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BMJ Open

Incidence and predictors of Tuberculosis among children on antiretroviral therapy in Amhara region, Ethiopia

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Complete List of Authors:	Mekonnen, Gebrehiwot ; Debre Tabor University, Department of Pediatrics and Child Health Nursing Legesse, Bruck Tesfaye; Wollega University, Department of Pediatrics and Neonatal Nursing Baye, Fikadie; Debre Tabor University, pediatric and child health nursing Wondie, Wubet ; Ambo University College of Medicine and Health Science, Department of Pediatrics and Child Health Nursing
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8	3	Gebrehiwot Berie Mekonnen1*, Bruck Tesfaye Legesse2, Fikadie Dagnew Baye1, and Wubet
9 10 11	4	Tazeb Wondie ³
12 13	5	Authors' affiliations:
14 15	6	¹ Department of Pediatrics and Child Health Nursing, College of Health Sciences, Debre Tabor
16 17	7	University, Debre Tabor, Ethiopia
18 19	8	² Department of Pediatrics and Neonatal Nursing, School of Nursing and Midwifery, Institutes of
20	9	Health Science, Wollega University, Nekemte, Ethiopia
21 22	10	³ Department of Pediatrics and Child Health Nursing, College of Medicine and Health Science,
23 24	11	Ambo University, Ambo, Ethiopia
25 26	12	* Corresponding Author, Address: geberehwot2004@gmail.com P.O Box: 272, Debre Tabor,
20 27 28	13	Ethiopia
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Abstract:

Introduction: Tuberculosis (TB) continues to be a significant public health issue, particularly in low- and middle-income countries. Globally, the end-TB strategy targets an 80% reduction in TB incidence by 2030. Despite this strategy, there is limited evidence on the incidence of TB among HIV-infected children in the study area after the test and treatment strategies in Amhara region. Hence, this study aimed to assess the incidence of TB and its predictors among HIV-infected children receiving antiretroviral therapy in the Amhara region.

Methods: A multicenter institution-based retrospective follow-up study was conducted on 421 HIV-infected children receiving antiretroviral (ART) treatment from July 2014 to March 2022. The study participants were selected using a simple random technique. National antiretroviral intake and follow-up forms were utilized to gather data through the KoBo Toolbox. STATA version 17 was used for data analysis. The Kaplan-Meier curve was applied to estimate failure time, and the log-rank test was employed for comparison among groups of predictors. To find TB predictors, Gompertz regression models, both bivariable and multivariable, were constructed. Ultimately, a 95% confidence interval-adjusted hazard ratio was calculated, and variables with a p-value less than 0.05 were considered statistically significant.

Results: A total of 421 children with a record completeness rate of 97.9% were analyzed in the study. The tuberculosis incidence rate in children on ART was 2.16 (95% CI: 1.52, 3.05) per 100 child-year observations. Those children who were on baseline anemic [AHR: 3.83 (95% CI: 1.46, 10.04)], never took TB preventive treatment (TPT) [AHR: 3.78 (95% CI: 1.44, 9.94)], wasted children [AHR: 2.53 (95% CI: 1.19, 5.38)], and not initiated antiretroviral therapy within seven days [AHR: 2.35 (95% CI: 1.15, 4.78)] were the significant predictors.

Conclusion: The incidence of TB in children on ART was relatively high. HIV-positive children presenting with anemia, who never took TPT, wasted, and late initiation of ART were prone to the occurrence of TB. Therefore, needs emphasis on prompt treatment of anemia and TB preventive therapy, counseling on nutritional improvement, and timely initiation of ART to avert TB.

Keywords: Antiretroviral therapy; HIV-infected children; incidence; predictors; test and treat Tuberculosis

53 Introduction

Globally, tuberculosis (TB) is a primary cause of morbidity and mortality, and it's a global emergency in all regions and affects every country in the world. Globally, TB incidence varies, with 30 high-burden countries accounting for 87% of cases [1]. Children and young adolescents (age below 15 years) account for 1.25 million (12%) of the total TB incidence across the globe every year [2].

TB remains an important public health problem, particularly in low and middle-income countries (LMIC) [3]. The risk of developing this global infectious disease is 18 times higher among HIVinfected individuals [4]. In addition to increasing the suffering of infected individuals, it remains the second leading cause of death from infectious disease, and the risk of death is threefold higher among HIV-infected individuals worldwide [3, 4].

Recently, the global occurrence of TB mortality in children increased significantly, which was 214,000 in 2023. Each day, 600 children lost their lives to this preventable disease. Approximately 31,000 deaths are related to people with HIV [1, 5]. In Sub-Saharan African countries, the HIV-TB burden has increased, despite the test and-treat policy in this region. The incidence rate of tuberculosis among HIV-infected children is 3.42 per 100-person year [6]. This problem has a significant economic burden in low- income ad middle- income countries [3]. Like in other Sub-Saharan countries, in Ethiopia, tuberculosis is a significant health problem among HIV-infected children, with an incidence of 4.33 per 100-person year [7].

The occurrence of tuberculosis (TB) among children on ART treatment is 24.2% to 32% in Nigeria [8-10], and 15.2% in Ethiopia [11], while the incidence of TB among children with HIV varies from 0.83 to 2.3 in China [12], 7 per 1000 person-years in Thailand [13], 4 in South Africa [14], , 2 to 2.63 in Ethiopia [15-17], and 17.4 in East Africa [18].

Some factors contribute to the causes of TB among children on ART treatment, such as extrapulmonary TB, severe immunosuppression, age less than two years, and WHO HIV clinical stage
[19-21]. Underweight [21], a low Cluster of Differentiation 4 (CD4) () count, anemia [22], and
virological failure [23] also contribute to the occurrence of TB among children on ART treatment.
To better understand the variety of contexts and the application of new approaches in factors that

81 affect the risk of tuberculosis (TB) in children living with HIV, additional investigation is 82 necessary.

The achievement of Ethiopia's Sustainable Development Goals (SDG s) and the end-TB strategy targets established by the World Health Organization (WHO) and the United Nations, which aim to reduce tuberculosis cases by 80% and deaths from tuberculosis by 90%, provide support for this study [2, 24]. The political declaration of the UN high-level meeting on TB held in WHO plans to reach TB Preventive Treatment (TPT) at least 90% of people with HIV in 2027 [25].

Ethiopia has adopted a test-and-treat strategy since June 10, 2014, for all children initiation of ART regardless of CD4 cell count and WHO clinical staging aiming at reduction of HIV-related mortality and morbidity [26]. Despite this intervention, there is paucity of evidence of the overall incidence of TB in children enrolled in the Amhara region after the test and treat strategy. In addition to previous studies, this finding covers a wide range of public institutions, and in this study, rapid initiation of ART and doultegravir (DTG)-contained drugs were incorporated as independent variables to the determine incidence of TB. Timely and recent evidence is very crucial. Therefore, by incorporating these new variables and new strategy needs further investigation. The finding will provide input for policy-makers and decision-makers on HIV/AIDS care and support at various levels. Therefore, this study aimed to assess the incidence of TB and its predictors among HIV-infected children enrolled in ART in the Amhara Region.

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99 Methods

⁸ 100 Study Design, setting, and period

A multicenter institution based retrospective follow-up study was conducted among HIV-positive
children enrolled at Amhara region comprehensive specialized hospitals from July 2014 to March
2022. The Amhara region is located in the Northwestern, Northeastern and North-central parts of
Ethiopia, with an estimated area of 159,173.66 square kilometers. The most recent estimated
population in this region is 30,848,988 [27]. In this region, there are 81 Hospitals; among those,
eight are comprehensive specialized and teaching hospitals, the University of Gondar, TibebeGhion, Felege Hiwot, Debre Markos, Debre Tabor, Dessie, Woldia, and Debre Birhan.

108 Those hospitals have been providing ART care and support as part of the National AIDS Control
109 Program. Among the total number of Comprehensive Specialized Hospitals, seven were included

in the study area, except Tibebe-Ghion, due to the inadequate study population. A total of 1095 children were newly enrolled in HIV care in the Amhara region from July 2014 to March 2022.

Population and eligibility

All HIV-positive children ages less than 15 who were enrolled in the pediatric HIV care clinic in Amhara Region Comprehensive Specialized Hospitals and had at least one month of ART follow-up were the source population. HIV-positive children aged less than 15 years who were enrolled in the pediatric HIV care clinic in Amhara Region between July 2014 and March 2022 were the study population. Children with HIV who already had TB before starting ART and records with incomplete baseline information (CD4 count, WHO staging, hemoglobin level, weight, and height) and unknown dates of ART initiation and TB occurrence were excluded from the study.

Sample size determination

The sample size was calculated using common significant predictor variables (height for age, WHO clinical staging, and ART adherence level). STATA version 17 and the cox proportional hazard model were used for sample size determination through the following assumptions: $Z\alpha/2$ = is the critical value of a standard normal distributed variable at 5% significance level = 1.96; Z $\beta/2$ = is the critical value of a standard normal distributed variable at 20% = 0.84; the probability of an event was 0.167 [28]; and the probability of withdrawal was 0.15 using an adjusted hazard ratio (AHR). (Supplementary table 1)

Sampling procedures, and sampling technique

From the calculated sample sizes, the largest sample size (430) was selected as a sample for this study. The sample was allocated proportionally to those comprehensively specialized hospitals in the Amhara region, and records were selected using simple random techniques. (Supplementary Figure 1:)

Variables of the study

The outcome variable for this study was the occurrence of TB during the follow-up period. The independent variables were socio-demographic characteristics: age, sex, residence, current parent's status, educational status of the caregiver, HIV disclosure status, and marital status of the caregiver. Baseline clinical, nutritional, and laboratory characteristics: CD4 count, WHO clinical staging, hemoglobin level, anthropometric indices, previous OIs, functional and developmental

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status. ART and medication-related characteristics: baseline ART regimen, DTG containing ART drugs, presence of regimen change, level of ART adherence, TPT, CPT, ART side effects, initiation of ART. **Operational definition of the variables** Events: The occurrence of TB among HIV-infected children during the follow-up period at any time after enrollment in the pediatric HIV care clinic, as confirmed by a health care professional. **TB** cases were diagnosed based on the national TB diagnosis guideline, using sputum or gastric aspirate microscopy, chest X-ray examination, and/or histopathology. Children, who were lost to follow-up, dropped out, transferred out, died due to any causes, or completed the study period before developing TB considered as a censored. **TB-free probability time** was considered between ART starting and the TB diagnosis date. Wasting: if the weight for height (WFH) Z-score is less than -2 SD for less than five years, or if the body mass index (BMI) for age Z-score is less than -2 SD for greater than five years [29]. The level of adherence to ART: good adherence is reported with compliance equal to or greater than 95% or \leq 3 missed doses per month as documented by the ART health personnel; fair reflected 85–94% compliance and between 4 and 8 missing doses per month) as documented by the ART health personnel; and poorly reflected less than 85% compliance or > 9 missed doses per month) as documented by the ART health personnel [29]. **Rapid initiation of ART:** ART initiation care and support on the same day of HIV confirmation or within seven days [30]. Anemia was defined as having a hemoglobin level of less than 10 mg/dl [31]. Data collection tool and procedures The data were collected retrospectively from the ART intake form, follow-up form, and children's charts using the data extraction tool adopted from Ethiopian ART guidelines newly registered at ART clinics during the period of July 2014 to March 2022 [29]. Data was extracted for one month, from May 17 to June 15, 2022. The variables consist of socio-demographic, clinical, laboratory, ART, and medication-related variables. Data were collected by seven bachelor's degree nurses

who had smartphones and who were familiar with the ART follow-up and taking basic ART training.

Data quality control

The data extraction tool was pretested on 5% of the sample size before the actual data collection period at the University of Gondar (UoG) Comprehensive Specialized Hospital. Moreover, one-day onsite training was given on how to review ART follow-up and medical records, data collection methods, and the objective of the study for data collectors and supervisors. Data were collected using the KoBo toolbox, which was prepared with relevant restrictions by trained nurses working in Hospitals. Besides, the data collector and principal investigators carefully monitored the entire data collection process and daily submission report.

Data processing and analysis

The KoBo toolbox was used, which was then exported and imported into STATA version 17 statistical software for final analysis. Additionally anthropometric indices were created using the WHO anthro and WHO anthroPlus software. To describe the data, descriptive statistics including mean (\pm SD), percentage, and frequency were employed. The Variance inflation factor (VIF) was used to check the association between predictor variables; the average VIF was found to be 1.18, it indicates no significant multicollinearity.

A separate graph of Kaplan-Meier survival functions and the log-rank test were estimated for each categorical variable to compare survival between different exposure groups. The proportional hazard assumption (PHA) was checked using both graphical and statistical global tests and revealed that the PHA was satisfied. The log-likelihood and Akaike Information Criteria (AIC) were applied to select the best-fitted model, and a model with a minimum AIC was considered the best-fitted model. Based on this, the Gompertz regression model with the lowest value (AIC = 236.02) was the best-fitted model. In addition, the goodness-of-model fitness was also checked using the Cox-Snell residual test. Variables having a p value less than 0.25 in the bivariable analysis were fitted into the multivariable Gompertz regression model. A hazard Ratio with a 95% CI was used to determine the strength of the association. Variables with a p<0.05 in multivariable analysis were considered statistically significant.

Page 9 of 27

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To handle and manage missing data, multiple imputations using multivariable chained equations (MVCE) were carried out to handle and manage missing data. The variables missing at random (MAR) are clarified by the "Little test" results for continuous variables and graphical patterns for categorical variables, making the application of multiple imputations straightforward. Furthermore, sensitivity analysis was performed utilizing both descriptive and inferential statistical techniques to confirm if a significant difference was detected between the outputs of the original and imputed data.

201 Patient and public involvement

Patients and public were not directly involved in the design, conduct and dissemination of thisstudy.

Results:

205 1. Socio-Demographic characteristics

A total of 430 medical records of HIV-infected children on ART were reviewed. Of these, 421 (97.9%) were included in this study, and the remaining percent were excluded from the analysis due to data incompleteness. The mean (SD) age of the study participant was 7.58 (\pm 4.02) years; one-third was found in the age group of 5-9 years. Nearly two-thirds (58.43%) were male, and 70% were from urban areas. (**Table 1:**)

211 Table 1: Socio-demographic characteristics of incidence of Tuberculosis among HIV-

212 infected children on ART at Amhara Regional State Comprehensive Specialized Hospitals,

Ethiopia, 2022 (n=421) Variables Categories Percentage (%) Frequency(n) Age <5 Years 28.98 5-9 Years 34.44 10-14 Years 36.58 Sex Female 41.57

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	Male	246	58.43
Residence			
	Rural	126	29.93
	Urban	295	70.03
Current parent status			
	Both parents alive	290	68.88
	One parent alive	113	26.84
	Both parents deceased	18	4.28
Educational Status of t	he caregiver		
	No formal education	144	34.2
	Primary	150	35.63
	Secondary	67	15.91
	Tertiary (College & above)	60	14.25
Marital status of the ca	aregiver		
	Married	228	54.16
	Unmarried	87	20.67
	Divorced	70	16.63
	Widowed	36	8.55
HIV status of the pare	nts		
	Non-reactive	158	37.53
	Reactive	263	62.47
Disclosure status the cl	hild		
	Yes	220	52.26
	No	201	47.74

2. Baseline clinical, laboratory, nutritional and ART medication related characteristics

At baseline, 79.9% of children were in WHO clinical stages I or II. The median CD4+ count was 421 (IQR: 403, 1017) cells/l, and one fifth (20.19%) had CD4+ below the threshold level. The median hemoglobin level was 12.3 (IQR: 10.7, 13.6) mg/dl, and 17.34% had less than 10 mg/dl hemoglobin level. Nearly 30% and 50% of children were wasted and stunted at baseline, respectively. Out of 421 HIV infected children, 296 (70.31%) had a good ART drug adherence level. More than two-thirds (63.42%) of children had never received TPT, and 45.13% of children never taken ART within seven days of its duration. (**supplementary table 2:**)

3. 3. Follow-up time and incidence of TB incidence

A total of 421 children followed from 1 to 89 months. The mean follow-up time was 42 months
(14.57 to 70.07 months). The total time at risk was 1484.75 child-year observations (CYO). New TB cases were observed in 32 (7.6%) children; the overall TB incidence rate was 2.16 (95% CI:
1.52, 3.05) per 100 CYO. (Supplementary figure 2:)

Page 11 of 27

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1 2		
3	232	The incidence rate of TB was 3.98 (95% CI, 1.99, 7.95) per 100 CYO in the six months of ART
4 5	233	initiation and decreased to 0.33 (95% CI, 0.05, 2.34) per 100 CYO after three years of ART
6 7	234	initiation. The cumulative probability of TB incidence at the end of two, four, and six years of the
8	235	study was 0.9636, 0.9309, and 0.9045, respectively. The incidence rate of TB was 8.09 (95% CI,
9 10	236	5.03, 13.01) per 100 CYO among anemic children, while it was 1.18 (95% CI, 0.7, 1.95) per 100
11 12	237	CYO among non-anemic children (Figure 1)
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Figure 1: Kaplan-Meier of TB free survival of anemic status (A), tuberculosis preventive therapy
(B), nutritional status (C), and initiation of antiretroviral therapy (D) main predictor variables
among children on ART in Amhara region comprehensive Specialized Hospitals

257 4. Model comparison

The proportional hazard assumption, semi-parametric, and parametric proportional hazard models were fitted to estimate the incidence of tuberculosis and its predictors among HIV-infected children in the Amhara region. The graphical test and global test (P-value = 0.2980) confirmed the proportional hazard assumption (PHA). The most fitted model was chosen using Akaike Page 13 of 27

BMJ Open

information criteria (AIC = 236.02), Bayesian information criteria (BIC = 304.74), and loglikelihood (-138.43). The results outperformed the Cox-proportional hazard and other parametric
models in all three comparison techniques. As a result, interpretations and conclusions were based
on the Gompertz model. (Supplementary table 3 :)

The Cox-Snell residual test checked the goodness of fit. (supplementary figure 3) The shared
frailty was estimated, (theta: 1.89e⁻⁰⁷), and the distribution of unmeasured variables is indifferent
between the comprehensive specialized hospitals.

7 269 **5.**

5. Predictors of incidence of Tuberculosis

In bi-variable parametric survival Gompertz regression: parental status of the care givers, educational status of the care givers, baseline of WHO clinical staging, CD4+ count, hemoglobin status, functional and developmental status, regimen change, ever taking TPT, ever taking CPT, ART adherence level, previous opportunistic infections, doultegravir (DTG) contained ART drug, wasting, and rapid initiation of ART were found to be significant predictors of TB among children in ART. In the final multivariable Gompertz regression model, only baseline hemoglobin, ever taking TPT, wasting, and rapid initiation of ART significantly increased the incidence of tuberculosis.

Anemic children had 3.83 times [AHR: 3.83 (95% CI: 1.46, 10.04)] higher risk of getting TB infections than those in non-anemic children. Likewise, the risk of developing TB for children who were not given TPT was 3.78 times [AHR: 3.78 (95% CI: 1.44, 9.94)] higher as compared with those who were given TPT at baseline. Additionally, the hazard of TB among children with wasted children at baseline was 2.53 times [AHR: 2.53 (95% CI: 1.19, 5.38)] more likely as compared to their well-nourished counterparts. Furthermore, children had late ART initiation 3.27 times [AHR: 3.27 (95% CI: 1.26, 8.46)] increased risk of developing TB compared to rapid initiation of ART (Table 3).

Table 3: Bi-variable and multivariable Gompertz cox-regression analysis of predictors of incidence of Tuberculosis among HIV-infected children on ART in Amhara Region Comprehensive Specialized Hospitals, Ethiopia, 2022 (n = 421).

Variables	Status		CHR (95% CI)	AHR (95% CI)	P value
	Event (n=32)	Censored (n=389)			
Parental stat	tus of the child				

Rapid Initiation	6 26	225 164	4.41(1.81, 10.74)	3.27(1.26, 8.46)	0.015		
Initiation of Antiretrovira	l thera	by					
No	26	326	0.46 (0.18, 1.14)	0.37 (0.13, 1.03)	0.059		
Yes	6	63	1	1			
Doultegravir (DTG) conta	ined dr	ugs					
Yes	15	83	3.43(1.71, 6.88)	1.32 (0.54, 3.19)	0.54		
No	17	306	1	1			
Previous opportunistic inf	ections						
Wasting	17	105	2.9(1.45, 5.81)	2.53(1.19, 5.38)	0.016		
No wasting	15	284	1	1			
Weight for height		1					
No	11	76	2.68(1.29, 5.57)	1.28(0.5, 3.27)	0.601		
Yes	21	324		1			
Ever taking cotrimoxazol	e preve	ntive the	erapy(CPT)				
No	25	129	7.55(3.26, 17.47)	3.78(1.44, 9.94)	0.007		
Yes	7	260		1			
Ever taking tuberculosis p	oreventi	ive treati	ment(TPT)				
No	17	190	1.63(0.81, 3.27)	0.77 (0.32, 1.87)	0.57		
Yes	15	199	1	1			
ART regimen change		122					
Sub-optimal	16	109	2.79(1.39, 5.59)	0.92(0.36, 2.4)	0.874		
Optimal	16	280			0.05:		
Adherence level of ART	1.0	000					
NO	16	122	2.39(1.19, 4.8)	1.66(0.77, 3.61)	0.196		
Yes	16	267			0.107		
Working and appropriate	motor	develop	mental status				
Yes	17	56	7.26(3.62, 14.56)	3.83 (1.46, 10.04)	0.006		
No	15	333		1			
Anemia							
Below threshold	11	74	2.89(1.39, 6.02)	1.59(0.59, 4.31)	0.357		
Above threshold	21	315			0.257		
CD4 cell count							
Stage III & IV	15	61	5.47 (2.73, 11.00)	1.71(0.62, 4.71)	0.299		
Stage I & II	17	328	1	1			
WHO Clinical staging							
Secondary and Tertiary	8	137	1	1			
Primary	15	117	2.05(0.87, 4.83)	0.97(0.33, 2.81)	0.96		
No formal education	9	135	1.27(0.49, 3.29)	0.72(0.25, 2.04)	0.53		
Educational status of the caregiver							
One or both parents dead	13	118	1.77 (1.88, 3.59)	0.8 (0.32, 2.02)	0.64		
	19	271	1	1			

Discussion

This study aimed to assess TB incidence rate and its predictors in children on ART in Amhara region comprehensive specialized Hospitals. In this study, HIV-infected children on ART were 2.16 (95% CI 1.52, 3.05) per 100 child-years observations(CYO), which is consistent with study conducted in Debre Markos 2.63 [32], in Northeast Ethiopia 2.0 [28], and Southern Ethiopia 2.6 per 100 CYO[33]. This finding is lower than study conducted in Northern Ethiopia [34], in Benishangul Gumuz region in Northwest Ethiopia [35, 36], in Adama Referral Hospital and Medical College [37], in South west Ethiopia [38], and in Tanzania [39]. This could be due to higher burden of tuberculosis in resource limited settings[40], and also might be due to the difference in sociodemographic and baseline clinical characteristics of the study participant. changes in the study period and setting.

However, our study is higher than studies conducted in New York City [41], in Ireland and the United Kingdom [42], and in China [43]. This could be because the general population in high-income countries has a low incidence rate of tuberculosis. In addition, the use of early TB diagnosis and prevention techniques, along with the accessibility of modern technologies, significantly lowers the incidence of tuberculosis [44]. Furthermore, there are higher cases of tuberculosis (TB) in Ethiopia due to poverty, overcrowding, large families, and subpar living conditions.

Children who were classified as anemic had a 3.83 times higher risk of getting TB infections than non-anemic children. Supported by Northern Ethiopia [34] and Benshangul Gumuz [36], this is because anemia highly prevalent in TB cases due to persistent inflammation or chronic diseases[45], and anemia appears to have predictive value for incident TB disease during ART [46].

Likewise, the risk of developing TB for children who were not getting TPT was 3.78 times higher as compared with those who were taking TPT at baseline. This finding is supported by different studies conducted in Ethiopia [34, 47], Tanzania [48], and global data [49]. TPT decreases mycobacterium load and reduces the progression of latent TB bacilli to active TB. Increases in mycobacterial load were associated with progressive impairment of mycobacterium specific-T-cell responses and increased the occurrence of active TB [50]. Additionally, the synergetic effect of ART and TPT in reducing active TB incidence is increased as a result of CD4+ T cell recovery

and viral load suppression [25]. Lower TPT intake is associated with an increased incidence of tuberculosis; in our study, only 63.42% of children with HIV took TPT.

The hazard of TB among children with wasting at baseline was 2.53 times more likely as compared to their counterparts. This finding is supported by studies conducted in Northern Ethiopia, Debre Markos [32, 34], and Southern Ethiopia [51]. This could be explained by the fact that malnutrition causes nutritionally acquired immune dysfunction and increases host susceptibility to infections. Under-nutrition also weakens the immune system through atrophy of the thymus, spleen, and lymph nodes and reduces cell-mediated immunity [52, 53]. Immunological and clinical recovery are directly associated with nutritional status [54].

Furthermore, children with late ART initiation had a 3.27 times increased risk of developing TB when compared to those with rapid ART initiation. This finding was in agreement with those of a study done in Ethiopia [32]. Initiation of ART early after confirmation of HIV-infection, even at a higher CD4 cell count, helps to reduce the occurrence of TB. This might be due to the early initiation of ART to reduce delays and improve viral suppression rates in children with HIV, increase retention care, and reduce HIV transmission [55].

Strength and limitation of the study

As a strength, this study was multicenter, covering wide ranges in geographical areas of specialized hospitals, and used a longer follow-up period for better estimation of the incidence of tuberculosis. There are certain inherent limitations to the current study. Owing to financial limitations, factors such as housing characteristics, the environment, and family history of smoking-related factors were evaluated retrospectively rather than prospectively in order to determine the incidence and predictors of TB following the start of ART. Additionally, the study excluded children who began antiretroviral therapy (ART) at the outset and got tuberculosis within a month or less. This may have led to an underestimation of the incidence of tuberculosis.

Conclusion and Recommendation

In this study, the incidence of TB was found to be high. Anemia, wasting, TB preventive therapy, and early initiation of ART were factors found to be significant predictors of TB incidence in HIV-infected children receiving ART. Additionally, clinicians should emphasize early screening and maximizing nutritional supplements for HIV-infected children to decrease the incidence of TB in those individuals. Furthermore, it needs emphasis on early detection and treatment of anemia and

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TB preventive therapy, counseling on nutritional improvement, and timely initiation of ART to avert TB. Abbreviations AHR: Adjusted Hazard Ratio; ART: Antiretroviral Therapy; CPT: Cotrimoxazole Preventive Therapy; CD4: Cluster of Differentiation 4; OIs: Opportunistic Infections; CYO: Child-Year-Observations; SD: Standard Deviation; TB: Tuberculosis; TPT: Tuberculosis Preventive Treatment; UoG: University of Gondar; WHO: World Health Organization; AIC: Akakie Information Criterion; BIC: Bayesian Information Criterion; PHA: proportional hazard assumption Ethical approval and consent to participate This study used secondary data or medical charts; the need for informed consent and ethical approval was waived by the Institutional Review Board of the University of Gondar, College of Medicine and Health Sciences, on behalf of the Ethical Review Committee of the School of Nursing (SN/212/2022). Finally, before collecting the data, a letter of permission to collect the data was obtained from each Comprehensive Specialized Hospital administrator to collect the data from each ART clinic. At the time of abstraction, personal identifiers (names and contact numbers) were excluded. The data were kept strictly confidential and used only for study purposes. All of the procedures were carried out by considering the Declaration of Helsinki. Patient and public involvement Patients and public were not directly involved in the design, conduct and dissemination of this study. Acknowledgment The authors acknowledge University of Gondar for ethical clearance, and each comprehensive specialized Hospitals, and data collectors. **Authors' contributions** GBM worked on developing the research idea, designing the study, being involved in proposal writing, training and supervising the data collectors, analyzing and interpreting the results, and For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

- preparing the manuscript. BTL, FDB, and WTW played their role in critically revising the proposal, participating in its design, analyzing and interpreting the results, and writing the manuscript. All authors were involved in reading and approving the final manuscript. Funding No funding Availability of data and materials Data will be available upon reasonable request from the corresponding author. **Consent for publication** Not applicable. **Competing interests** The authors declare that they have no competing interests. Supplementary figure 1: schematic diagram of the sampling procedure for the incidence and predictors of Tuberculosis among HIV-infected children on ART in Amhara Region Comprehensive Specialized Hospitals, Ethiopia Supplementary Figure 2: overall Kaplan-Meier estimate of TB-free probability in children on ART in Amhara Region comprehensive specialized Hospitals Supplementary Figure 3: The goodness of fit test for the Gompertz regression model for the incidence of TB among children on ART in Amhara region comprehensive specialized Hospitals **Supplementary Table 1:** Estimated sample size determination by predictor variables for incidence of tuberculosis among HIV-infected children on ART, by using STATA version 17, cox-model Supplementary Table 2: Baseline clinical, nutritional, and laboratory characteristics of incidence of Tuberculosis among HIV-infected children on ART in Amhara Regional State Comprehensive Specialized Hospitals, Ethiopia Supplementary Table 3: Summary of model comparison between Semi parametric and parametric cox-regression model using log-likelihood, AIC, and BIC criteria **References:** Orginization, W.H., WHO consolidated guidelines on tuberculosis, in Module 5: Management of 1. tuberculosis in children and adolescents. 2022, WHO. Orginization, W.H., Global tuberculosis report. 2023, WHO: Geneva. 2. 3. World Health Organization(WHO). Global Tuberculosis Report. . 2023; Available from: https://reliefweb.int/report/world/global-tuberculosis-report-2023?gad source=1. 4. World Health Organization (WHO). Global HIV programme. 20121; Available from: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/treatment/tuberculosis. Verkuijl, S., et al., Global reporting on TB in children and adolescents: how far have we come and 5. what remains to be done? IJTLD OPEN, 2024. 1(1): p. 3-6. Wondmeneh, T.G. and A.T. Mekonnen, The incidence rate of tuberculosis and its associated 6. factors among HIV-positive persons in Sub-Saharan Africa: a systematic review and meta-analysis. BMC Infectious Diseases, 2023. 23(1): p. 613.

BMJ Open

 Azanaw, M.M., et al., incidence and predictors of tuberculosis among HIV patients ofter initiation of antiretrowiral treatment in Ethiopia: a systematic review and meta-analysis. Tropical Medicine and Health, 2021. 49(1): p. 18. Daniel, O., et al., HIV-TB co-infection in children: associated factors and access to HIV services in lagos, Nigeria. 2015. 5(3): p. 165-169. Ebonyi, A.O., et al., Previdence of and risk factors for pulmonary tuberculosis among newly diagnosed HIV-1 infected Nigerian children. 2016. 5(1): p. 21. Amuta, E., I. Tsaku, and I. Akyala. A retrospective study on the epidemiological trend of human immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state, Nigeria. 2013. Kebede, F., et al., incidence and predictors of pulmonary tuberculosis in HIV-infected children ofter highly active antiretroviral therapy (HART) in China: a retrospective study. 2009–2019. 2022. Mu, W., et al., incidence and associated factors of pulmonary tuberculosis in HIV-infected children ofter highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. 20(9): p. 1127-1135. Salvadori, N., et al., incidence of tuberculosis and associated mortolity in a cohort of human immunodeficiency virus (Jud 22: p. 484-5. Wondifraw, E.B., et al., incidence and predictors of tuberculosis among children on antiretroviral therapy a retrospective cohort study. 2018. 11: p. 1-7. Endalamaw, A., et al., incidence and predictors of tuberculosis, 2022; A multicenter retrospective follow-up study. 2023. [21]. Endalamaw, A., et al., incidence of MD Stage 3 and 4 events, tuberculosis in children on antiretroviral therapy a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoniaid preventive therapy and antiretroviral therapy and the incidence of Luberculosis in people living with HIV in Ethiolos. 2014. 38(5): p	1 2			
 All F. Ashaw, M.M., et al., Incidence and predictors of tuberculosis among Hiv patients of the Initiation of antiretroviral treatment in Ethiopia: a systematic review and meta-analysis. Tropical Medicine and Health, 2021. 49(1): p. 18. Daniel, O., et al., HIV TB co-infection in children: associated factors and access to HIV services in Logos, Nigeria. 2015. 5(3): p. 155-169. Ebonyi, A.O., et al., Prevalence of and risk factors for pulmonary tuberculosis among newly diagnosed HIV-1 infected Nigerian children. 2016. 6(1): p. 21. Amuta, E., I. Tsaku, and I. Akyala, A retrospective study on the epidemiological trend of human immunodeficiency Virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasorawa state, Nigeria. 2013. Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopio: a multicenter historical cohorts study 2009–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 148-5. Wondiffraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy: a retrospective cohort study. 2014. 9(3): p. 014-57. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2014. 9(3): p. 01457. Cararnello, A., et al., Incidence of VMO Stage 3 and events, tuberculosis, i	∠ 3	447	-	A second baba she have the second
 of antiretrovinal treatment in thiopia: a systematic review and meta-analysis. Iropical Medicine and Netath, 2021. 49(1): p. 18. Daniel, O., et al., <i>HIV-TB co-inflection in children: associated factors and access to HIV services in Lagos, Nigeria,</i> 2015. 5(3): p. 165-169. Ebonyi, A.O., et al., <i>Prevalence of and risk factors for pulmonary tuberculosis among newly diagnosed HIV-1 infected Nigerian children.</i> 2016. 6(1): p. 21. Amuta, E., I., Tsaku, and I. Akyala, <i>Artospective study on the epidemiological trend of human immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state, Nigeria.</i> 2013. Kebede, F., et al., <i>Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART).</i> Northwest Ethiopia: a multicenter historical cohorts study 2009-2019. 2022. 2022. Mu, W., et al., <i>Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after high yac tube antiretroviral therapy (HAART) in China: a retrospective study.</i> 2014. 26(9): p. 1127-1135. Salvadori, N., et al., <i>Incidence on tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy.</i> 2017. 6(2): p. 161-167. Brennan, A., et al., <i>Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort.</i> 2014. 22: p. 484-5. Wondifraw, E.B., et al., <i>Incidence and predictors of tuberculosis among children on antiretroviral therapy on the incidence of tuberculosis and children and antiretroviral therapy and antiretroviral therapy on the incidence of tuberculosis in poptalis, 2022; A multicenter retrospective follow-up study. 2022. 8(12).</i> C. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, <i>Incidence of tuberculosis, and mortality in untreated, HIV-infected children enoling in care befora 1 year of age: an ICDFS (interpretival t</i>	4	41/	7.	Azanaw, M.M., et al., Incidence and predictors of tuberculosis among HIV patients after initiation
 and Health, 2021, 49(1): p. 18. Daniel, O., et al., <i>HV-YB co-infection in children: associated factors and access to HIV services in Lagos, Nigeria.</i> 2015. 5(3): p. 165-169. Ebonyi, A.O., et al., <i>IPrevalence of and risk factors for pulmonary tuberculosis among newly diagnosed HIV-1 infected Nigerian children.</i> 2016. 6(1): p. 21. Amuta, E., I. Tsaku, and I. Akyala, A retrospective study on the epidemiological trend of human immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state, Nigeria. 2013. Kebede, F., et al., <i>Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019.</i> 2022. 2022. Mu, W., et al., <i>Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a retrospective study.</i> 2014. 26(9): p. 1127-1135. Salvadori, N., et al., <i>Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy.</i> 2017. 6(2): p. 161-167. Brennan, A., et al., <i>Rick factors associated int B in children receiving ART in a South Africa multicenter HIV cohort.</i> 2014. 22: p. 484-5. Wondifraw, E.B., et al., <i>Incidence of WHO Stage 3 and 4 events, tuberculosis in children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals.</i> 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., et al., <i>Bregela, and N.J.B.A.</i>, Tezera. <i>Incidence of tuberculosis in children on ontiretroviral therapy: a retrospective cohort study.</i> 2018. 11: p. 1-7. Yirdaw, K.D., et al., <i>Bicher Gel Store Study and antiretroviral therapy on the incidence of tuberculosis and humoin mumodeficiency virus at therapy in children on ontiretroviral therapy: a</i>	5	418		of antiretroviral treatment in Ethiopia: a systematic review and meta-analysis. Tropical Medicine
 Daniel, O., et al., HIV-TB co-inflection in children: associated factors and access to HIV services in Lagos, Nigeria. 2015. 5(3): p. 165-169. Ebonyi, A.O., et al., Prevalence of and risk factors for pulmonary tuberculosis among newly diagnosed HIV-1 infacted Nigerian children. 2016. 6(1): p. 21. Amuta, E., I., Tsaku, and I. Akyala, A retrospective study on the epidemiological trend of human immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state, Nigeria. 2013. Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART). Northwest Ethiopia: a multicenter historical cohorts study 2008–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children filer highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondiffaw, E.B., et al., Incidence of WHO Stage 3 and 4 sevents, bacicalized hospitals, 2022; A multicenter HV cohort. 2014. 22: p. 148-5. Wondiffaw, K.B., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis in children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., E.H. Engeda, and N.J.B.C.n. Terera, Incidence of tuberculosis in children on antiretroviral therapy on a the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(6): p. 104557. Ciaranello, A., et al., Incidence of WHO Stage 3 an	6	419	_	and Health, 2021. 49 (1): p. 18.
 Lagos, Nigeria. 2015. 5(3): p. 165-169. Ebonyi, A.O., et al., <i>Prevalence of and risk factors for pulmonary tuberculosis among newly diagnosed HIV-1 infected Nigerian children</i>. 2016. 6(1): p. 21. Amuta, E., I. Tsaku, and I. Akyala, <i>A retrospective study on the epidemiological trend of human immunoefficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nosarawa state, Nigeria</i>. 2013. Kebede, F., et al., <i>Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019. 2022. 2022.</i> Mu, W., et al., <i>Incidence and associated factors of pulmonary tuberculosis in HIV-infected children ofter highly active antiretroviral therapy (HAART) in China: a retrospective study.</i> 2014. Salvadori, N., et al., <i>Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy.</i> 2017. 6(2): p. 161-167. Brennan, A., et al., <i>Risk factors associated with Tb in children receiving ART in a South African multicenter HV cohort.</i> 2014. 22: p. 484-5. Wondifraw, E.B., et al., <i>Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeost Ethiopia comprehensive specialized hospitals.</i> 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamay, A., et al., <i>Reneficial effect of isoniaid preventive therapy and antiretroviral therapy on the incidence of Huberculosis and a elefore 1 year of age: an eleb& <i>I (International therapy on the incidence of WHO Stage 3 and 4 events</i>, tuberculosis in children on antiretroviral therapy on the incidence of WHO Stage 3 and 4 events, tuberculosis in children or antiretroviral therapy on the incidence of WHO Stage 3 and 4 events, tuberculosis in children for <i>follow preventive therapy and antiretroviral therapy on the incidence of Hubercu</i></i>	7	420	8.	Daniel, O., et al., HIV-TB co-infection in children: associated factors and access to HIV services in
 9. Ebonyi, A.O., et al., <i>Prevalence of and risk factors for pulmonary tuberculosis among newly</i> <i>diagnosed HV-1 infected Nigerian children</i>, 2016. 6(1): p. 21. 11. 424 10. Amuta, E., I. Tsaku, and I. Akyala, <i>A retrospective study on the epidemiological trend of human</i> <i>immunodeficiency virus</i> (<i>HIV</i>) <i>and pulmonary tuberculosis</i> (<i>PTB</i>) <i>co-infection in Nasarawa state</i>, <i>Nigeria</i>. 2013. 11. Kebede, F., et al., <i>Incidence and predictors of pulmonary tuberculosis among children who</i> <i>received antiretroviral therapy</i> (<i>ART</i>), <i>Northwest Ethiopia: a multicenter historical cohorts study</i> 2009–2019. 2022. 2022. 12. Mu, W., et al., <i>Incidence and associated factors of pulmonary tuberculosis theory children who</i> <i>received antiretroviral therapy</i> (<i>HART</i>) in <i>China: a retrospective study</i>. 2014. 26(9): p. 1127-1135. 13. Salvadori, N., et al., <i>Ricidence of tuberculosis and associated mortality in a cohort of human</i> <i>immunodeficiency virus infected children initiating antiretroviral therapy</i>. 2017. 6(2): p. 161-167. 14. Brennan, A., et al., <i>Risk foctors associated with TB in children receiving ART in a South African</i> <i>multicenter HIV cohort</i>. 2014. 22: p. 484-5. 15. Wondifraw, E.B., et al., <i>Incidence and predictors of tuberculosis anong children on antiretroviral</i> <i>therapy at northeost Ethiopia comprehensive specialized hospitals</i>, 2022; <i>A multicenter</i> <i>retrospective follow</i> pus tudy. 2022. 14. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, <i>Incidence of tuberculosis on antiretroviral therapy on <i>antiretroviral therapy: a retrospective cohort study</i>. 2014. 32(6): p. e10457.</i> 14. Ciaranello, A., et al., <i>Incidence of WHO Stoge 3 and 4 events</i>, <i>tuberculosis, and matility in</i> <i>untrected</i>, <i>HHV-infected children norbing in care of face an ipeola on</i>	8	421		<i>Lagos, Nigeria.</i> 2015. 5 (3): p. 165-169.
 diagnosed HIV-1 infected Nigerian children. 2016. 6(1): p. 21. Amuta, E., I. Tsaku, and I. Akyala, A retrospective study on the epidemiological trend of human immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state, Nigeria. 2013. Kebede, F., et al., incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children ofter highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk foctors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondifraw, E.B., et al., incidence and predictors of tuberculosis among children on antiretroviral therapy at northeest Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, incidence of tuberculosis in children on antiretroviral therapy or attrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isonicid preventive theropy on and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. Caranello, A., et al., Incidence and WD Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IEDEA (International Epidemiologic Databases to Evoluate AIDS) East Africa regional andysis. 2014. 33(6): p. e623. A	9	422	9.	Ebonyi, A.O., et al., Prevalence of and risk factors for pulmonary tuberculosis among newly
 Amuta, E., I. Tsaku, and I. Akyala, A retrospective study on the epidemiological trend of human immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state, Nigeria. 2013. Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who received antitertorival therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children ofter highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondifraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized haspitals, 2022, A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoliaid preventive threapy and antiretroviral therapy on antiretroviral therapy. Class. J. Eucle Children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Fuoluet ALDS) East Africa regional analysis. 2014. 33(6): p. 623. Katalello, A., et al., Maintrition associated with utberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 33(5): p. 60197145. Katalello, K.A., N. Bithan Tebeje, a	10	423		diagnosed HIV-1 infected Nigerian children. 2016. 6 (1): p. 21.
 immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state, Nigeria. 2013. Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., E.H., Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in popel living with HIV in Ethiopia. 2014. 9(8): p. e104557. Atale Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated. HIV-infected children enrolling in care before 1 year of age: an IEEA (International Epidemiologic Datobases to Evaluate AIDS) Fast Africa regional analysis. 2014. 3(6): p. 623. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.o. Ekubagewargies, Survival and predictors of mortality among chi	11	424	10.	Amuta, E., I. Tsaku, and I. Akyala, A retrospective study on the epidemiological trend of human
 Migeria 2013. Nigeria 2013. Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. Z6(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondifraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Hoo Endalamaw, A., E.H. Engeda, and N.J.B.I.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective of isonical preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. Claranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an teDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.o. Ekubagewargles, Survival and predictors of mortality momog children co-infected with tuberculosis and mamin munundeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 1	12	425		immunodeficiency virus (HIV) and pulmonary tuberculosis (PTB) co-infection in Nasarawa state,
 Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a restrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., Et al., Bredea, and N.J.B.r. n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoniaid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IEDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P. Ekubagewargles, Survival and predictors of mortality among children co-infected with tuberculosis and human deficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. Hicks, R., et al., Malhurtition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected wit	13	426		Nigeria. 2013.
 received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019. 2022. 2022. Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Rik factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondifraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy on study. 2022. 8(12). Wondifraw, K.B., et al., Incidence and predictors of tuberculosis in children on antiretroviral therapy or study. 2022. 8(12). Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isonizid preventive therapy and antiretroviral therapy on their cidence of WHO Stage 3 and 4 events, tuberculosis, and martality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. Ata University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2016. 11(4): p. e015291. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.o. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2016. 11(4): p. e0152941.	14	427	11.	Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who
 2009–2019. 2022. 2022. 2029–2019. 2022. 2022. 2029–2019. 2022. 2022. 2029–2019. 2022. 2022. 2029–2019. 2022. 2022. 2020. 2019. 2022. 2021. 2020. 2019. 2022. 2022. 2020. 2019.	15	428		received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study
 Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected children offer highly active antiretrovirol therapy (HAART) in China: a retrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondifraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northest Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopi	10	429		2009–2019. 2022. 2022 .
 children after highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014. 26(9): p. 1127-1135. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondifraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamav, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoniaid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. Giaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of gae: an IEDEA (International Epidemiologic Databases to Evaluate AIDS). East Africa regional analysis. 2014. 33(6): p. 623. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid	12	430	12.	Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected
 26(9): p. 1127-1135. 13. Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. 14. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. 15. Wondifraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeosts Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). 16. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. 17. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. 18. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. 19. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. 20. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(1): p. e0152941. 21. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid and cortimoxazole preventive therapy in children living with HIV in northern Ethiopia: a retrospective,	19	431		children after highly active antiretroviral therapy (HAART) in China: a retrospective study. 2014.
 Ala Salvadori, N., et al., Incidence of tuberculosis and associated mortality in a cohort of human immunodeficiency virus-infected children initiating antiretroviral therapy. 2017. 6(2): p. 161-167. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22: p. 484-5. Wondifraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tetera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoniaid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. Caranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an leDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.o. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniaid and actiminoxazole preventive therapy in children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(4): p. e0152941. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of huberculosis in the absence of isoniaid and actiminoxazole preventive therapy in	20	432		26 (9): n 1127-1135
 435 1. Bartrown, M., et al., Rickarder J. 1998. 436 14. Brennan, A., et al., Risk factors associated with TB in children receiving ART in a South African multicenter HIV cohort. 2014. 22; p. 484-5. 437 15. Wondfiraw, E.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study. 2022. 8(12). 440 16. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. 441 17. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV infoin. 2014. 9(8): p. e104557. 443 18. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. 447 19. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. 445 20. Hicks, R., et al., Molnutritino associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. 445 21. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(4): p. e0152941. 456 22. Nan, L., et al., Incident tuberculosis and risk facto	21	433	13	Salvadori N et al Incidence of tuberculosis and associated mortality in a cohort of human
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 430 Inducted Internet Internet Procession (2014) 214, 22, p. 464-3. 431 IS. Wondifraw, R.B., et al., Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study, 2022, 8(12). 440 16. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018, 11; p. 1-7. 441 17. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014, 9(8); p. e104557. 443 ta. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6); p. 623. 444 19. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.o. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5); p. e0197145. 451 20. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9); p. 1074-1083. 452 454 African MDR-TB and HIV co-infected children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(4); p. e0152941. 455 454 Stama, L., et al., Tuberculosis, before and after antiretroviral therapy among HIV-infected children in Nigeria: what are the risk factors? 2016. 11(5); p. e0156177. 456 22. Nan, L., et al., Tuberculosis, before and after antiretroviral therapy among HIV-infected children in Nigeria: what	24	435	14.	multicenter HIV cohort 2014 22: p 494 E
 437 15. Woldmaw, E.S., et al., Include and predictors of audertability induction of induction of the approximate of a different of different	25	430	15	Mondiframe E.B., et al. Incidence and predictors of tuborculosis among children on antiretrouiral
 436 Interlop at Notifiest Ethiopia Completions performance inspirate, 2022, A multicenter retrospective follow-up study. 2022. 8(12). 440 16. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. 441 17. Virdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. 443 18. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. 444 19. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. 445 20. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. 453 21. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(4): p. e0152941. 454 455 22. Nan, L., et al., Incident tuberculosis, before and ofter antiretroviral therapy among HIV-infected children in Dar es Salaam, Tanzania. 2013. 27(8): p. 1273. 458 23. Anigilaje, E.A., et al., Tuberculosis, before and ofter antiretroviral therapy among HIV-infected children in Nigeria: what are the risk factors? 2016. 11(5): p. e0156177. 460 24.	26	437	15.	therapy at parthaset Ethiopia comprehensive energialized herpitale, 2022; A multisenter
 439 retrospective follow-up study. 2022. 8(12). 440 16. Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. 441 17. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. 443 18. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. 447 19. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. 451 20. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. 453 21. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(4): p. e0152941. 454 455 retrospective follow-up study. 2016. 11(4): p. e0152941. 455 454 Anigilaje, E.A., et al., Tuberculosis, before and after antiretroviral therapy among HIV-infected children in Nigeria: what are the risk factors? 2016. 11(5): p. e0156177. 456 24. Health, M.o., Health Sector Transformation Plan II(HSTP- II). February, 2021: Addis Ababa. 457 458 25. Assembly, U.N.G., Political declaration of the high-level meeting on the fi	27	438		inerapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter
 440 16. Endalamaw, A., E.H. Engeda, and N.J.B.T.n. (E2era, Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. 441 17. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. 444 18. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. 447 19. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.o. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. 450 451 20. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. 453 454 454 455 455 456 456 457 456 458 451 456 454 457 456 458 458 458 459 450 450 451 451 451 451 452 454 455 455 456 454 457 456 457 458 458 458 459 459 450 450 451 451 451 452 453 454 455 454 455 455 456 456 457 458 458 458 457 459 451	28	439	4.6	retrospective follow-up study. 2022. 8(12).
 antiretroviral therapy: a retrospective cohort study. 2018. 11: p. 1-7. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid and cotrimoxacole preventive therapy in children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(4): p. e0152941. Ana, L., et al., Incident tuberculosis and risk factors among HIV-infected children in Dar es Salaam, Tanzania. 2013. 27(8): p. 1273. Anagliaje, E.A., et al., Tuberculosis, before and after antiretroviral therapy among HIV-infected tuberculosis. 2 September 2023, WHO. p. 1-15. Kasembly, U.N.G., Political declaration of the high-level meeting on the fight against tuberculosis. 25 September 2023, WHO. p. 1-15. FMOH, National guidlines for comprhensive HIV prevention ,care and treatment in Ethiopia. 2014, FMOH: Addis Ababa. p. 1-165. 	29	440	16.	Endalamaw, A., E.H. Engeda, and N.J.B.r.n. Tezera, <i>Incidence of tuberculosis in children on</i>
 442 17. Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. 2014. 9(8): p. e104557. 444 18. Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in untreated, HIV-infected children enrolling in care before 1 year of age: an leDEA (International Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33(6): p. 623. 447 19. Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of mortality among children co-infected with tuberculosis and human immunodeficiency virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective follow-up study. 2018. 13(5): p. e0197145. 451 20. Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083. 453 21. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a retrospective follow-up study. 2016. 11(4): p. e0152941. 455 Salaam, Tanzania. 2013. 27(8): p. 1273. 458 23. Anigliaje, E.A., et al., Tuberculosis, before and after antiretroviral therapy among HIV-infected children in Nigeria: what are the risk factors? 2016. 11(5): p. e0156177. 460 24. Health., M.O., Health Sector Transformation Plan II(HSTP- II). February, 2021: Addis Ababa. 461 25. Assembly, U.N.G., Political declaration of the high-level meeting on the fight against tuberculosis. 25 September 2023, WHO. p. 1-15. 463 26. FMOH, National guidlines for comprhensive HIV prevention ,care and treatment in Ethiopia. 2014, FMOH: Addis Ababa. p. 1-165. 	30 21	441	. –	antiretroviral therapy: a retrospective cohort study. 2018. 11 : p. 1-7.
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35445untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International36446Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33 (6): p. 623.3744719.Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of38448mortality among children co-infected with tuberculosis and human immunodeficiency virus at39449University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective40450follow-up study. 2018. 13 (5): p. e0197145.4145120.Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South42452African MDR-TB and HIV co-infected children. 2014. 18 (9): p. 1074-1083.4345321.Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of454isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a455retrospective follow-up study. 2016. 11 (4): p. e0152941.4745622.4845745823.49458459children in Nigeria: what are the risk factors? 2016. 11 (5): p. e0156177.46024.46125.462children in Nigeria: what are the risk factors? 2016. 11 (5): p. e0156177.46326.4642014, FMOH: Addis Ababa. p. 1-15.5546326.56464572014, FMOH: Addis Ababa. p. 1-165.<	34	444	18.	Ciaranello, A., et al., Incidence of WHO Stage 3 and 4 events, tuberculosis, and mortality in
36446Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis. 2014. 33 (6): p. 623.3744719.Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.o. Ekubagewargies, Survival and predictors of38448mortality among children co-infected with tuberculosis and human immunodeficiency virus at39449University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective40450follow-up study. 2018. 13 (5): p. e0197145.4145120.Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South4345321.Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of444455retrospective follow-up study. 2016. 11 (4): p. e0152941.4745622.Nan, L., et al., Incident tuberculosis and risk factors among HIV-infected children in Dar es48457Salaam, Tanzania. 2013. 27 (8): p. 1273.4945823.Anigilaje, E.A., et al., Tuberculosis, before and after antiretroviral therapy among HIV-infected50459children in Nigeria: what are the risk factors? 2016. 11 (5): p. e0156177.5146024.Health., M.o., Health Sector Transformation Plan II(HSTP- II). February, 2021: Addis Ababa.53462tuberculosis. 25 September 2023, WHO. p. 1-15.5445326.FMOH, National guidlines for comprhensive HIV prevention ,care and treatment in Ethiopia.544542014, FMOH: Addis Ababa. p. 1-165.	35	445		untreated, HIV-infected children enrolling in care before 1 year of age: an IeDEA (International
3744719.Atalell, K.A., N. Birhan Tebeje, and D.T.J.P.O. Ekubagewargies, Survival and predictors of38448mortality among children co-infected with tuberculosis and human immunodeficiency virus at39449University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. A retrospective40450follow-up study. 2018. 13(5): p. e0197145.4145120.Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South43452African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083.4445321.Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of454isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a455retrospective follow-up study. 2016. 11(4): p. e0152941.4745622.4745622.48457Salaam, Tanzania. 2013. 27(8): p. 1273.4945823.459children in Nigeria: what are the risk factors? 2016. 11(5): p. e0156177.5146024.524535326.5425.46326.5455.5425.554635626.5758582014, FMOH: Addis Ababa. p. 1-165.582014, FMOH: Addis Ababa. p. 1-165.	36	446		<i>Epidemiologic Databases to Evaluate AIDS) East Africa regional analysis.</i> 2014. 33 (6): p. 623.
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42452African MDR-TB and HIV co-infected children. 2014. 18(9): p. 1074-1083.4345321.Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of4445321.Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, High incidence of tuberculosis in the absence of45454isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a46455retrospective follow-up study. 2016. 11(4): p. e0152941.4745622.Nan, L., et al., Incident tuberculosis and risk factors among HIV-infected children in Dar es48457Salaam, Tanzania. 2013. 27(8): p. 1273.4945823.Anigilaje, E.A., et al., Tuberculosis, before and after antiretroviral therapy among HIV-infected50459children in Nigeria: what are the risk factors? 2016. 11(5): p. e0156177.5146024.Health., M.o., Health Sector Transformation Plan II(HSTP- II). February, 2021: Addis Ababa.5346125.Assembly, U.N.G., Political declaration of the high-level meeting on the fight against54462tuberculosis. 25 September 2023, WHO. p. 1-15.5546326.FMOH, National guidlines for comprhensive HIV prevention ,care and treatment in Ethiopia.564642014, FMOH: Addis Ababa. p. 1-165.5716	41	451	20.	Hicks, R., et al., Malnutrition associated with unfavorable outcome and death among South
 453 21. Alemu, Y.M., G. Andargie, and E.J.P.O. Gebeye, <i>High incidence of tuberculosis in the absence of</i> 454 <i>isoniazid and cotrimoxazole preventive therapy in children living with HIV in northern Ethiopia: a</i> 455 <i>retrospective follow-up study.</i> 2016. 11(4): p. e0152941. 47 456 22. Nan, L., et al., <i>Incident tuberculosis and risk factors among HIV-infected children in Dar es</i> 48 457 <i>Salaam, Tanzania.</i> 2013. 27(8): p. 1273. 49 458 23. Anigilaje, E.A., et al., <i>Tuberculosis, before and after antiretroviral therapy among HIV-infected</i> 459 <i>children in Nigeria: what are the risk factors?</i> 2016. 11(5): p. e0156177. 460 24. Health., M.o., <i>Health Sector Transformation Plan II(HSTP- II).</i> February, 2021: Addis Ababa. 461 25. Assembly, U.N.G., <i>Political declaration of the high-level meeting on the fight against</i> 462 <i>tuberculosis.</i> 25 September 2023, WHO. p. 1-15. 463 26. FMOH, <i>National guidlines for comprhensive HIV prevention ,care and treatment in Ethiopia.</i> 464 2014, FMOH: Addis Ababa. p. 1-165. 	42	452		African MDR-TB and HIV co-infected children. 2014. 18 (9): p. 1074-1083.
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53101201101	52	461	25	Assembly, U.N.G., Political declaration of the high-level meeting on the fight against
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 55 463 2014, FMOH: Addis Ababa. p. 1-165. 56 16 57 16 58 16 	54	402 162	26	EMOH National auidlines for comprehensive HIV prevention care and treatment in Ethionia
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Page 20 of 27 BMJ Open: first published as 10.1136/bmjopen-2024-093808 on 13 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .

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Federal Democratic Republic of Ethiopia Central Statistical Agency, <i>Population Projection of Ethiopia for All Regions At Wereda Level from 2014 – 2017.</i> . Archived from the original on 6 June 2018. , 2018.
Wondifraw, E.B., et al., <i>Incidence and predictors of tuberculosis among children on antiretroviral therapy at northeast Ethiopia comprehensive specialized hospitals, 2022; A multicenter retrospective follow-up study.</i> Heliyon, 2022. 8 (12).
FMOH, National Comprehensive HIV Prevention, Care and Treatment Training for Healthcare Providers, M.o. Health, Editor. Revised on August, 2021, Ethiopian Federal Ministry of Health Addis Ababa. p. 1-502.
Le Thuy, World Health Organization Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. 2018.
Chanie, E.S., et al., Incidence of advanced opportunistic infection and its predictors among HIV infected children at Debre Tabor referral Hospital and University of Gondar Compressive specialized hospitals, Northwest Ethiopia, 2020: A multicenter retrospective follow-up study. Heliyon, 2021. 7 (4): p. e06745.
Endalamaw, A., E.H. Engeda, and N. Tezera, <i>Incidence of tuberculosis in children on antiretroviral therapy: a retrospective cohort study</i> , BMC research notes, 2018, 11 : p. 1-7.
Yirdaw, K.D., et al., <i>Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia.</i> PloS one, 2014. 9 (8): p. e104557.
Alemu, Y.M., G. Andargie, and E. Gebeye, <i>High Incidence of Tuberculosis in the Absence of Isoniazid and Cotrimoxazole Preventive Therapy in Children Living with HIV in Northern Ethiopia: A Retrospective Follow-Up Study.</i> PLoS One, 2016. 11 (4): p. e0152941.
Kebede, F., et al., <i>Incidence and predictors of pulmonary tuberculosis among children who received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study 2009–2019.</i> Journal of Tropical Medicine, 2022. 2022 .
Fassikaw, K., et al., <i>HIV/AIDS associated tuberculosis occurance on art initiated children in North West Ethiopia 2020.</i> Journal of Pulmonary & Respiratory Medicine, 2021. 11 : p. 6. Beshir, M.T., et al., <i>Incidence and predictors of tuberculosis among HIV-positive children at</i>
Adama Referral Hospital and Medical College, Oromia, Ethiopia: a retrospective follow-up study. Epidemiology and health, 2019. 41 .
Tiruneh, F. and Y. Deyas, How Far Does Highly Active Antiretroviral Treatment Reduce TB Incidence among Children? A Marginal Structural Modeling Analysis, Southwest Ethiopia. Ethiopian Journal of Health Sciences, 2020, 30 (5)
Li, N., et al., <i>Incident tuberculosis and risk factors among HIV-infected children in Tanzania</i> . Aids, 2013. 27 (8): p. 1273-1281.
Bagcchi, S., WHO's global tuberculosis report 2022, in The Lancet Microbe. 2023. p. e20. Thomas, P., et al., Tuberculosis in human immunodeficiency virus-infected and human
<i>immunodeficiency virus-exposed children in New York City.</i> The Pediatric infectious disease journal, 2000. 19 (8): p. 700-706.
Turkova, A., et al., <i>Prevalence, incidence, and associated risk factors of tuberculosis in children with HIV living in the UK and Ireland (CHIPS): a cohort study.</i> The Lancet HIV, 2015. 2 (12): p. e530-e539.
Mu, W., et al., <i>Incidence and associated factors of pulmonary tuberculosis in HIV-infected children after highly active antiretroviral therapy (HAART) in China: a retrospective study.</i> AIDS care, 2014. 26 (9): p. 1127-1135.
Scott, C., et al., <i>Tuberculosis trends—United States, 2014.</i> Morbidity and Mortality Weekly Report, 2015. 64 (10): p. 265.

tiated children in North ositive children at pective follow-up study. ment Reduce TB thwest Ethiopia. ildren in Tanzania. Aids, e. 2023. p. e20. d and human infectious disease berculosis in children HIV, 2015. 2(12): p. is in HIV-infected rospective study. AIDS Mortality Weekly

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1 2			
3	F12	45	Cil Contono I, et al. Tubarcularic accordiated anomia is linked to a distinct inflammatory profile
4	513	45.	Gil-Santana, L., et al., Tuberculosis-associated anemia is linked to a distinct inflammatory profile
5	514	10	that persists after initiation of antitubercular therapy. Scientific reports, 2019. 9 (1): p. 1381.
6	515	46.	Kerkhoff, A.D., et al., The predictive value of current naemoglobin levels for incident tuberculosis
7	516		and/or mortality during long-term antiretroviral therapy in South Africa: a conort study. BMC
8	517	47	medicine, 2015. 13 (1): p. 1-13.
9	518	47.	Geremew, D., et al., The protective effect of isoniazid preventive therapy on tuberculosis
10	519		incidence among HIV positive patients receiving ART in Ethiopian settings: a meta-analysis. BMC
11	520		infectious diseases, 2019. 19 (1): p. 1-9.
13	521	48.	Sabasaba, A., et al., Effect of isoniazid preventive therapy on tuberculosis incidence and
14	522		associated risk factors among HIV infected adults in Tanzania: a retrospective cohort study. BMC
15	523	40	infectious diseases, 2019. 19 (1): p. 1-8.
16	524	49.	Ayieko, J., et al., Efficacy of isoniazid prophylactic therapy in prevention of tuberculosis in
17	525		children: a meta–analysis. BMC infectious diseases, 2014. 14 (1): p. 1-10.
18	526	50.	Day, C.L., et al., Patients with tuberculosis disease have Mycobacterium tuberculosis-specific CD8
19	527		T cells with a pro-apoptotic phenotype and impaired proliferative capacity, which is not restored
20	528		following treatment. PloS one, 2014. 9 (4): p. e94949.
21 22	529	51.	Tekese, D., et al., Incidence and predictors of tuberculosis among children receiving antiretroviral
22	530		therapy in the Wolaita Zone: A retrospective cohort study. PLOS ONE, 2023. 18 (9): p. e0291502.
24	531	52.	Bourke, C.D., J.A. Berkley, and A.J. Prendergast, <i>Immune dysfunction as a cause and</i>
25	532		consequence of mainutrition. Trends in immunology, 2016. 37 (6): p. 386-398.
26	533	53.	Katona, P. and J. Katona-Apte, <i>The interaction between nutrition and infection</i> . Clin Infect Dis,
27	534		2008. 46 (10): p. 1582-8.
28	535	54.	Ezeamama, A.E., et al., Age, sex, and nutritional status modify the CD4+ 1-cell recovery rate in
29	536		HIV-tuberculosis co-infected patients on combination antiretroviral therapy. Int J Infect Dis,
30 31	537		2015. 35 : p. 73-9.
32	538	55.	Asa E. Radix, M., MPH, PhD, Clinical Guidelines program, Rapid ART Initiation. February 9, 2023:
33	539		MEDICAL CARE CRITERIA COMMITTEE.
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Supplementary table 1: Estimated sample size determination by predictor variables for incidence of tuberculosis among HIV-infected children on ART, by using STATA version 17, cox-model

Variables	AHR	Powe r	Probability of withdrawal	Probability of event	Sample size (n)
Height for Age Z score	2.14	80%	0.15	0.167	383
WHO clinical staging	3.23	80%	0.15	0.167	161
ART adherence	2.05	80%	0.15	0.167	430

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Page 25 01 27	incidence of	Tuberculosis among HIV-infect	ted children on ART in	Amhara Regional Sta
	Comprehensiv	ve Specialized Hospitals, Ethiop	pia	-
1	Variables	Categories	Frequency	Percent (%)
2	CD4 cell cou	int	i v	
3		Above threshold	336	79.81
4		Below threshold	85	20.10
5	Anomio	Delow threshold	05	20.17
6	Anemia	NT	249	00 ((
7		No	348	82.66
8		Yes	73	17.34
9	Functional st	tatus (n=299)		
10		Working	201	67.22
11		working	201	07.22
12		Ambulatory	95	31.77
13		Bedridden	3	1.00
14	Development	tal status (n=122)		
15	20,000	Annronriate	82	67 21
16		Dolovod	35	28.60
17		Derayed	55	4 1
18	**7 /*	Regressed	5	4.1
19	Wasting		• • • •	
20		No	299	71.02
21		Yes	122	28.98
22	Stunting			
23 74		No	218	51.78
25		Yes	203	48.22
26	Previous On	portunistic infections		
27		No	323	76 72
28		Vas	08	12.12
29			90	23.20
30	WHO Clinica	al staging		(2.00
31		Stage I	261	62.00
32		Stage II	84	19.95
33		Stage III	55	13.06
34		Stage IV	21	4.99
35	ART drug ad	lherence level		
36	0	Good	296	70.31
37		Fair	68	16.15
38		Poor	57	13 54
39	Tuborculosis	nrovantiva Traatmant (TPT)	takon	10.51
40	1 uber curosis	Vac		(2.42
41		Yes	20/	03.42
42		NO	154 🥏	36.58
45	Cotrimoxazo	ole preventive Therapy (CPT)	taken	
44 45		Yes	345	81.95
46		No	76	18.05
47	ART side eff	ect		
48		No	275	65.32
49		Yes	146	34.68
50	Presence rea	imen change	1.0	•
51	i i counce i eg	men enange		

Supplementary table 2: Baseline clinical, nutritional, and laboratory characteristics of Page 23 of 27 ite

No Initiated ART within seven days	214 207	50.83 49.17
Yes	231	54.87
No	190	45.13
DTG contained ART drugs		
Yes	69	16.39
No	352	83.61

Supplementary table 3: Summary of model comparison between Semi parametric and parametric cox-regression model using log likelihood, AIC, and BIC criteria

Methods	Cox-model	Weibul	Exponential	Gompertz	Lognormal	Log-logistic
Log-likelihood	-168.36	-139.6	-139.62	-138.43	-141.27	-139.96
AIC	294.64	240.79	238.94	236.02	238.19	240.53
BIC	355.28	309.52	303.62	304.74	306.92	309.26

* Akakie Information Criterion (AIC), Bayesian Information Criterion (BIC)

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Supplementary figure 1: schematic diagram of the sampling procedure for the incidence and predictors of Tuberculosis among HIV-infected children on ART in Amhara Region Comprehensive Specialized Hospitals, Ethiopia

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Supplementary figure 2: overall Kaplan-Meier estimate of TB-free probability in children on ART in Amhara Region comprehensive specialized Hospitals

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Supplementary figure 3: The goodness of fit test for the Gompertz regression model for the incidence of TB among children on ART in Amhara region comprehensive specialized Hospitals

Incidence of Tuberculosis and its predictors among children on antiretroviral therapy in Amhara region, Ethiopia: A multicentre institution-based retrospective follow-up study

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3	1	Incidence of Tuberculosis and its predictors among children on antiretroviral therapy in Amhara
5 6 7	2	region, Ethiopia: A multicentre institution-based retrospective follow-up study
8 9	3	Gebrehiwot Berie Mekonnen ^{1*} , Bruck Tesfaye Legesse ² , Fikadie Dagnew Baye ¹ , and Wubet
10 11 12	4	Tazeb Wondie ³
13 14	5	Authors' affiliations:
15 16	6	¹ Department of Pediatrics and Child Health Nursing, College of Health Sciences, Debre Tabor
17 18	7	University, Debre Tabor, Ethiopia
19 20	8	² Department of Pediatrics and Neonatal Nursing, School of Nursing and Midwifery, Institutes of
20	9	Health Science, Wollega University, Nekemte, Ethiopia
22 23	10	³ Department of Pediatrics and Child Health Nursing, College of Medicine and Health Science,
24	11	Ambo University, Ambo, Ethiopia
25 26	12	* Corresponding Author, Address: geberehwot2004@gmail.com P.O Box: 272, Debre Tabor,
27 28	13	Ethiopia
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25 Abstract:

Introduction: Tuberculosis (TB) continues to be a significant public health issue, particularly in low- and middle-income countries. Globally, the end-TB strategy targets an 80% reduction in TB incidence by 2030. Despite this strategy, there is limited evidence on the incidence of TB among HIV-infected children in the study area after the test and treatment strategies in the Amhara region. Hence, this study aimed to assess the incidence of TB and its predictors among children on antiretroviral therapy (ART) in the Amhara region, which is the second largest region in Ethiopia and located in the Northwestern, Northeastern, and North-central parts of Ethiopia.

Methods: A multicentre institution-based retrospective follow-up study was conducted on 421 HIV-infected children receiving ART from July 2014 to March 2022. The study participants were selected using a simple random technique. National antiretroviral intake and follow-up forms were utilized to gather data through the KoBo Toolbox. STATA version 17 was used for data analysis. The Kaplan-Meier curve was applied to estimate failure time, and the log-rank test was employed to compare groups of predictors. To find TB predictors, Gompertz regression models, both bivariable and multivariable, were constructed. Ultimately, a 95% confidence interval-adjusted hazard ratio was calculated, and variables with a p-value less than 0.05 were considered statistically significant.

Results: A total of 421 children with a record completeness rate of 97.9% were analyzed in the study. The tuberculosis incidence rate in children on ART was 2.16 (95% CI: 1.52, 3.05) per 100 child-year observations. Those children who were on baseline anemic [AHR: 3.83 (95% CI: 1.46, 10.04)], never took TB preventive treatment (TPT) [AHR: 3.78 (95% CI: 1.44, 9.94)], wasted children [AHR: 2.53 (95% CI: 1.19, 5.38)], and not initiated antiretroviral therapy within seven days [AHR: 2.35 (95% CI: 1.15, 4.78)] were the significant predictors.

48 Conclusion: The incidence of TB in children on ART was relatively high. HIV-positive children
49 presenting with anaemia, who never took TPT, wasted, and late initiation of ART were prone to
50 the occurrence of TB. Therefore, prioritizing anaemia treatment, TB preventive therapy,
51 nutritional counseling, and timely ART initiation is essential to curb the TB burden.

52 Keywords: Antiretroviral therapy; HIV-infected children; incidence; predictors; test and treat,
53 Tuberculosis

² ³ 55 Strength and limitations of the study

- As a strength, this study was multicentre, covering wide ranges in geographical areas of
 specialized comprehensive hospitals
 - Due to the nature of retrospective follow-up study, factors such as housing characteristics, the environment, and family history of smoking-related factors were not evaluated
 - The study excluded children who started ART and developed tuberculosis within a month, potentially underestimating tuberculosis incidence
 - Since the study was conducted in tertiary level of health care (comprehensive specialized hospitals) subjected to biases related to healthcare accessibility

III | Page

Introduction

TB remains an important public health problem, particularly in low-and middle-income countries
(LMIC) [1]. Globally, TB incidence in 30 high-burden countries accounts for 87% of cases [2].
Children and young adolescents (aged below 15 years) account for 1.25 million (12%) of the
total TB incidence across the globe every year [3].

The risk of developing this global infectious disease is 18 times higher among HIV-infected individuals [4]. It remains the second leading cause of death from infectious disease, and the risk of death is threefold higher among HIV-infected individuals worldwide [1, 4]. Recently, the global occurrence of TB mortality in children increased significantly, which was 214,000 in 2023. Each day, 600 children lost their lives to this preventable disease. Approximately 31,000 deaths are related to people with HIV [2, 5].

In Sub-Saharan African countries, the HIV-TB burden has increased, despite the test-and-treat policy in this region. The incidence rate of tuberculosis among HIV-infected children is 3.42 per 100-person year [6]. This problem has a significant economic burden in low and middle- income countries [1]. Similar to other Sub-Saharan countries, tuberculosis remains a major health issue among HIV-infected children in Ethiopia, with an incidence rate of 4.33 cases per 100 person-years [7].

The occurrence of tuberculosis (TB) among children on ART treatment is 24.2% to 32% in Nigeria [8-10] and 15.2% in Ethiopia [11], while the incidence of TB among children with HIV varies from 0.83 to 2.3 in China [12], 7 per 1000 person-years in Thailand [13], 4 in South Africa [14], 2 to 2.63 in Ethiopia [15-17], and 17.4 in East Africa [18].

Some studies showed that severe immunosuppression, age less than two years, WHO clinical staging [19-21], underweight [21], a low Cluster of Differentiation 4 (CD4) cell count, anaemia [22], and virological failure [23] contribute to the occurrence of TB among children on ART treatment. To better understand the variety of contexts and the application of new approaches in factors that affect the risk of TB in children living with HIV, additional investigation is necessary.

The achievement of Ethiopia's Sustainable Development Goals (SDGs) and the end-TB strategy
targets established by the World Health Organization (WHO) and the United Nations, which aim

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to reduce tuberculosis cases by 80% and deaths from tuberculosis by 90%, provide support for
this study [3, 24]. The political declaration of the UN high-level meeting on TB held in WHO
plans to reach TB Preventive Treatment (TPT) at least 90% of people with HIV in 2027 [25].

Ethiopia has adopted a test-and-treat strategy since June 10, 2014, for all children initiating ART
regardless of CD4 cell count and WHO clinical staging, aiming at the reduction of HIV-related
mortality and morbidity [26].

Despite this intervention, there is a paucity of evidence of the overall incidence of TB in children enrolled in the Amhara region after the test and treat strategy. In addition to previous studies, this finding covers a wide range of public institutions, and in this study, rapid initiation of ART and Dolutegravir (DTG)-contained ART drugs were incorporated as independent variables to identify the incidence of TB. The current study population also consists of newly enrolled pediatric HIV care patients, rather than ever enrolled on antiretroviral therapy. Timely and recent evidence is very crucial. Furthermore, more research is required to incorporate these variables and new strategies. The findings will help decision-makers and policymakers at different levels with HIV/AIDS care and assistance.

Therefore, this study aimed to assess the incidence of TB and its predictors among HIV-infected
 children enrolled in ART in the Amhara Region.

37 111 Methods

³⁹ 112 Study Design, setting, and period ⁴⁰

A multicentre institution-based retrospective follow-up study was conducted among HIV-positive children enrolled at Amhara region comprehensive specialized hospitals from July 2014 to March 2022. In Ethiopia, Comprehensive Specialized Hospitals represent the highest level of healthcare facilities (Tertiary level of health services) which provides advanced medical services, specialized care, and training centre for health professionals.

The Amhara region is located in the Northwestern, Northeastern, and North-central parts of
Ethiopia, with an estimated area of 159,173.66 square kilometers. The most recent estimated
population in this region is 30,848,988 [27]. In this region, there are 81 hospitals; among those,

eight are comprehensive specialized and teaching hospitals: the University of Gondar, Tibebe-Ghion, Felege Hiwot, Debre Markos, Debre Tabor, Dessie, Woldia, and Debre Birhan.

123 Those hospitals have been providing ART care and support as part of the National AIDS Control 124 Program. Among the total number of Comprehensive Specialized Hospitals, seven were included 125 in the study area, except Tibebe-Ghion, due to an insufficient number of study participants. A 126 total of 1095 children were newly enrolled in HIV care in the Amhara region from July, 2014 to 127 March, 2022.

⁶ 128 **Population and eligibility**

The source population for this study comprised all HIV-infected children who were enrolled in the pediatric HIV care clinics at comprehensive specialized hospitals in the Amhara Region and had a minimum of one month of ART follow-up. HIV-positive children who were newly enrolled in the pediatric HIV care clinic in Amhara Region from July, 2014 to March, 2022 were the study population. Children with HIV who already had TB before starting ART and records with incomplete baseline information (CD4 count, WHO staging, haemoglobin level, weight, and height) and unknown dates of ART initiation and TB occurrence were excluded from the study. (Supplementary Figure 1)

3 137 Sample size determination

The sample size was determined based on key predictors, including height for age, WHO clinical staging, and ART adherence level. Using STATA version 17 and the Cox model, the calculation was performed under the following assumptions, a critical value ($Z\alpha/2$) of 1.96 for a 5% significance level, a critical value ($Z\beta/2$) of 0.84 for 20% power, an event probability of 0.167 [28], and the probability of withdrawal was 0.15 using an adjusted hazard ratio (AHR). (Table 143 1)

Table 1: Estimated sample size determination by predictor variables for HIV-infected children
on ART, by using STATA version 17, cox-model

Variables	Hazard Ratio	Power	Probability of withdrawal	Probability of event	Sample (n)	size
Height for Age Z score	2.14	80%	0.15	0.167	383	

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WHO clinical staging	3.23	80%	0.15	0.167	161
ART adherence	2.05	80%	0.15	0.167	430

Sampling procedures, and sampling technique

From the calculated sample sizes, the largest sample size (430) was selected as a sample for this study. The sample was allocated proportionally to those comprehensively specialized hospitals in the Amhara region, and records were selected using simple random techniques. (Supplementary Figure 2)

Variables of the study

The outcome variable for this study was the occurrence of TB during the follow-up period. The independent variables were socio-demographic characteristics: age, sex, residence, current parent's status, educational status of the caregiver, HIV disclosure status, and marital status of the caregiver. Baseline clinical, nutritional, and laboratory characteristics: CD4 count, WHO clinical staging, haemoglobin level, anthropometric indices, previous OIs, functional and developmental status. ART and medication-related characteristics: baseline ART regimen, DTG containing ART drugs, presence of regimen change, level of ART adherence, TPT, CPT, ART side effects, initiation of ART.

Operational definition of the variables

Events: The occurrence of TB among HIV-infected children during the follow-up period at any time after enrollment in the pediatric HIV care clinic, as confirmed by a health care professional. Tuberculosis (TB) is defined as a diagnosis of either pulmonary tuberculosis (PTB) or extra-pulmonary tuberculosis (EPTB) as documented in children's medical records during the study period.

Censored: Children, who were lost to follow-up, dropped out, transferred out, died due to any causes, or completed the study period before developing TB.

Pulmonary Tuberculosis (PTB): was diagnosed based on the national TB diagnosis guideline, which primarily affects the lungs, and diagnosis is based on clinical symptoms, chest X-ray findings, sputum smear microscopy, or molecular tests such as GeneXpert, or histopathology.

Page 9 of 32

BMJ Open

Extra-pulmonary Tuberculosis (EPTB): Defined as TB that affects organs outside the lungs, such as lymph nodes, pleura, bones and joints, meninges, or the abdomen. Diagnosis may involve biopsy, imaging, or fluid analysis. Wasting: if the weight for height (WFH) Z-score is less than -2 SD for less than five years, or if the body mass index (BMI) for age Z-score is less than -2 SD for greater than five years [29]. **ART adherence levels:** categorized as follows: good (\geq 95% compliance or \leq 3 missed doses per month), fair (85–94% compliance or 4–8 missed doses per month), and poor (<85% compliance or ≥ 9 missed doses per month), as recorded by ART health personnel [29]. **Rapid initiation of ART** refers to starting antiretroviral therapy on the same day as HIV diagnosis or within seven days afterward [30]. Urban areas are officially designated towns with municipal structures and better access to services like education, healthcare, electricity, and water[31]. **Rural areas** are primarily agricultural or pastoral, with limited infrastructure such as roads, electricity, healthcare, and schools, and characterized by dispersed settlements[31].

Anaemia was defined as having a haemoglobin level of less than 10 mg/dl [32].

Data collection tool and procedures

Data were retrospectively collected using a data extraction tool based on Ethiopian ART guidelines. Information was obtained from ART intake form, follow-up form, and children's medical charts for patients newly enrolled at ART clinics from July 2014 to March 2022 [29]. Data was extracted for one month, from May 17 to June 15, 2022. The variables include socio-demographic, clinical, laboratory, ART-related, and medication-related factors. Data collection was conducted by seven bachelor's degree nurses who had smartphones and prior experience with ART follow-up, as well as basic training in ART management.

Data quality control

The data extraction tool was pretested on 5% of the sample size at the University of Gondar Comprehensive Specialized Hospital prior to the actual data collection. Additionally, one-day onsite training was conducted for data collectors and supervisors, covering topics such as reviewing ART follow-up and medical records, data collection techniques, and the study's objectives. Data collection was carried out using the KoBo toolbox, which was prepared with relevant restrictions by trained nurses working in Hospitals. Besides, the data collector and

principal investigators carefully monitored the entire data collection process and dailysubmission report.

203 Data processing and analysis

The KoBo toolbox [33] was used for data collection, then exported and imported into STATA version 17 statistical software [34] for final analysis. Additionally anthropometric indices were created using the WHO anthro and WHO anthroPlus software. To describe the data, descriptive statistics including mean (±SD), percentage, and frequency were employed. The Variance inflation factor (VIF) was used to check the association between predictor variables; the average VIF was found to be 1.18, which indicates no significant multicollinearity.

A separate graph of Kaplan-Meier survival functions and the log-rank test were estimated for each categorical variable to compare survival between different exposure groups. The proportional hazard assumption (PHA) was checked using both graphical and statistical global tests and revealed that the PHA was satisfied. The log-likelihood and Akaike Information Criteria (AIC) were applied to select the best-fitted model, and a model with a minimum AIC was considered the best-fitted model.

In our survival analysis, we consider parametric models including the Exponential, Weibull, Log-normal, Log-logistic, and Gompertz regression models. Models were evaluated based on the Akaike Information Criterion (AIC) to identify the best fit. The Gompertz model, with the lowest AIC value of 236.02, was selected as the best-fitted model. This indicates that among the models considered, the Gompertz model provided the best balance between model fit and complexity.

In addition, the goodness-of-model fitness was also checked using the Cox-Snell residual test. Variables having a p-value less than 0.25 in the Bivariable analysis were fitted into the multivariable Gompertz regression model. A hazard Ratio with a 95% CI was used to determine the strength of the association. Variables with a p<0.05 in multivariable analysis were considered statistically significant.

To handle and manage missing data, multiple imputations using multivariable chained equations (MVCE) were carried out to handle and manage missing data. The variables missing at random (MAR) are clarified by the "Little test" results for continuous variables and graphical patterns for

Page 11 of 32

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1 cal variables, making the application of multiple imputations straightforward. nore, sensitivity analysis was performed utilizing both descriptive and inferential I techniques to confirm if a significant difference was detected between the outputs of nal and imputed data. and public involvement

and the public were not directly involved in the design, conduct and dissemination of y.

s:

cio-Demographic characteristics

of 430 medical records of HIV-infected children on ART were reviewed. Of these, 421 were included in this study, and the remaining percent were excluded from the analysis ata incompleteness. The mean (SD) age of the study participant was 7.58 (± 4.02) years; d was found in the age group of 5-9 years. Nearly two-thirds (58.43%) were male, and re from urban areas. (Table 2)

Socio-demographic characteristics of HIV-infected children on ART in Amhara comprehensive specialized hospitals, Ethiopia, 2022 (n=421)

Variables	Categories	Frequency(n)	Percentage (%
Age Sex Residence			
-	Less than 5 Years	122	28.98
	5-9 Years	145	34.44
	10-14 Years	154	36.58
Sex			
	Female	175	41.57
	Male	246	58.43
Residence			
	Rural	126	29.93
	Urban	295	70.03
Current parent s	tatus		
-	Both parents alive	290	68.88
	One parent alive	113	26.84
	Both parents deceased	18	4.28
Educational State	us of the caregiver		
	No formal education	144	34.2
	Primary	150	35.63
	Secondary	67	15 91

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	Tertiary (College &	above) 60	14.25
Marital status o	f the caregiver		
	Married	228	54.16
	Unmarried	87	20.67
	Divorced	70	16.63
	Widowed	36	8.55
HIV status of th	e parents		
	Non-reactive	158	37.53
	Reactive	263	62.47
Disclosure statu	s the child		
	Yes	220	52.26
	No	201	47.74

2. Baseline clinical, laboratory, nutritional and ART medication related characteristics

At baseline, 79.9% of children were in WHO clinical stages I or II. The median CD4+ count was 421 (IQR: 403, 1017) cells/l, and one-fifth (20.19%) had CD4+ below the threshold level. The median haemoglobin level was 12.3 (IQR: 10.7, 13.6) mg/dl, and 17.34% had less than 10 mg/dl haemoglobin level. Nearly 30% and 50% of children were wasted and stunted at baseline, respectively. Out of 421 HIV-infected children, 296 (70.31%) had a good ART drug adherence level. More than two-thirds (63.42%) of children had never received TPT, and 45.13% of children had never taken ART within seven days of its duration. (**Supplementary table 1**)

3. Follow-up time and incidence of TB incidence

A total of 421 children followed from 1 to 89 months. The mean follow-up time was 42 months (14.57 to 70.07 months). The total time at risk was 1484.75 child-year observations (CYO). New TB cases were observed in 32 (7.6%) children; the overall TB incidence rate was 2.16 (95% CI: 1.52, 3.05) per 100 CYO. (Figure 1)

The incidence rate of TB was 3.98 (95% CI, 1.99, 7.95) per 100 CYO in the six months of ART initiation and decreased to 0.33 (95% CI, 0.05, 2.34) per 100 CYO after three years of ART initiation. The cumulative probability of TB incidence at the end of two, four, and six years of the study was 0.9636, 0.9309, and 0.9045, respectively. The incidence rate of TB was 8.09 (95% CI, 5.03, 13.01) per 100 CYO among anemic children, while it was 1.18 (95% CI, 0.7, 1.95) per 100 CYO among non-anemic children. (Supplementary Figure 3, 4, 5, and 6)

265 4. Model comparison

Page 13 of 32

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The proportional hazard assumption, semi-parametric, and parametric proportional hazard models were fitted to estimate the incidence of tuberculosis and its predictors among HIV-infected children in the Amhara region. The graphical test and global test (P-value = 0.2980) confirmed the proportional hazard assumption (PHA). The most fitted model was chosen using Akaike information criteria (AIC = 236.02), Bayesian information criteria (BIC = 304.74), and log-likelihood (-138.43). The results outperformed the Cox-proportional hazard and other parametric models in all three comparison techniques. As a result, interpretations and conclusions were based on the Gompertz model. (Supplementary Table 2)

- The Cox-Snell residual test checked the goodness of fit. (Figure 2) The shared frailty was
 estimated, (theta: 1.89e⁻⁰⁷), and the distribution of unmeasured variables is indifferent between
 the comprehensive specialized hospitals.
- 24 277 5. Predictors of incidence of Tuberculosis
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In bi-variable parametric survival Gompertz regression: parental status of the caregivers, educational status of the caregivers, baseline of WHO clinical staging, CD4+ count, haemoglobin status, functional and developmental status, regimen change, ever taking TPT, ever taking CPT, ART adherence level, previous opportunistic infections, dolutegravir (DTG)-contained ART drugs, wasting, and rapid initiation of ART were found to be significant predictors of TB among children in ART. In the final multivariable Gompertz regression model, only baseline haemoglobin, ever taking TPT, wasting, and rapid initiation of ART significantly increased the incidence of tuberculosis.

Anaemic children had 3.83 times [AHR: 3.83 (95% CI: 1.46, 10.04)] higher risk of getting TB infections than those in non-anemic children. Likewise, the risk of developing TB for children who were not given TPT was 3.78 times [AHR: 3.78 (95% CI: 1.44, 9.94)] higher as compared with those who were given TPT at baseline. Additionally, the hazard of TB among children with wasted children at baseline was 2.53 times [AHR: 2.53 (95% CI: 1.19, 5.38)] more likely as compared to their well-nourished counterparts. Furthermore, children had late ART initiation 3.27 times [AHR: 3.27 (95% CI: 1.26, 8.46)] increased risk of developing TB compared to rapid initiation of ART (Table 3).

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	s among child	aren ol		in Am	nara Region C	omprenensive Spe	cialized
Hospitals, E	tniopia, 2022 (n = 421	.).				
Variables	Status				CHR (95% CI)	AHR (95% CI)	P value
	Event (n=32)	Cer	nsored (1	n=389)			
Parental stat	tus of the child						
Both parents	alive	19	271	1		1	
One or both p	parents dead	13	118	1.77 (1.88, 3.59)	0.8 (0.32, 2.02)	0.64
Educational	status of the c	aregive	er		, ,		
No formal ed	lucation	9	135	1.27(0.49, 3.29)	0.72(0.25, 2.04)	0.53
Primary		15	117	2.05(0.87, 4.83)	0.97(0.33, 2.81)	0.96
Secondary an	d Tertiary	8	137	1	, ,	1	
WHO Clinic	al staging					1	
Stage I & II		17	328	1		1	
Stage III & I	V	15	61	5.47	(2.73, 11.00)	1.71(0.62, 4.71)	0.299
CD4 cell cou	unt						
Above thresh	hold	21	315	1		1	
Below thresh	old	11	74	2.89(1.39, 6.02)	1.59(0.59, 4.31)	0.357
Anaemia							
No		15	333	1		1	
Yes		17	56	7.26(3.62, 14.56)	3.83 (1.46, 10.04)	0.006
Working an	d appropriate	motor	developi	mental s	status		
Yes		16	267	1		1	
No		16	122	2.39(1.19, 4.8)	1.66(0.77, 3.61)	0.196
Adherence l	evel of ART		_				
Optimal		16	280	1		1	
Sub-optimal		16	109	2.79(1.39, 5.59)	0.92(0.36, 2.4)	0.874
ART regime	n change		1				
Yes		15	199	1		1	
No		17	190	1.63(0.81, 3.27)	0.77 (0.32, 1.87)	0.57
Ever taking	tuberculosis p	reventi	ve treat	ment(Tl	PT)		
Yes		7	260	1		1	
No	~ .	25	129	7.55(3.26, 17.47)	3.78(1.44, 9.94)	0.007
Ever taking	Cotrimoxazol	e preve	entive th	erapy(C	(T4)	-	
Yes		21	324	1			
No	• • •	11	76	2.68(1.29, 5.57)	1.28(0.5, 3.27)	0.601
Weight for h	neight	1 -	0.01				
No wasting		15	284	1			0.015
Wasting		17	105	2.9(1	.45, 5.81)	2.53(1.19, 5.38)	0.016
Previous opp	portunistic info	ections	0.00	4			
No		17	306	1			0.7
Yes		15	83	3.43(1.71, 6.88)	1.32 (0.54, 3.19)	0.54

Doultegravir (DTG)	contained d	rugs			
Yes	6	63	1	1	
No	26	326	0.46 (0.18, 1.14)	0.37 (0.13, 1.03)	0.059
Initiation of Antiretr	oviral thera	ıpy			
Rapid Initiation	6	225			
Late Initiation	26	164	4.41(1.81, 10.74)	3.27(1.26, 8.46)	0.015

297 * Significant at a 0.05, 1: reference, *CHR, crude hazard ratio, AHR, Adjusted hazard ratio

298 Discussion

This study aimed to assess the TB incidence rate and its predictors in children on ART inAmhara region comprehensive specialized Hospitals.

In this study, HIV-infected children on ART were 2.16 (95% CI 1.52, 3.05) per 100 child-years observations(CYO), which is consistent with study conducted in Debre Markos 2.63 [35], in Northeast Ethiopia 2.0 [36], and Southern Ethiopia 2.6 per 100 CYO[37]. This finding is lower than study conducted in Northern Ethiopia [38], in Benishangul Gumuz region in Northwest Ethiopia [39, 40], in Adama Referral Hospital and Medical College [41], in Southwest Ethiopia [42], and in Tanzania [43]. This could be due to higher burden of tuberculosis in resource-limited settings[44], and also might be due to the difference in sociodemographic and baseline clinical characteristics of the study participant, changes in the study period and setting.

However, our study is higher than studies conducted in New York City [45], in Ireland and the United Kingdom [46], and in China [47]. This could be because the general population in high-income countries has a low incidence rate of tuberculosis. In addition, the use of early TB diagnosis and prevention techniques, along with the accessibility of modern technologies, significantly lowers the incidence of tuberculosis [48]. Furthermore, there are higher cases of tuberculosis (TB) in Ethiopia due to poverty, overcrowding, large families, and subpar living conditions.

Children who were classified as anemic had a 3.83 times higher risk of getting TB infections than non-anemic children. Supported by Northern Ethiopia [38] and Benshangul Gumuz [40], this is because anaemia highly prevalent in TB cases due to persistent inflammation or chronic diseases[49], and anaemia appears to have predictive value for incident TB disease during ART [50].

Likewise, the risk of developing TB for children who were not getting TPT was 3.78 times higher as compared with those who were taking TPT at baseline. This finding is supported by different studies conducted in Ethiopia [38, 51], Tanzania [52], and global data[53]. TPT decreases mycobacterium load and reduces the progression of latent TB bacilli to active TB. Increases in mycobacterial load were associated with progressive impairment of mycobacterium specific T-cell responses and increased the occurrence of active TB [54].

Additionally, the synergetic effect of ART and TPT in reducing active TB incidence is increased as a result of CD4+ T cell recovery and viral load suppression [25]. Lower TPT intake is associated with an increased incidence of tuberculosis; in our study, only 63.42% of children with HIV took TPT.

The hazard of TB among children with wasting at baseline was 2.53 times more likely as compared to their counterparts. This finding is supported by studies conducted in Northern Ethiopia, Debre Markos [35, 38], and Southern Ethiopia [55]. This could be explained by the fact that malnutrition causes nutritionally acquired immune dysfunction and increases host susceptibility to infections.

Under-nutrition also weakens the immune system through atrophy of the thymus, spleen, and lymph nodes and reduces cell-mediated immunity [56, 57]. Immunological and clinical recovery are directly associated with nutritional status [58].

Furthermore, children with late ART initiation had a 3.27 times increased risk of developing TB when compared to those with rapid ART initiation. This finding was in agreement with those of a study done in Ethiopia [35]. Initiation of ART early after confirmation of HIV-infection, even at a higher CD4 cell count, helps to reduce the occurrence of TB. This could be attributed to the early initiation of ART, which helps minimize delays, enhances viral suppression rates in children with HIV, improves retention in care, and reduces the risk of HIV transmission [59].

This study was conducted in a tertiary-level, comprehensive specialized hospitals, which may introduce biases related to healthcare accessibility, particularly in LMIC with significant geographic and socioeconomic disparities. These hospitals primarily serve urban populations and provide advanced medical services, potentially limiting the generalizability of findings to

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children in rural areas. A substantial proportion of ART children in the region, especially thosewith limited access to healthcare, were not represented.

351 Strength and limitations of the study

As a strength, this study was multicentre, covering wide ranges in geographical areas of specialized hospitals, and used a longer follow-up period for better estimation of the incidence of tuberculosis. There are certain inherent limitations to the current study. Owing to financial limitations, factors such as housing characteristics, the environment, and family history of smoking-related factors were evaluated retrospectively rather than prospectively in order to determine the incidence and predictors of TB following the start of ART. Additionally, the study excluded children who began antiretroviral therapy (ART) at the outset and got tuberculosis within a month or less. This may have led to an underestimation of the incidence of tuberculosis.

24 360 Conclusion and Recommendation

In this study, the incidence of TB was found to be high. Anaemia, wasting, TB preventive therapy, and early initiation of ART were factors found to be significant predictors of TB incidence in HIV-infected children receiving ART. Additionally, clinicians should emphasize early screening and maximizing nutritional supplements for HIV-infected children to decrease the incidence of TB in those individuals. Furthermore, it needs emphasis on early detection and treatment of anaemia and TB preventive therapy, counseling on nutritional improvement, and timely initiation of ART to avert TB. Future studies should include data from community-level health facilities to ensure more representative and equitable findings.

39
40369Abbreviations

AHR: Adjusted Hazard Ratio; ART: Antiretroviral Therapy; CPT: Cotrimoxazole Preventive Therapy; CD4: Cluster of Differentiation 4; OIs: Opportunistic Infections; CYO: Child-Year-Observations; SD: Standard Deviation; TB: Tuberculosis; TPT: Tuberculosis Preventive Treatment; UoG: University of Gondar; WHO: World Health Organization; AIC: Akakie Information Criterion; BIC: Bayesian Information Criterion; PHA: proportional hazard assumption

376 Ethical approval and consent to participate

This study used secondary data or medical charts; the study was approved by the Institutional Review Board of the University of Gondar, College of Medicine and Health Sciences, on behalf of the Ethical Review Committee of the School of Nursing (SN/212/2022) with a waiver of informed consent. Finally, before collecting the data, a letter of permission to collect the data was obtained from each Comprehensive Specialized Hospital administrator to collect the data from each ART clinic. At the time of abstraction, personal identifiers (names and contact numbers) were excluded. The data were kept strictly confidential and used only for study purposes. All of the procedures were carried out by considering the Declaration of Helsinki. Patient and public involvement

Patients and the public were not directly involved in the design, conduct and dissemination ofthis study.

388 Acknowledgment

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390 specialized Hospital, and data collectors.

391 Authors' contributions

GBM worked on developing the research idea, designing the study, being involved in proposal writing, training and supervising the data collectors, analyzing and interpreting the results, and preparing the manuscript. BTL, FDB, and WTW played their role in critically revising the proposal, participating in its design, analyzing and interpreting the results, and writing the manuscript. All authors were involved in reading and approving the final manuscript. GBM is responsible for the overall content as the guarantor.

45 398 Funding

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⁵⁰ 400 Availability of data and materials

52 401 Data will be available upon reasonable request from the corresponding author.

54 402 Consent for publication
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403 Not applicable.

1 2						
3 4	404	Competing interests				
5	405	The authors declare that they have no competing interests.				
$\begin{array}{c}1\\2\\3\\4\\5\\6\\7\\8\\9\\10\\11\\23\\14\\15\\16\\7\\8\\9\\10\\12\\23\\24\\25\\26\\27\\28\\9\\01\\32\\33\\45\\36\\7\\8\\9\\01\\12\\33\\45\\46\\45\\46\end{array}$	406 407 408	Figure 1: Overall Kaplan-Meier estimate of TB-free probability in children on ART in Amhara Region comprehensive specialized Hospitals, Ethiopia Figure 2: The goodness of fit test for the Gompertz regression model for the incidence of TB				
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12 13	410	Supplementary Figure 1. Diagram for study population selection for HIV-infected children on				
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10 11 12 13 14 15 16 17 18 9 20 21 22 23 25 26 27 28 29 31 23 34 35 37 38 9 40 41 42 34 45 46 47 48 9 50 152 35 45 56 7 89 60	428	Ethiopia				
46 47	429	Supplementary Table 2: Summary of model comparison between Semi parametric and				
48 49	430	parametric Cox-regression model using log-likelihood, AIC, and BIC criteria				
50	431	References:				
51 52 53 54 55 56	432 433 434 435	 World Health Organization(WHO). <i>Global Tuberculosis Report</i>. 2023; Available from: https://reliefweb.int/report/world/global-tuberculosis-report-2023?gad_source=1. Orginization, W.H., <i>WHO consolidated guidelines on tuberculosis</i>, in <i>Module 5: Management of tuberculosis in children and adolescents</i>. 2022, WHO. 				
57 58		15 Page				
59 60		For peer review only - http://bmiopen.bmi.com/site/about/quidelines.xhtml				
00						

2			
3	436	3.	Orginization, W.H., Global tuberculosis report, 2023, WHO: Geneva,
4	437	4.	World Health Organization (WHO). <i>Global HIV programme</i> . 20121: Available from:
5	438		https://www.who.int/teams/global-hiv-hepatitis-and-stis-
6 7	439		programmes/hiv/treatment/tuberculosis.
/ 8	440	5.	Verkuijl, S., et al., Global reporting on TB in children and adolescents: how far have we come and
9	441		what remains to be done? IJTLD OPEN, 2024, $1(1)$; p. 3-6.
10	442	6.	Wondmeneh, T.G. and A.T. Mekonnen. The incidence rate of tuberculosis and its associated
11	443		factors amona HIV-positive persons in Sub-Saharan Africa: a systematic review and meta-
12	444		analysis. BMC Infectious Diseases. 2023. 23 (1): p. 613.
13	445	7.	Azanaw, M.M., et al., Incidence and predictors of tuberculosis among HIV patients after initiation
14	446		of antiretroviral treatment in Ethiopia: a systematic review and meta-analysis. Tropical Medicine
15	447		and Health 2021 49 (1): p 18
16	448	8	Daniel, O., et al., HIV-TB co-infection in children: associated factors and access to HIV services in
17 10	449	0.	Lagos, Nigeria, 2015, 5(3): p. 165-169.
10	450	9	Ebonyi A Ω et al. Prevalence of and risk factors for nulmonary tuberculosis among newly
20	451	5.	diagnosed HIV-1 infected Nigerian children 2016 6 (1): n 21
21	452	10	Amuta F. I. Tsaku, and I. Akvala. A retrospective study on the enidemiological trend of human
22	453	10.	immunodeficiency virus (HIV) and nulmonary tuberculosis (PTB) co-infection in Nasarawa state
23	453		Nigeria 2013
24	455	11	Kebede E et al Incidence and predictors of nulmonary tuberculosis among children who
25	456		received antiretroviral therapy (ART) Northwest Ethiopia: a multicenter historical cohorts study
26	457		2009–2019 2022 2022
27	458	12	Mu W et al. Incidence and associated factors of nulmonary tuberculosis in HIV-infected
20	450 159	12.	children after highly active antiretroviral therapy (HAART) in China: a retrospective study 2014
30	460		26 (9): n 1127-1135
31	461	13	Salvadori N et al Incidence of tuberculosis and associated mortality in a cohort of human
32	462	15.	immunodeficiency virus-infected children initiating antiretroviral therapy 2017 6(2): p 161-167
33	462	1/	Brennan A et al. Risk factors associated with TB in children receiving ART in a South African
34	405	17.	multicenter HIV cohort 2014 22: n 484-5
35	465	15	Wondifraw F B et al. Incidence and predictors of tuberculosis among children on antiretroviral
30 27	466	15.	therapy at northeast Ethionia comprehensive specialized hospitals 2022: A multicenter
38	467		retrospective follow-up study 2022 8(12)
39	468	16	Endalamaw $A \in H$ Engeda and N I B r n Tezera <i>Incidence</i> of tuberculosis in children on
40	469	10.	antiretroviral therapy: a retrospective cohort study 2018 11 : p 1-7
41	405	17	Virdaw KD et al. Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on
42	471	17.	the incidence of tuberculosis in people living with HIV in Ethionia 2014 9(8): p. e104557
43	472	18	Ciaranello A et al Incidence of WHO Stage 3 and 4 events tuberculosis and mortality in
44	172	10.	untreated HIV-infected children enrolling in care before 1 year of gae: an IEDEA (International
45 46	473		Enidemiologic Databases to Evaluate AIDS) East Africa regional analysis 2014 33 (6): p. 623
40 17	475	19	Atalell K A N Birban Teheje and D T I P o Ekubagewargies Survival and predictors of
48	475	15.	mortality among children co-infected with tuberculosis and human immunodeficiency virus at
49	470 177		University of Gondar Comprehensive Specialized Hospital Northwest Ethiopia. A retrospective
50	477 178		follow-un study 2018 13 (5): n e01971/15
51	470 470	20	Hicks R et al Malnutrition associated with unfavorable outcome and death among South
52	480	20.	African MDR-TR and HIV co-infected children 2014 18 (9) n 1074-1083
53	400 401	21	Alemu YM G Andargie and FIPO Gebeve High incidence of tuberculosis in the absence of
54 55	487	4 1.	isoniazid and cotrimoxazole preventive therapy in children living with HIV in porthern Ethiopia: a
22 56	483		retrospective follow-up study 2016 11 (4): p. e0152941
50 57	COF		$\mathbf{L}_{\mathbf{L}} = \mathbf{L}_{\mathbf{L}} = $
58			16 Page
59			

60

60

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484	22.	Nan, L., et al., Incident tuberculosis and risk factors among HIV-infected children in Dar es
485		Salaam, Tanzania. 2013. 27 (8): p. 1273.
486	23.	Anigilaje, E.A., et al., <i>Tuberculosis, before and after antiretroviral therapy among HIV-infected</i>
487		<i>children in Nigeria: what are the risk factors?</i> 2016. 11 (5): p. e0156177.
488	24.	Health., M.o., Health Sector Transformation Plan II(HSTP- II). February, 2021: Addis Ababa.
489	25.	Assembly, U.N.G., Political declaration of the high-level meeting on the fight against
490		tuberculosis. 25 September 2023, WHO. p. 1-15.
491	26.	FMOH, National guidlines for comprhensive HIV prevention ,care and treatment in Ethiopia.
492	27	2014, FMOH: Addis Ababa. p. 1-165.
493	27.	Ethionia for All Bogions At Morada Loval from 2014 2017 Archived from the original on 6
494 405		
495	70	Julie 2018. , 2018. Mondifram, E.B. et al. Incidence and predictors of tubersulosis among shildren on antiretrouiral
490	28.	therapy at porthoast Ethiopia comprehensive specialized bespitals, 2022; A multicenter
497		retrospective follow up study. Holiven, 2022, 9 (12)
490	20	FRIOSPECIAE Joinow-up Study. Heliyon, 2022. 8(12).
499 500	29.	Providers M. a. Haalth. Editor. Bayisad on August. 2021. Ethiopian Edderal Ministry of Health
500		Addic Ababa, p. 1, 502
501	30	Auus Ababa. p. 1-502.
502	50.	initiation of antiretroviral therapy 2018
504	31	Ethionia C S A o Population and Housing Census Report: 2013: Addis Ababa Ethionia
505	32	Chanie F S et al. Incidence of advanced opportunistic infection and its predictors among HIV
506	52.	infected children at Debre Tabor referral Hospital and University of Gondar Compressive
507		specialized hospitals. Northwest Ethiopia, 2020: A multicenter retrospective follow-up study
508		Helivon, 2021, 7 (4).
509	33.	Initiative., H.H., KoBoToolbox [Internet]. Cambridge. MA: Harvard University: 2023. Available
510		from: https://www.kobotoolbox.org. 2023.
511	34.	StataCorp., Stata Statistical Software: Release 14. College Station, TX: StataCorp LLC. 2021.
512	35.	Endalamaw, A., E.H. Engeda, and N. Tezera, Incidence of tuberculosis in children on antiretroviral
513		therapy: a retrospective cohort study. BMC research notes, 2018. 11: p. 1-7.
514	36.	Wondifraw, E.B., et al., Incidence and predictors of common opportunistic infection among HIV-
515		infected children attending antiretroviral treatment clinic at Northeast Ethiopia, public hospitals
516		2022: A multicenter retrospective follow-up study. Annals of Medicine and Surgery, 2022. 84: p.
517		104910.
518	37.	Yirdaw, K.D., et al., Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on
519		the incidence of tuberculosis in people living with HIV in Ethiopia. PloS one, 2014. 9 (8): p.
520		e104557.
521	38.	Alemu, Y.M., G. Andargie, and E. Gebeye, High Incidence of Tuberculosis in the Absence of
522		Isoniazid and Cotrimoxazole Preventive Therapy in Children Living with HIV in Northern Ethiopia:
523		A Retrospective Follow-Up Study. PLoS One, 2016. 11(4): p. e0152941.
524	39.	Kebede, F., et al., Incidence and predictors of pulmonary tuberculosis among children who
525		received antiretroviral therapy (ART), Northwest Ethiopia: a multicenter historical cohorts study
526		2009–2019. Journal of Tropical Medicine, 2022. 2022 .
527	40.	Fassikaw, K., et al., HIV/AIDS associated tuberculosis occurance on art initiated children in North
528		West Ethiopia 2020. Journal of Pulmonary & Respiratory Medicine, 2021. 11: p. 6.
529	41.	Beshir, M.T., et al., Incidence and predictors of tuberculosis among HIV-positive children at
530		Adama Referral Hospital and Medical College, Oromia, Ethiopia: a retrospective follow-up study.
531		Epidemiology and health, 2019. 41 .
		17 Page
		For peer review only - http://bmiopen.bmi.com/site/about/guidelines.xhtml

1

58

59

2			
3	532	42.	Tiruneh, F. and Y. Deyas, How Far Does Highly Active Antiretroviral Treatment Reduce TB
4	533		Incidence amona Children? A Marainal Structural Modelina Analysis. Southwest Ethiopia.
5	534		Ethiopian Journal of Health Sciences, 2020, 30 (5).
6	535	43	Li, N., et al., Incident tuberculosis and risk factors among HIV-infected children in Tanzania. Aids
/	536	131	2013 27 (8): n 1273-1281
8	537	11	Bagechi S WHO's global tuberculosis report 2022 in The Lancet Microbe 2023 n e20
9 10	520	44. 15	Themas D. et al. Tuberculosis in human immunodeficiency virus infected and human
10	520	45.	immunodoficionou virus evaced children in New York City. The Dedictric infectious disease
12	539		inimunouejiciency virus-exposed children in New York City. The Pediatric Infectious disease
13	540	10	Journal, 2000. 19(8): p. 700-706.
14	541	46.	Turkova, A., et al., Prevalence, Inclaence, and associated risk factors of tuberculosis in children
15	542		with HIV living in the UK and Ireland (CHIPS): a cohort study. The Lancet HIV, 2015. 2 (12): p.
16	543		e530-e539.
17	544	47.	Mu, W., et al., Incidence and associated factors of pulmonary tuberculosis in HIV-infected
18	545		children after highly active antiretroviral therapy (HAART) in China: a retrospective study. AIDS
19	546		care, 2014. 26 (9): p. 1127-1135.
20	547	48.	Scott, C., et al., <i>Tuberculosis trends—United States, 2014</i> . Morbidity and Mortality Weekly
21	548		Report, 2015. 64 (10): p. 265.
22	549	49.	Gil-Santana, L., et al., Tuberculosis-associated anemia is linked to a distinct inflammatory profile
23	550		that persists after initiation of antitubercular therapy. Scientific reports, 2019. 9(1): p. 1381.
24 25	551	50.	Kerkhoff, A.D., et al., The predictive value of current haemoglobin levels for incident tuberculosis
25 26	552		and/or mortality during long-term antiretroviral therapy in South Africa: a cohort study. BMC
20	553		medicine, 2015. 13 (1): p. 1-13.
28	554	51.	Geremew, D., et al., The protective effect of isoniazid preventive therapy on tuberculosis
29	555		incidence amona HIV positive patients receiving ART in Ethiopian settings; a meta-analysis. BMC
30	556		infectious diseases. 2019. 19 (1): p. 1-9.
31	557	52.	Sabasaba, A., et al., Effect of isonigzid preventive therapy on tuberculosis incidence and
32	558	01	associated risk factors among HIV infected adults in Tanzania: a retrospective cohort study BMC
33	559		infectious diseases 2019 19 (1): n 1-8
34	560	53	Avieko I et al. Efficacy of isoniazid prophylactic therapy in prevention of tuberculosis in
35	561	55.	children: a meta-analysis BMC infectious diseases 2014 14(1): p. 1-10
36 27	562	5/	Day CL et al. Patients with tuberculosis disease have Mycobacterium tuberculosis-specific CD8
3/ 20	562	54.	T cells with a pro-apoptotic phenotype and impaired proliferative capacity, which is not restored
20	505		following treatment plos one 2014 0 (4): n c04040
40	504		Johowing treatment. Plos one, 2014. 9 (4). p. 694949.
41	505	55.	therease, D., et al., incluence and predictors of tuberculosis among children receiving antiretroviral
42	500	50	inerapy in the woland zone: A retrospective conort study. PLOS ONE, 2023. 18(9): p. e0291502.
43	567	50.	Bourke, C.D., J.A. Berkley, and A.J. Prendergast, <i>Immune dysjunction as a cause and</i>
44	568		consequence of mainutrition. Trends in immunology, 2016. 37 (6): p. 386-398.
45	569	57.	Katona, P. and J. Katona-Apte, The Interaction between nutrition and infection. Clin Infect Dis,
46	570		2008. 46 (10): p. 1582-8.
47	5/1	58.	Ezeamama, A.E., et al., Age, sex, and nutritional status modify the CD4+ 1-cell recovery rate in
48	572		HIV-tuberculosis co-infected patients on combination antiretroviral therapy. Int J Infect Dis,
49 50	573		2015. 35 : p. 73-9.
50 51	574	59.	Asa E. Radix, M., MPH, PhD, Clinical Guidelines program, Rapid ART Initiation. February 9, 2023:
57	575		MEDICAL CARE CRITERIA COMMITTEE.
53			
54	576		
55			
56			
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Figure 1: Overall Kaplan-Meier estimate of TB-free probability in children on ART in Amhara Region comprehensive specialized Hospitals, Ethiopia

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Supplementary Figure 1: Diagram for study population selection for HIV-infected children on ART in Amhara Region Comprehensive Specialized Hospitals, Ethiopia



Supplementary Figure 2: Schematic diagram of the sampling procedure for among HIVinfected children on ART in Amhara Region Comprehensive Specialized Hospitals, Ethiopia

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Supplementary Figure 3: Kaplan-Meier TB-free survival of anemic status a main predictor variables among children on ART in Amhara region comprehensive Specialized Hospitals, Ethiopia



Supplementary Figure 4: Kaplan-Meier TB-free survival of tuberculosis preventive therapy a main predictor variables among children on ART in Amhara region comprehensive Specialized Hospitals, Ethiopia



Supplementary Figure 5: Kaplan-Meier TB-free survival of Nutritional status a main predictor variables among children on ART in Amhara region comprehensive Specialized Hospitals, Ethiopia

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Supplementary Figure 6: Kaplan-Meier TB-free survival of Initiation of Antiretroviral therapy a main predictor variables among children on ART in Amhara region comprehensive Specialized Hospitals, Ethiopia

Page 31 of 32	Supplementa infected child Ethiopia	ry table 1: Baseline clinical, nutrition BMJ Oper Iren on ART in Amhara Regional Sta	hal, and laboratory ate Comprehensive	e Specialized Hospitals,
1	Variables	Categories	Frequency	Percent (%)
2	CD4 cell cou	int		
3		Above threshold	336	79.81
4		Below threshold	85	20.19
5	Anemia			
6	1 monnu	No	348	87 66
7		Vos	72	17 34
8	Eurofien al at	105	13	17.34
9	Functional st	atus (n=299)		
10		Working	201	67.22
11		A h h - 4	05	21 77
12		Ambulatory	95	31.//
14		Bedridden	3	1.00
15	Development	al status (n=122)		
16		Appropriate	82	67.21
17		Delayed	35	28.69
18		Regressed	5	4.1
19	Wasting			
20	8	No	299	71.02
21		Ves	122	28.98
22	Stunting		1	20.70
23	Stunting	No	210	51 79
24		No	210	31.70
25		Y es	203	48.22
26	Previous Opp	portunistic infections		
27		No	323	76.72
28		Yes	98	23.28
29	WHO Clinica	al staging 🛛 🗸 🗸		
31		Stage I	261	62.00
32		Stage II	84	19.95
33		Stage III	55	13.06
34		Stage IV	21	4.99
35	ART drug ad	lherence level		
36	inter unug uu	Good	296	70 31
37		Fair	68	16 15
38			57	12.54
39	Т Ь Ы		31	13.34
40	I uberculosis	preventive Treatment (TPT) taken		(2.12)
41		Yes	267	63.42
42		No	154 🛁	36.58
43	Cotrimoxazo	le preventive Therapy (CPT) taken		
44		Yes	345	81.95
45		No	76	18.05
40	ART side effe	ect		
48		No	275	65.32
49		Yes	146	34.68
50	Presence regi	imen change	1.10	• 1100
51	i reșence regi	men enunge		
52				
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Page	32	of	32
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Yes No Initiated ART within seven days Yes No	214 207 231 190	50.83 49.17 54.87 45.13
DTG contained ART drugs Yes No	69 352	16.39 83.61



Supplementary Table 2: Summary of model comparison between Semi parametric and parametric Cox-regression model using log-likelihood, AIC, and BIC criteria

Methods	Cox-model	Weibul	Exponential	Gompertz	Lognormal	Log-logistic
Log-likelihood	-168.36	-139.6	-139.62	-138.43	-141.27	-139.96
AIC	294.64	240.79	238.94	236.02	238.19	240.53
BIC	355.28	309.52	303.62	304.74	306.92	309.26

* Akakie Information Criterion (AIC), Bayesian Information Criterion (BIC)