Zaidi ya sekondari
37. Kazi: a) Nimejiajiri b) Nimeajiriwa c) Sijaajiriwa
38. Hali ya maambukizi ya VVU a) Ndio b)Hapana
39. Matumizi ya ARTs a) Ndio b) Hapana
40. Je,haliya VVU inajulikana kwa mtoto? a) Ndio b) hapana
41. Unafahamu kuhusu dawa ya kuzuia kifua kikuu? a) Ndio b) Hapana
42. Umewahi kupata elimu juu ya dawa ya kuzuia kifua kikuu? a) Ndio kama ataweza kujibu maswali yote haya mawili (Je inatumika kwa muda gani? Je inalengo gani?) b) Hapana
43. Umewahi kutumia isoniazidi dawa ya kuzuia kifua kikuu? a) Ndio b) Hapana
44. Umewahi kuugua kifua kikuu? a) Ndio b) Hapana

ASANTE KWA KUSHIRIKI

9.3 Informed consent form

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES (MUHAS)

AN INFORMED CONSENT FORM FOR STUDY ON ISONIAZID PREVENTIVE THERAPY UPTAKE AMONG HIV POSITIVE CHILDREN ATTENDING IN DAR-ES-SALAAM

INTRODUCTION

My name is Dr Emilia Karugaba a resident at Muhimbili University of Health and Allied Sciences, Dar es Salaam. I'm researching the level of IPT uptake and the associated factors in HIV infected children attending CTC clinic at MNH and Mwananyamala Hospital. I am going to give you information and invite you to be part of this research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. If you have questions, please ask me or any doctor/nurse.

Purpose of the research

The purpose of this research is to determine the level of uptake of IPT, adherence and factors associated with IPT use. This research will involve a questionnaire that will assess the social demographic data of the child and parent/caregiver and will trace clinical profile from CTC cards, from the parents/care-giver, screen for TB symptoms, crosschecking and counting INH pills remained from last prescription and anthropometric measurements. You sign this consent form and answer the questions in the questionnaire as best as you can. It will take approximately 3 minutes.

We are inviting all children together with parents/caregivers who attend CTC clinics at MNH and Mwananyamala Hospital to participate clinics at MNH and Mwananyamala in order to come up with best solutions to improve IPT uptake since from the literature and the evidence available, INH is safe and effective for preventing active TB and recommended to all PLWHIV including children.

What does participation involves?

Your participation in this research is entirely voluntary. Whether you choose to participate or not, all the services you receive at this hospital will continue and nothing will change.

CONFIDENTIALITY

Information about you that will be collected during the research will be kept confidential and no-one but the researchers will be able to see it, no names will be used but identification numbers only. We will not be sharing the identity of those participating in the research.

RISKS

By participating in this research you will not be subject to any risk.

BENEFITS

Your child will be management will not be interrupted and your participation is likely to help us find the answer to the research question and you will get to be aware of IPT.

CERTIFICATE OF CONSENT

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Name of Participant_____

Signature of Participant _____

Date _____

Day/month/year

IF ILLITERATE

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Illiterate participants should include their thumb-print as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness_____ AND Thumb print of participant

Signature of witness _____

Date _____

Day/month/year

9.4 Fomu ya ridhaa kwa mzaz/mlezii kwa kiswahili

Namba ya utambulisho……

KICHWA CHA HABARI: MATUMIZI YA DAWA YA ISONIAZID YA KUZUIA MASHAMBULIZI YA KIFUA KIKUU KWA WATOTO WENYE VVU DAR ES SALAAM

Utangulizi:

Habari, naitwa Dkt. Emilia Karugaba mwanafunzi wa shahada ya uzamili ya udaktari wa watoto katika Chuo cha Sayansi Shirikishi cha Muhimbili.

Nafanya utafiti kuangalia matumizi ya dawa ya isoniazid ya kuzuia kifua kikuu kwa watoto wanaoishi na virusi vya UKIMWI (VVU) wanaohudhuria kliniki za CTC katika hospitali ya taifa ya Muhimbili, Amana, Temeke na Mwananyamala. Nitakupa maelekezo na kukualika kushiriki katika utafiti huu, kabla ya kuamua unaweza kuomba maelekezo zaidi kutoka kwa daktari yeyote au muuguzi atakupa maelekezo ya kutosha.

Lengo la utafiti huu: lengo nikutambua kiwango cha matumizi ya dawa ya Isoniazid kwa lengo la kuzuia kifua kikuu kwa watoto wenye maambukizi ya virusi vya UKIMWI wanaohudhuria kliniki za CTC katika hospitali ya taifa ya Muhimbili, Temeke, Amana na Mwananyamala. Hii itasaidia kutafuta ufumbuzi wa namna gani ya kuboresha matumizi ya dawa hii kwani tafiti zimethibitisha kuwa ni dawa ambayo ni salama na madhubuti katika kuzuia ugonjwa wa kifua kikuu katika watu wanaoishi na VVU.

Kushiriki kutahusisha nini:

Kama unakubali mwanao kushiriki katika utafiti huu, tutakuuliza, maswali kuhusiana na mwanao na familia yako. Baadhi ya maelezo kuhusiana na ugonjwa wake, maelezo mengine ya ugonjwa yatafwatiliwa katika kadi ya kliniki, dawa ya Isoniazid itakaguliwa na kuhesabiwa kujua matumizi na vipimo kama uzito na urefu vitachukuliwa. Kushiriki kwako ni kwa hiari na mwanao atapata huduma zote stahiki hata kama hutashiriki kwenye utafiti.

Usiri wa taarifa: taarifa zote zitakazopatikana katika utafiti huu, zitabaki kuwa siri, tutatumia namba ya hospitali na namba ya utambulisho ya utafiti huu kwaajili ya kuwatambua washiriki wa utafiti bila kutumia majina katika utafiti huu au katika machapisho yoyote ya kiutafiti yatakayotokana na utafiti huu hapo baadae.

Madhara ya kushiriki

Kwa kushiriki kwenye utafiti huu hautapata madhara yeyote.

Tamko la ridhaa

Mimi …… nimesoma/nimesomewa yaliyomo kwenye hii fomu ya ridhaa. Maswali yangu yote yamejibiwa nanimepewa nakala ya hii fomu ya ridhaa. Nina kubali kwa hiari yangu mwenyewe kuruhusu mtoto wangu ashiriki katika utafiti huu.

Saini ya mzazi/mlezi…… Tarehe ……..

Tamko la shahidiwamzazi/mleziasiyejuakusoma au kuandika

Mimi…… nimeshuhudia …….Mzazi/ mleziwa motto akisomewa fomu hii ya ridhaa kwa usahihi. Mzazi/ mlezi aliyepata nafasi ya kuuliza maswali yote ambayo yote yalijibiwa. Ninathibitisha kuwa mzazi/ mlezi wa motto ameruhusu kwa hiari yake mtoto wake ashiriki katika utafiti.

Saini ya shahidi …….……. Tarehe:…….

Dole gumba la mzazi/mlezi

9.5 Assent form

TITLE: ISONIAZID PREVENTIVE THERAPY UPTAKE AND FACTORS ASSOCIATED WITH IPT USE AMONG HIV POSITIVE CHILDREN IN DAR-ES-SALAAM

Hello, I am Dr Emilia Karugaba, a resident in Paediatrics and Child Health researching Isoniazid Preventive Therapy uptake among children attending paediatrics CTC clinics at Dar es Salaam.

A research is a way to learn about people and if you decide you want to be a part of this study, you and/or your caregiver will be asked a few questions. If you do not want to be in this research study, you will continue to receive the treatment and care you will need.

Your documents will not have your identity on it and whatever information you give us will be kept confidential.

You do not have to be in this study if you do not want to. If you decide to stop after we begin, that is okay too.

If you decide you want to be in this study, please sign your name.

I, ---------- want to be in this research study.

---------- ----------

Sign your name here Date

9.6 Fomu ya ridhaa ya mtoto

Namba ya utambulisho----------

KICHWA CHA HABARI: MATUMIZI YA DAWA YA ISONIAZID YA KUZUIA MASHAMBULIZI YA KIFUA KIKUU KWA WATOTO WENYE VVU DAR ES SALAAM

Habari, naitwa Dkt Emilia L Karugaba, mwanafunzi wa shahada ya uzamili ya udaktari wa watoto katika Chuo cha Sayansi Shirikishi cha Muhimbili.

Nafanya utafiti kuangalia kiwango cha utumiaji wa dawa ya Isoniazid katika kujikinga na mshambulio wa kifua kikuu. Nitakupa maelezo nakukualika kushiriki katika utafiti huu, kabla ya kuamua unaweza kuongea na mtu yeyote kupata maelezo ya kutosha, kama kuna maneno hujaelewa vizuri unaweza kumuuliza daktari au muuguzi yeyote.

Utafiti ni njia ya kujifunza juu ya watu na ikiwa unaamua unataka kuwa sehemu ya utafiti huu, wewena/au mlezi wako ataulizwa maswali machache. Ikiwa hutaki kuwa katika utafiti huu, utaendelea kupata matibabu na huduma unayohitaji. Nyaraka hazitakuwa na utambulisho wako juu yake na taarifa yoyote unayotoa itachukuliwa siri. Huna ulazima wakuwa katika utafiti huu ikiwa hutaki. Ikiwa utaamua kuacha baada ya kuanza, hiyo ni sawa pia.

Ikiwa unaamua unataka kuwa katika utafiti huu tafadhali saini jina lako.

Mimi, ---------- nataka kuwa katika utafiti huu.

---------- ----------

Andika jina lako hapa Tarehe

10. ETHICAL CLEARANCE APPROVAL.

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR OF POSTGRADUATE STUDIES

P.O. Box 65001
DAR ES SALAAM
TANZANIA
Web: www.muhas.ac.tz

Tel G/Line: +255-22-2150302/6 Ext. 1015
Direct Line: +255-22-2151378
Telefax: +255-22-2150465
E-mail: dpgs@muhas.ac.tz

Ref. No. DA.287/298/01A/

28th October, 2019

Dr. Emilia L. Karugaba
MMed. Paediatrics and Child Health
MUHAS.

RE: APPROVAL OF ETHICAL CLEARANCE FOR A STUDY TITLED: "FACTORS INFLUENCING UPTAKE OF ISONIAZID PREVENTIVE THERAPY AMONG CHILDREN LIVING WITH HIV ATTENDING HIV CLINICS IN DAR ES SALAAM: A CROSS-SECTIONAL STUDY"

Reference is made to the above heading.

I am pleased to inform you that, the Chairman has, on behalf of the Senate, approved ethical clearance for the above-mentioned study. Hence you may proceed with the planned study.

The ethical clearance is valid for one year only, from **25th October, 2019 to 24th October, 2020.** In case you do not complete data analysis and dissertation report writing by **24th October, 2020,** you will have to apply for renewal of ethical clearance prior to the expiry date.

Dr. Emmanuel Balandya
ACTING: DIRECTOR OF POSTGRADUATE STUDIES

cc: Director of Research and Publications
cc: Dean, School of Medicine, **MUHAS**