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Factors associated with uptake of isoniazid preventive therapy among children living with HIV in Mwanza region, Tanzania: a cross-sectional study

Ally Tuwa[1,2], David Okia[1], Ritah Nantale[1*], Hyasinta Jaka[2,3,4], Jimmy Patrick Alunyo[1], David Mukunya[1], Joseph KB Matovu[1,5] and Dan Kibuule[6]

Abstract

Background Tuberculosis (TB) is a leading cause of death among children living with HIV (CLHIV). Isoniazid preventive therapy (IPT) reduces the incidence of TB by 70% and mortality by 50% among CLHIV. However, in most developing countries including Tanzania, the uptake of IPT is suboptimal, below the 90% WHO-global uptake target. We assessed the factors associated with IPT uptake among CLHIV in Mwanza region, Tanzania.

Methods This was a multicenter facility-based cross-sectional study among CLHIV aged 1 to 10 years in seven districts of Mwanza region, Tanzania from 1st November 2021 to 20th January 2022. Data were collected using a structured interview-administered questionnaire including information on children and caregivers' demographics, caregivers' health related information and children's clinical information. Our outcome variable was uptake of IPT, defined as initiation on IPT either during the time of the study or within past three years before this study We conducted modified Poisson regression to assess the association between IPT uptake and selected exposures in Stata version 15.0.

Results A total of 415 CLHIV were enrolled, the median age of the children was 7 years (Interquartile range: 5–8). The uptake of IPT was 91% ($n=377$). The majority of children's caregivers were HIV positive (86%, $n=387$) and were aware about IPT (63.6%, $n=264$). Factors associated with IPT uptake included; having an employed caregiver [Adjusted Prevalence Ratio (aPR): 1.06 95% Confidence Interval (CI): 1.00-1.13] and attending the ART clinic every month [aPR: 1.00; 95% CI: 0.87–1.00] .

Conclusions The uptake of IPT uptake among CLHIV in Mwanza, Tanzania exceeds the global WHO-target of ≥ 90%. Monthly ART clinic visits could be essential in promoting IPT uptake among CLHIV.

Keywords Children, HIV, Isoniazid preventive therapy, Tanzania, Tuberculosis

*Correspondence:
Ritah Nantale
ritahclaire24@gmail.com

Full list of author information is available at the end of the article

Background

Children living with HIV are 18 times more likely to develop active tuberculosis (TB) disease than people without HIV [1]. This is a major public health concern, given that TB is a leading cause of death among people living with HIV [2, 3]. A co-infection of HIV with TB is associated with poor prognosis in children [2]. In 2019, the World Health Organization (WHO) estimated that over 1.2 million children (children aged less than 15 years) fell ill with TB globally, accounting for 12% of all incident cases [1]. In 2020, over 215 000 people including children died of HIV-associated TB globally [4]. Tanzania is among the 30 WHO-identified high TB burden countries, an estimated TB incidence rate of 237 cases per 100,000 population was reported in 2019 with 54% (74,067) of the cases notified [1, 5].

The WHO recommended the roll-out of Isoniazid preventive therapy (IPT) as a chemoprophylaxis to reduce the risk of the TB among high risk populations including children living with HIV [6, 7]. In high TB burden countries, it is recommended that children living with HIV should be initiated on antiretroviral therapy (ART) as well as IPT to prevent pediatric TB [8]. In fact, ART alone reduces the incidence of TB by up to 65% [9], but the combination of ART and IPT reduces the overall incidence and mortality from TB by up to 90% due to the synergism between them [10]. In children living with HIV, IPT reduces mortality by 50% and incidence by more than 70% in high TB-burden countries [11–13].

However, the uptake of IPT (i.e., enrolment and completion) in most developing countries with a high TB burden remains below the WHO recommended target of 90% [14]. Studies conducted in Ethiopia and Nigeria reported a low IPT coverage among people living with HIV [15, 16]. The factors for the low uptake of IPT included stock-outs of isoniazid, poor adherence, anticipation of isoniazid resistance, pill burden, and adverse effects [15, 16]. In Tanzania, IPT use in children living with HIV was rolled-out in 2009, and scaled up in 2011 to 10 regions including Mwanza [17]. In Tanzania, including Mwanza Region, there is paucity of data regarding IPT uptake among children living with HIV. We assessed the factors associated with IPT uptake among children living with HIV in Mwanza, Tanzania to inform the national and global TB strategies towards ending TB by 2030.

Methods

Study design and setting

This was a multicenter facility-based cross-sectional study involving quantitative methods of data collection from 1st November, 2021 to 20th January, 2022. The study was conducted in the Mwanza region among seven districts including Nyamagana, Ilemela, Magu, Misungwi, Sengerema, Kwimba and Buchosa. The study included seven Care and Treatment Clinic (CTC)/ Antiretroviral therapy (ART) centers at the district level as a representative of the Mwanza region based on the predetermined selection criteria.

Study population and sample

All children living with HIV aged 1 to 10 years registered for care and their respective caregivers in the selected ART centers. Children living with HIV (CLHIV) aged 1 to 10 years registered for care from 1st January 2019 up to 20th January 2022 eligible for IPT initiation were included whereas CLHIV diagnosed with TB and contraindicated to IPT as per national guidelines for example severe liver disease or known adverse reaction to isoniazid were excluded in this study.

The sample size of children living with HIV included in this study was 415 based on the Cochran formula for a definite population. A stratified random sampling method was used to include the proportion of CLHIV to be recruited at each health facility (Table 1).

Data collection procedure

Data were collected using a structured administered questionnaire designed in Kobo Toolbox (https://www.kobotoolbox.org/). The first part of the questionnaire included socio-demographic information of caregivers and their health-related information. The second part of the questionnaire was designed into three components including children's socio-demographics, clinical information and medical records. Study questionnaires were translated to Swahili language to ensure more accurate responses. One trained health care provider was hired as

Table 1 Shows the number of participants enrolled into the study at each health facility of the district

District	Health facility	Registered CLHIV	Enrolled study participants
Nyamagana	Baylor	593	218
Sengerema	Sengerema D/H	160	60
Magu	Magu D/H	99	36
Ngudu	Kwimba D/H	85	31
Buchosa	Nyehunge H/C	80	30
Ilemela	Buzuruga H/C	60	22
Misungwi	Misungwi D/H	50	18
Total		1127	415

a research assistant at each selected health care facility to capture the raw data from caregivers of children living with HIV eligible to IPT initiation during the day of the HIV clinic visit from 1st November, 2021 to 20th January 2022.

Measures

The outcome variable was uptake of IPT among children living with HIV, defined as children living with HIV who had been initiated on IPT at either the time of the study or within past three years before the conduction of this study. Children who had not started on IPT at the time of the study were considered as no uptake of IPT. The exposure variables were caregiver's characteristics including age, sex of the caregiver, relationship to child, marital status, educational level, employment status, HIV status of the caregivers, history of IPT use (yes vs. no) and awareness about IPT (yes vs. no).

Children characteristics including age, sex of the child, child on ART (Child receiving ART or not as per clinic records), clinic visit schedule, WHO clinical HIV stage and latest HIV viral load. Latest HIV viral load was categorized into suppressed, non-suppressed and not documented. Viral suppression was defined as having less than 1000 copies of HIV per milliliter of blood as per the child's latest viral load report.

Data analysis

Categorical data were summarized using frequencies and percentages and continuous data using means (SD) or medians (IQR) as appropriate. We used modified Poisson regression analysis with robust standard errors to perform multivariable analysis. Variables with a p-value < 0.2 at the bivariable level and those known to be associated with IPT uptake from literature were entered into the multivariable model to estimate prevalence ratios between selected exposures and IPT uptake. Statistical significance was set at a p-value less than 0.05. Data were analyzed in Stata version 15.0.

Results

Characteristics of caregivers and children living with HIV

Of the 415 CLHIV enrolled in the study, the majority of their caregivers were female (89.4%, n=371), were biological parents (84.8%, n=352), and aged 30 to 50 years (65.1%, n=270). Most caregivers were not married (60.7%, n=252), attained primary school (47.9%, n=199) and were unemployed (64.3%, n=267). The majority of the caregivers were HIV positive (86.5%, n=387), 63.6% (n=264) were aware about isoniazid preventive therapy (IPT), and 54.0% (n=224) had used IPT in the past.

The median age of enrolled children was 7 years (IQR 5–8), more than two thirds (76.1%, n=316) of the children were in the age group of 5–10 years and 51.1% (n=212) were male. Majority of the children were on ART (97.1%, n=403), attended ART clinic visits monthly (98.8%, n=410) and had a suppressed viral load (71.8%, n=298). More than a quarter (28.9%, n=120) were in WHO clinical stage 3 of HIV. The details are in Table 2.

Uptake of isoniazid preventive therapy among children living with HIV in Mwanza region, Tanzania

A total of 377 out of the 415 CLHIV eligible to IPT (90.8%) were found to be either on IPT at the time of the study or received IPT in the past 3 years. Majority [79.8% (331/377)] CLHIV had received IPT 3 years ago.

Caregiver factors associated with uptake of isoniazid preventive therapy among children living with HIV in Mwanza region, Tanzania

Children with employed caregivers were 1.06 times more likely to be on IPT as compared to their counterparts. [Adjusted Prevalence Ratio (APR): 1.06; 95% CI: 1.00-1.13] (Table 3).

Child related factors associated with uptake of isoniazid preventive therapy in Mwanza region, Tanzania

Attending the ART clinic on a monthly basis [APR: 1.0; 95% CI: 0.87–1.00] was associated with uptake of IPT (Table 4).

Discussion

In this study, we assessed the level of isoniazid preventive therapy (IPT) uptake and associated factors among children living with HIV in Mwanza, Tanzania. The observed IPT uptake (91%) was above the global WHO-target of 90%. This finding is comparable to other studies conducted in Gambia [18] and Rwanda [19], that reported uptake rates of 91% and 89% respectively. The integration of IPT into the programmatic delivery of healthcare might explain the high uptake reported in our study. Further, the collaborative efforts from partners, less or non-side effect of IPT, availability of training for health workers and guidelines at health facilities may also explain the high uptake in this study.

However, the IPT uptake observed in this study (91%) is higher than the 26.8%, 53.2% and 64.3% in South Africa, Kenya and Ethiopia respectively [20–22]. The variation in uptake could be due to the different study designs used in the various studies.

Children with employed caregivers were more likely to be on IPT than their counterparts. This current study is the first study to report this finding. This could be related to the ability of employed caregivers to meet out of pocket costs including transport costs to meet clinic visits consistently compared to their counterparts and having increased perceived benefits of IPT uptake among children living with HIV.

Table 2 Characteristics of caregivers and CLHIV ($n=415$)

Caregivers		Children	
Characteristic	**Frequency (%)**	**Characteristic**	**Frequency (%)**
Age in years	*Median 33 (IQR 28–38)*	*Age in years*	*Median 7 (IQR 5–8)*
< 30	138 (33.3)	< 5	99 (23.9)
30–50	270 (65.1)	5–10	316 (76.1)
> 50	7 (1.7)		
Sex		**Sex**	
Female	371 (89.4)	Female	203 (48.9)
Male	44 (10.6)	Male	212 (51.1)
Relationship to the child		**Child on ART**	
Parents relationship	352 (84.4)	Yes	403 (97.1)
Other relationship	63 (15.2)	No	12 (2.9)
Marital status		**Clinic visits (months)**	
Not married	252 (60.7)	Monthly	410 (98.8)
Married	163 (39.3)	Every after 3 months	5 (1.2)
Education		**WHO clinical stage**	
No formal education	43 (10.4)	Stage 1	106(25.5)
Primary	199 (47.9)	Stage 2	82 (19.8)
Secondary	165 (39.8)	Stage 3	120 (28.9)
Higher education	8 (1.9)	Stage 4	107 (25.8)
Employment status		**Latest high viral load**	
Not employed	267 (64.3)	Suppressed	298 (71.8)
Employed	148 (35.7)	Non suppressed	38 (9.2)
HIV status of the caregiver		Not documented	79 (19.0)
Negative	56 (13.5)		
Positive	355 (86.5)		
Unknown	4 (1.0)		
History of IPT use			
Yes	224 (54.0)		
No	191 (46.0)		
Aware of IPT			
Yes	264 (63.6)		
No	151(36.4)		

We also found out that children who were scheduled to attended the clinic on a monthly basis were more likely to be on IPT as compared to children who attended the clinic every three months. Monthly visits may allow close monitoring of ART adherence, opportunistic infections and IPT uptake. However, a study by Mwangi et al., in Kenya revealed that frequency of clinic visits was not associated with IPT uptake [22].

Strengths and limitations of the study

Our study is the first of its kind to be conducted in Mwanza, Tanzania including all the districts thus, it provides a distinctive picture regarding IPT uptake among CLHIV in Mwanza region. The study was done at both public and private facilities (Baylor Clinic Centre) to get the true picture of IPT uptake in both settings.

However, we could not rule out selection bias of the health facilities because in every district of Mwanza only one health facility was selected, therefore the results may not be correctly representing the true picture of all health facilities of Mwanza. Although this was minimized by applying sampling techniques namely stratified and systematic random sampling.

Furthermore, some of the children' clinical characteristics data were captured from their Care and Treatment Clinic 2 file which is liable to misclassification bias, though this was minimized by clearly defining the study variables.

For information captured from patient file, some HIV viral load data were missing which could result in overestimation or underestimation of result.

Conclusion

This study demonstrated a high IPT uptake among children living with HIV in relation to the set global uptake target. Monthly ART clinic visits could be essential in promoting IPT uptake among CLHIV.

Table 3 Caregiver related factors associated with uptake of isoniazid preventive therapy among children living with HIV in Mwanza region, Tanzania

Variable	Isoniazid Preventive Therapy (IPT) uptake		Crude PR	*p*-value	Adjusted PR	*p*-value
	Yes, n (%)	No, n (%)				
Sex						
Male	43(11.4)	1(2.6)	1		1	
Female	334(88.6)	37(97.4)	0.92(0.87–0.97)	0.004*	0.95 (0.89-1.00)	0.066
Age (years)						
< 30	128(33.9)	10(26.3)	1			
30–50	243(64.5)	27(71.1)	0.97(0.91–1.03)	0.336		
> 50	6(1.6)	1(2.6)	0.92(0.68–1.26)	0.614		
Educational level						
Informal	37(9.8)	5(13.2)	1			
Higher	9(2.4)	0(0.0)	1.13(1.02–1.27)	0.026		
Secondary	152(40.3)	13(34.2)	1.02(0.91–1.15	0.735		
Primary	179(47.5)	20(52.6)	1.04(0.93–1.18)	0.465		
Marital status						
Unmarried	229(60.7)	23(60.5)	1			
Married	148(39.3)	15(39.5)	0.99(0.94–1.03)	0.979		
Employment status						
Unemployed	237(62.9)	30(78.9)	1		1	
Employed	140(37.1)	8(21.1)	1.07(1.01–1.13)	0.030	1.06(1.00-1.13)	**0.046**
Relationship to the child						
Other relationship	55(14.6)	8(21.1)	1			
Parents relationship	322(85.4)	30(78.9)	1.05(0.95–1.15)	0.358		
HIV Status						
Negative	50(13.3)	6(15.8)	1			
Positive	324(85.9)	31(81.6)	1.02(0.93–1.13)	0.655		
Unknown	3(0.8)	1(2.6)	0.84(0.47–1.49)	0.551		
Aware of IPT						
No	134(35.5)	17(44.7)	1			
Yes	243(64.5)	21(55.3)	1.04(0.97–1.11)	0.285		
History of IPT use						
No	178(47.2)	13(34.2)	1		1	
Yes	199(52.8)	25(65.8)	0.95(0.89–1.01)	0.120	0.96(0.90–1.02)	0.179

PR: prevalence ratio; CI: confidence interval

Table 4 Child related factors associated with uptake of isoniazid preventive therapy in Mwanza, Tanzania

Variable	Isoniazid Preventive Therapy (IPT) uptake		Crude PR	*p*-value	Adjusted PR	*p*-value
	Yes, n (%)	No, n (%)				
Age (years)						
< 5 years	87(23.1)	12(31.6)	1		1	
≥ 5 years	290(76.9)	28(68.4)	1.04(0.96–1.13)	0.290	1.04(0.96–1.13)	0.362
Gender						
Male	185(49.1)	18(47.4)	1			
Female	192(50.9)	20(52.6)	0.99(0.93–1.06)	0.841		
HIV WHO clinical stage						
Stage 1	94(24.9)	12(31.6)	1		1	
Stage 2	74(19.6)	8(21.1)	1.02(0.92–1.12)	0.728	1.01(0.92–1.12)	0.830
Stage 3	113(30.0)	7(18.4)	1.06(0.98–1.15)	0.148	1.06(0.97–1.15)	0.185
Stage 4	96(25.5)	11(28.9)	1.01(0.92–1.11)	0.807	1.00(0.92–1.11)	0.855
Clinic visits (months)						
After 3 months	5(1.3)	0(0.0)	1		1	
Every month	372(98.7)	38(100.0)	0.91 (0.88–0.94)	< 0.001	1.00(0.87-1.00)	**< 0.001**
Latest high viral load						
Non suppressed	35(11.3)	3(13.6)	0.98(0.89–1.08)	0.743		
Suppressed	279(89.7)	19(86.4)	1			

Abbreviations

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
CLHIV	Children living with HIV
CTC	Care and Treatment Clinic
HIV	Human immunodeficiency virus
IPT	Isoniazid preventive therapy
LTBI	Latent TB infection
MOHCDGEC	Ministry of Health, Community Development, Gender, Elderly, and Children
NTP	National TB programme
PLHIV	People living with HIV
TST	Tuberculin skin test
WHO	World Health Organization

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Author contributions
AT, DO, HJ, RN and DK conceived the idea, drafted part of the manuscript, and interpreted the results. DM, JPA and JKBM drafted part of the manuscript, interpreted results, reviewed and drafted the subsequent versions. All authors have read and agreed to the final version of the manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Ethical approval and consent to participate
We obtained ethical approval from the research and ethical review committee (REC) of Mbale regional referral hospital Uganda, REC approval number MRRH-2021-79 and CREC Catholic University Health and Allied Science Tanzania, approval number CREC/503/2021. Permission to conduct the study was also requested from the regional medical officer (RMO), district medical officer (DMO), medical officer in charge (MOI) and the ART centre in charge. Confidentiality and privacy for study participant's information was maintained throughout the study. Informed consent was obtained from study participants and from the legal guardians of the participants below 8 years of age. All methods were carried out in accordance with relevant guidelines and regulations.

Author details
[1]Department of Community and Public Health, Busitema University Faculty of Health Sciences, Mbale, Uganda
[2]Department of Community and Research, Mwanza College of Health and Allied Sciences- MWACHAS, P.O.BOX 476, Mwanza, Tanzania
[3]Department of Internal Medicine, Gastroenterology and Hepatology Unit, Catholic University of Health and Allied Sciences-CUHAS, P.O.BOX 1464, Bugando, Mwanza, Tanzania
[4]Community Health and Development Foundation-CHADF, P.O.BOX 476, Buyombe, Ilemela, Mwanza, Tanzania
[5]Department of Disease Control and Environmental Health, Makerere University School of Public Health, P.O. Box 7072, Kampala, Uganda
[6]Department of Pharmacology and Therapeutics, Busitema University Faculty of Health Sciences, Mbale, Uganda

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