ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

INCIDENCE AND PREDICTORS OF TUBERCULOSIS AMONG HIV POSITIVE CHILDREN IN ADAMA REFERRAL HOSPITAL AND MEDICAL COLLEGE, EAST SHOA ETHIOPIA, 2018. A RETROSPECTIVE FOLLOW UP STUDY

BY: MASINO TESSU (BSC)

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A THESIS SUBMITTED TO THE SCHOOL OF POST GRADUATE STUDIES OF ADDIS ABABA UNIVESITY, COLLEGE OF HEALTH SCIENCES SCHOOL OF NURSING AND MIDWIFERY IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE DEGREE MASTERS IN PEADIATRIC AND CHILD HEALTH NURSING

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This thesis by Masino Tessu is accepted in its present form by the board of examiners as satisfying thesis requirement for the degree of masters in pediatric and child health nursing.

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STATEMENT OF DECLARATION

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Acronyms and abbreviations

AAU-Addis Ababa university

ART-Anti retroviral therapy

CDC-Center of disease control

CPT-Cotrimoxazole preventive therapy

HAART-Highly active antiretroviral treatment

HAZ-Height for age z score

Hgb-Hemoglobin

HIV/AIDS-Human immune deficiency virus, acquired immune deficiency syndrome

IPT-Isoniazide preventive therapy

NISDI- National and international site development initiative

OIs -opportunistic infections

TB-Tuberculosis

TREAT- Therapeutic research, education and aids training

UNAIDS-United Nations Programme on HIV/ Acquired Immune Deficiency Syndrome

UNICEF-United nation international children emergency fund

WAZ-Weight for age z score

WHZ- Weight for height z score

WHO-World health organization

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ABSTRACT

Background: Tuberculosis is an infectious disease caused by the bacillus Mycobacterium tuberculosis. It typically affects the lungs (pulmonary TB) but can affect other sites as well. Tuberculosis is a common condition in HIV-infected children; however, its effect on survival of HIV infected children after confirmed of HIV/AIDS is not well understood. There are few or no studies done on incidence and predictors of TB among HIV positive children particularly in the study area.

Objectives:- The aim of the study is to assess the incidence and predictors of tuberculosis among HIV positive children in Adama referral hospital and medical college.

Methods: Five years retrospective study follow up study method was conducted using a checklist to gather data from 428 randomly selected children's charts. The data extraction tool was developed from the standardized ART entry and follow up form currently used by the ART clinics. Data was cleared and entered into Epi-data version 4.2.0.0 and exported to stata version 14.1 for further statistical analysis. Data was analyzed by bivariate and multivariate analysis using Cox regression proportional hazard model. Survival were calculated and compared with the Kaplan Meier and log rank test.

Result: Out of the 466 charts reviewed, 428 patient records were included in the analysis. The total follow-up period was 1109.55 Person-Year (PY). A total of 67 new TB cases were observed during the follow up period. Hence, the incidence rate in this cohort was found to be 6.03 per 100 child-years observation. Base line Hemoglobin level<10g/dl (AHR:7.04, 95% CI:1.03-48.15),not taking CPT at baseline (AHR: 2.41,95% CI: 1.07, 5.45),not taking IPT (AHR: 8.23,95% CI:2.11,32.06), not appropriately vaccinated (AHR:3.73, 95% CI:1.59,8.76) moderate underweight (AHR:5.19, 95% CI: 1.89,14.21) and moderate wasted (AHR: 2.86, 95% CI : 1.02, 7.99) were independent predictors of TB occurrence.

Conclusion and recommendation:-Incidence of tuberculosis was high especially during the PRE ART groups on HIV chronic care. Baseline moderate underweight and moderate wasting, not taking prophylaxis's(CPT and IPT),inappropriate vaccination and anemia (Hgb≤10mg/dl) found to be the independent predictor of TB occurrence among HIV positive children. Therefore, close follow up of HIV exposed children to make early diagnosis and treatment initiation before the development of malnutrition and anemia is important.

Keywords: Incidence, Predictors, Tuberculosis, children, HIV/AIDS, Adama, Ethiopia.

1. INTRODUCTION

1.1. Background

Tuberculosis(TB) is a contagious and air borne disease caused by the bacillus Mycobacterium tuberculosis. It mainly affects the lungs (pulmonary TB) but can affect other sites as well**(1)**. Relatively, small proportion of people are infected with Mycobacterium tuberculosis will develop TB disease; but , the probability of developing TB is much higher among people infected with the human immunodeficiency virus (HIV). From natural history of the disease studies, among sputum smear-positive and HIV-negative cases of pulmonary TB, around 70% died within 10 years; among culture-positive (but smear-negative) cases, 20% died within 10 years**(2)**. Tuberculosis (TB) remains a major global health problem for millions of people each year and one of the top 10 causes of death worldwide, ranking above HIV/AIDS as one of the leading causes of death from an infectious disease. This is the fact that with a timely diagnosis and correct treatment, most people who develop TB disease can be cured. Globally according to World Health Organization(WHO) report in 2014 an estimated, 1 million children developed TB and TB is the first cause of death among people living with HIV (PLHIV) even in an era of scale up of antiretroviral therapy (ART), causing one third of all HIV-related deaths**(3)**.

Another WHO report in 2015, showed that there were an estimated 10.4 million new (incident) TB cases worldwide and among this 1.0 million (10%) occur in children. People living with HIV accounted for 1.2 million (11%) of all new TB cases. Overall,90% of cases were adults and 10% children for both sex respectively**(4)**. Children experience more rapid HIV disease progression than adults, making them highly susceptible to opportunistic infections like TB**(5)**. The variety of presentation, difficulty in obtaining samples for laboratory testing and pauci bacillary nature of disease mean that confirming a TB diagnosis in children is challenging problem. Recent indirect approaches to burden estimation have used mathematical modeling of exposure and disease progression risks to predict pediatric TB incidence**(6)**. Children living with HIV are particularly at risk, as are those suffering from malnutrition, common childhood infections and intestinal worms. Children are most likely to be infected with TB by their parents and other close relatives especially in overcrowded living conditions, which increases a child's risk of infection and causes severe disability**(7)**.

1.2. Statement of the problem

Tuberculosis (TB) is a leading cause of death and common presenting illness among people living with HIV**.** At least one in four HIV-related deaths is a result of TB and many of these deaths occur in developing countries**(8)**. People living with HIV are around 30 times more likely to develop TB than HIV negative people. HIV weakens people's immune systems, increasing the risk of opportunistic infections such as TB **(7, 8)**.The incidence of TB among children between the age of 0 and 14 years worldwide was estimated to be 1 Million in 2014, accounting for approximately 10% of the total TB burden **(9)**.

Worldwide report of 2015 showed that TB was responsible for more deaths than other infectious disease like HIV and an estimated 1.4 million people who were HIV negative and 0.4 million HIV positive were died of TB respectively. So, there were a total of 1.8 million TB related deaths. An estimated 239,000 children were died of TB in 2015 **(10)**. In same year as UNAIDS report there were a total of 1.1 million HIV related deaths. The 1.1 million HIV related deaths compares with 1.4 million people dying from TB. So, TB now annually causes more deaths worldwide than HIV**(11)**.

Childhood TB is often called "the hidden epidemic" due to the difficulties involved in finding and treating the disease in this population both in developed and developing countries. In high TB burden settings, children account for an estimated 15–20% of TB cases **(12, 13)**. The WHO estimates that HIV prevalence among children with TB, in countries with moderate to high prevalence, ranges from 10 to 60%. Paediatric TB and HIV have overlapping clinical manifestations, which could lead to missed or late diagnosis **(14)**.

Tuberculosis is largely a disease of poverty and children with the disease frequently live in poor communities with few health services**(15)**. In the African sub-region various risk factors for mortality have been identified in children with TB-HIV co-infection, before or during ART; some of these children had received anti tuberculosis treatment (ATT) prior to Antiretroviral therapy(ART) initiation while others had not**(16)**. Ethiopia ranks seventh among the world's 22 high-burden tuberculosis (TB) countries Prevention and control of TB has created additional challenge and a major strain to health care systems in many of developing countries including Ethiopia due its linkage with HIV/AIDS **(17)**. Besides, challenges with the diagnosis of childhood TB in the absence of

accurate diagnostic tools, the main barriers to providing children access to TB service are related to weaknesses in the health system. However, children with signs and symptoms of TB, that are similar to those of other common illnesses such as pneumonia or acute malnutrition, will usually present to child health services at the primary care level. Health care workers at this level often lack awareness and knowledge of risk factors for signs and symptoms of the disease **(18)**. Capacity in childhood TB usually is restricted to higher-level care facilities such as national referral hospitals and urban settings **(19, 20)**.

Markers of advanced HIV disease (advanced WHO stage, under-nutrition and low CD4%) were predictive of prevalent and incident of TB. Earlier initiation of ART, before advanced HIV disease, could reduce the TB burden among HIV-infected children**(21)** .

The majority of these HIV-associated TB cases and deaths are in the African Region carrying most of the global burden. ART coverage among known HIV-infected TB patients in 2014 was 77%, which shows an increase from previous years, however it is still far from the WHO recommendation that all HIV-positive people with TB should receive it **(22, 23)**.

Ethiopia is among the countries most heavily affected by the HIV and TB. There are an estimated 1.3 million people living with the virus and nationally 68,136 of them were children under 15 years **(24)**. in Addis Ababa selected health centers 26.8% **(25)** and in university of Gondar medical hospital (20%) new cases of TB/HIV co-infection occurred**(26)** as finding shows. Mycobacterium Tuberculosis transmission in health care setting, at home and in the community is one of the primary research questions in the area of TB prevention. To have better survival of children before and after initiation of ART, knowing effect of tuberculosis is important. Therefore, aim of this study would be assessing the effect of tuberculosis in survival of HIV positive children before and after initiation of ART.

1.3. Significance of the study

Tuberculosis and HIV/AIDS fuels one another. TB contributes to immune impairment, making the body vulnerable to frequent illnesses and increasing demand for energy and nutrients, thereby accelerating disease progression. Therefore the effect of tuberculosis on survival of HIV infected children is not well known before and after initiation of ART. There are no studies done on incidence of tuberculosis and HIV co-infection in children in the Adama Hospital Medical College. So these results will help people working in the field to understand the epidemiological distribution of HIV/AIDS infection in newly diagnosed TB patients and its contribution to clinical disease . This evidence and information will be used for governmental and non -governmental organizations which work in the area of HIV/AIDS specifically on ART and TB at national, regional and district level. The result of this study will be also used for further research as base line information.

2. LITERATURE REVIEW

2.1. Incidence of tuberculosis among HIV positive children on ART

Even if TB seriously affected Sub-Saharan Africa, it is a major public health problem throughout the world. About a third of the world's population is estimated to be infected with tubercle bacilli and hence at risk of developing active disease**(27)**. ART reduces pulmonary tuberculosis(PTB) in human immunodeficiency virus (HIV) infected children. Recent ART recommendations have increased the number of children on ART. In 2009, an estimated 2.5 million children aged <15 years were living with the HIV, 80% of those in sub-Saharan Africa(SSA) **(28)**.

Different studies have been conducted in developed as well as in developing countries to determine the incidence and predictors of tuberculosis among HIV positive children. A Retrospectively and prospectively collected data done in the Therapeutic Research Education and AIDS Training(TREAT)Asia Pediatric HIV Observational Database (TAPHOD) cohort study were analyzed and showed that Of 2280 children in the cohort, 1752 were ever reported to have received ART. Before commencing any ART, Opportunistic infections (OIs) occurred at a rate of 89.5 per 100 person-years and of OIs TB was the leading. The incidence rate was 28.8 infections per 100 person-years during mono- or dual-therapy and 10.5 infections per 100 person-years during HAART **(29)**.

Another a systematic review and meta-analysis done worldwide showed that TB incidence in HIV cohorts ranged from 0.3 to 25.3 per 100 person-years. TB incidence was lower in HIV-infected children on ART. Following initiation of ART, TB incidence declined rapidly over 12 months of treatment**(30)**.

Further retrospective cohort study done in china revealed that among 3365 children on ART 77 (2.3%) children were diagnosed with PTB after ART during 7.3 years cohort observation. Overall incidence was 0.83 (0.65–1.01)/100 person-years (py), with the peak of 3.6/100 py in the first 3 months after ART **(31)**.

In addition a prospective study done in Latin America among 1114 HIV-infected infants, children, and adolescents followed for nine years,69 patient classified as having confirmed or presumed tuberculosis were included in this case series; 52.2% had laboratory-confirmed tuberculosis, 15.9% had clinically confirmed disease and 31.9% had presumed tuberculosis , of this 25(36%) prior to ART initiation ,3(4%) within 3days of ART treatment 39(57%) after 3 days of ART,2(3%) missed art date treatment developed tuberculosis **(32)**.

Additionally, different institution based retrospective cohort studies have been conducted in resource-limited settings to determine the incidence of tuberculosis among HIV positive children. Of which, a study done in Tanzania on incident tuberculosis and risk factors among HIV infected children revealed that 376 out of 5040 children met the case definition for TB. The overall incidence of TB was 5.2/100 person-years**(33)**. Similarly, a retrospective study done in the University of Gondar Referral Hospital among 271 HIV positive children 54 new TB cases occurred. The overall incidence density of TB was 4.9 per 100 PY**(26)**.

2.2. Predictors of tuberculosis among HIV positive children's on care and ART

2.2.1. Baseline socio-demographic factors and ART

Despite children on ART, they have still high rate of tuberculosis infection when compare with HIV free children. Most of the child Tuberculosis infections were occurred in early periods after initiation of ART**(32)**.

A Systematic Review and Meta-analysis done on the incidence of opportunistic (OIs) and other infections in ART-naive and -exposed children shows that tuberculosis is the second most common infections next to bacterial pneumonia in Among HIV-infected Children in Low- and Middle-income Countries with the prevalence of combined TB 17(12.36%) in ART-naive children and combined TB type 20(8.84%) ART-exposed children **(34)**. In different studies, age is the most common socio-demographic significant predictor associated with early child tuberculosis after initiation of ART. Being age above 5 year**(35, 36)** , age 1-5 year**(37, 38)**,age 12–35month**(39)** were associated with tuberculosis infection after initiation of ART.

A retrospective study done in Nigeria shows that being male gender was a significant predictors of incident of TB**(38)**. On Univariate analysis having more than one child in the household has an association for the development of tuberculosis**(33)**. A retrospective study done in Tanzania and Nigeria shows on multivariate analysis being male has an association for the development of tuberculosis**(33, 38)** respectively. A retrospective study done Nigeria living in urban area has an association for the occurrence of tuberculosis among HIV positive children**(39)**.

2.3.2. Clinical and laboratory factors

Declining of CD4 level of the child is considered as predictor of incidence of tuberculosis in different studies. A Systematic Review and Meta-analysis done worldwide in low and middle income

countries**(29, 34, 40)** were important predictors of time to TB occurrence. Another retrospective studies done in Tanzania **(33)** and Nigeria **(37)** were important predictors of time to TB occurrence . Advanced WHO clinical stage (III and IV) of the child is considered as predictor of incidence of tuberculosis in different studies. A retrospective studies done in Tanzania **(33)**, Democratic Republic of Congo**(35, 37, 38, 41)** were important predictors of TB occurrence. Similarly institution based retrospective cohort studies conducted in northern part Ethiopia also showed that ambulatory functional status and having base line anemia**(26, 33)** were important predictors of time to TB occurrence. Furthermore a retrospective study done in Nigeria**(39)** shows past history of TB in children was significantly associated of development of tuberculosis.

2.3.3. ART and other medication factors

A prospective cohort study done in four Latin American countries, shows The vast majority (87.0%) of TB cases were diagnosed prior to enrollment into International National Site Development Initiative (NISDI); only nine cases of TB (13.0%) were diagnosed after study enrollment. Two (2.9%) cases did not have ART start dates available, 25 (36.2%) cases of TB were diagnosed prior to the start of ART, three (4.3%) had the diagnosis of TB and ART initiation occur within three days of each other, and 39 (56.5%) cases were on ART. Eleven of the 39 cases on ART prior to TB diagnosis had been on HAART for less than three months when TB manifested itself and another five cases were diagnosed between three and six months following initiation of HIV treatment **(32)**.

Another a prospective cohort study conducted in Kenya showed that recent ART initiation remained a significant predictor for incident TB **(42)**. Another an institutional based retrospective cohort study done in northern part of Ethiopia in Ahmara region show that Absence of cotrimoxazole preventive therapy and absence of isoniazid preventive therapy were an independent predictor for increased incidence of TB respectively **(43)**. Additionally a retrospective cohort study done in northern part of Ethiopia show that Inappropriate vaccination with was an important predictors of time to TB occurrence**(26)**.

2.3.4. Nutritional factors

A retrospective cohort studies done in Tanzania shows severe wasting was independently associated with a higher risk of TB **(33)**. A retrospective cohort studies which have been conducted in northern part of Ethiopia showed that Nutritional status underweight was associated with increased incidence of TB after initiation of ART**(43)**.

2.3. Conceptual frame work

The following conceptual framework shows association between independent variables with dependent variable which is developed after reviewing many literatures (24,27-40). According to these literatures, Socio-demographic, ART and other medications, nutritional status and base line clinical and laboratory variables affect Tuberculosis incidence of children in continuum of HIV care.

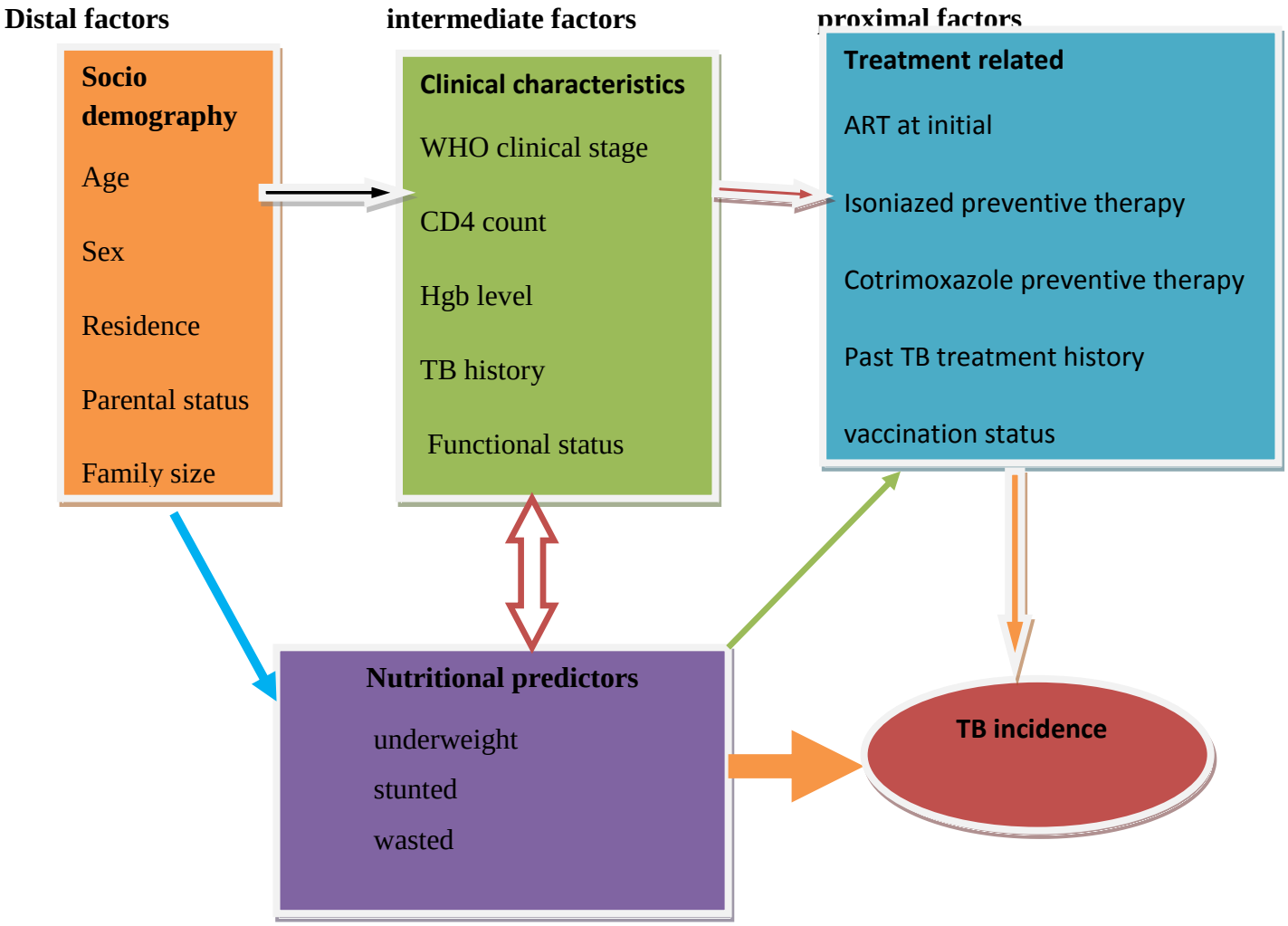

Figure 1: Conceptual frame work for the occurrence of tuberculosis among Children Living with HIV on chronic HIV care at Adama referral hospital medical college, East Shoa Ethiopia,2018, adapted from different literatures.

3. OBJECTIVES

3.1. General Objective

To assess the incidence and predictors of tuberculosis among children living with HIV on chronic HIV care in Adama referral hospital and medical college, East Shoa Ethiopia January1st,2013 to December 31th, 2017.

3.2. Specific Objectives

1) To estimate incidence rate of tuberculosis among children living with HIV in Adama referral hospital and medical college January 1st, 2013 to December 31th, 2017 .
2) To estimate the survival time of children to develop tuberculosis among children living with HIV in Adama referral hospital and medical college January 1st, 2013 to December 31th,2017 .
3) To identify predictors of tuberculosis incidence among children living with HIV in Adama referral hospital and medical college January 1st, 2013 to December 31th, 2017.

4. METHODS AND MATERIALS

4.1. Study area and period

The study was conducted in Adama referral hospital and medical college located at the center of Adama Town in HIV/AIDS care clinic from February 28th to March13th, 2018 . Adama town, located at 99 km southeast of Addis Ababa and is an administrative center for East Shoa Zone in Oromia Regional State. Adama Hospital and medical college was one of the first three hospitals in Oromia that started providing ART services since 2005. HIV infection is confirmed by serological testing or DNA PCR used in infants under 18 months of age. At ART clinic, HIV positive children are screened for opportunistic infections, evaluated for clinical staging and eligibility for ART by ART physician or nurse. Patients were managed in accordance with WHO recommendations **(44)**.The ART case team in the hospital comprised of ART trained physicians; ART trained nurses, pharmacist, laboratory technicians, data clerks, and drug adherence counselors. A total of 1309 children have been enrolled since March 2005, 633 children ever started ART since January 2013**(45)**. The study subjects was followed from January 1st 2013 to December 31th 2017.

4.2. Study design

A five years institution based retrospective follow up study was conducted.

4.3. Source population

All Children living with HIV/AIDS, age ≤ 14 years and confirmed of HIV/AIDS at Adama referral hospital and medical college, registered to chronic HIV Care and support program.

4.4. Study population

The study population was those children living with HIV who were enrolled to chronic HIV Care in Adama referral hospital and medical college, from January 1st, 2013 to December 31th, 2017.

4.5. Inclusion and Exclusion criteria

Inclusions:

All children aged ≤ 14 years who were newly enrolled in to chronic HIV Care clinic from January 1st,2013 to December 31th, 2017.

Exclusions:

children on HIV care clinic with incomplete baseline information like CD4 and hemoglobin were excluded.

HIV positive children who started anti-TB treatment at the beginning of the follow-up was excluded .

4.6. Sample size determination

For the first objective, a single population proportion formula was used to calculate the sample size by considering the following statistical assumptions:

- ✓ P = proportion of tuberculosis incidence among HIV positive children, 20%**(26)**
- ✓ Z α/2 = the corresponding Z score of 95% CI
- ✓ d= Margin of error (5%)

$$N = \frac{(Z_{\frac{\alpha}{2}})^2 \times p(1-p)}{(d)^2}$$

N= $(1.96)^2$ *0.2*0.8/ $(0.05)^2$ = 246 then after adding 10 % contingency rate the final sample size was 270.

For the second objective, the sample size was determined using double population proportion formula by considering anemia, ambulatory functional status and not appropriately vaccinated as the major predictor variables**(26)**. Moreover, ambulatory functional was considered as independent predictor since it gives the maximum sample size (Table1). Sample size was calculated by using open Epi info version 7 statistical package.

$$n_1 = \frac{\left[Z_{\alpha/2}\sqrt{\left(1+\frac{1}{r}\right)P(1-P)} + Z_{\beta}\sqrt{\frac{P_1(1-P_1)+P_2(1-P_2)}{r}}\right]^2}{(P_1-P_2)^2}$$

$$where, p = \frac{p1+rp2}{r+1}, if\ r = 1\ then\ p = \frac{p1+p2}{2}$$

P1: is percent of exposed with the outcome

P2: is percent of non-exposed with the outcome

r : is the ratio of non-exposed to exposed1:1

$Z_{\alpha/2}$: is taking CI 95%, Z_{β}: 80% power

Table 1:sample size calculation to assess the incidence of tuberculosis and its predictors among HIV positive children on ART in Adama Referral Hospital and Medical College, East Shoa Ethiopia, 2018.

Variables	Assumptions	Total sample size	After adding 10%
Anemia	P1=35.7% P2=17%	194	213(26)
Ambulatory functional status	P1=25% P2=13.8%	424	466(26)
Not appropriately vaccinated	P1=58.5% P2=10.6%	38	42(26)

P1: is percent of exposed with the outcome $Z_{\alpha/2}$: is taking CI 95%

P2: is percent of non-exposed with the outcome Z_{β}: 80% power

r is the ratio of non-exposed to exposed 1:1

- ✓ Then the largest sample size (N= 466) was selected as the final sample size for the study.

4.7. Sampling procedures

Children living with HIV who were registered from January 1st, 2013 to December 31th, 2017 in children chronic HIV care clinic in Adama referral hospital and medical college were included in the study and followed them for five years. This period was selected in order to have a nearest five year follow up study periods. The facility started full implementation of standardized formats, documentation and recording system in regular manner since this period. This is critical as the study was based on secondary data and it is also important to make sure that important variables for the study should be available for all enrolled subjects in the study. Sampling technique for study subject was by using simple random sampling technique from the list of 633 children who ever confirmed of HIV /AIDS and started ART service at ART- Unit.

4.8. Variables of the Study

Dependent variables: TB occurrence and its time of occurrence

Independent variables

Socio-demographic characteristics: Age, Sex, Residence, parental status, Family size, care givers.

Baseline clinical characteristics: WHO clinical Stage, CD4 counts(Immunodeficiency), Hemoglobin level (Hgb)(anemia), Functional status.

Follow-up clinical and treatment related characteristics: initial HAART regimen, Prior history of tuberculosis treatment, isoniazide preventive therapy, cotrimoxazole preventive therapy, Vaccination status, nutritional status.

4.9. Operational definitions

Entry date- First date for each observation within study period at date of HIV/AIDS confirmation .

End date- Last date for each observation within the study period that subject visited last.

Survival - The time from date of HIV/AIDS confirmation to occurrence of TB .

Time scale- Survival time was in month.

Events -Incident TB, which is defined in this study as the occurrence of TB in children living with HIV any time after enrolled into children chronic HIV care. The type of TB can be smear positive pulmonary, smear negative pulmonary, extra-pulmonary or disseminated tuberculosis as identified by signs and symptoms, laboratory, X-ray diagnosis and/or started anti TB treatment.

Censored - children living with HIV was censored by the first date of lost, drop out, transfer out and died by other causes before the end of the follow up period and completed the follow up period without developed the event.

- ✓ Lost-patients missing their appointment for follow up or drug pick up at least for one to three months.
- ✓ Drop out- patients missing their appointment for follow up or drug pick up for more than three months.
- ✓ Transferred out - those patients who are transferred to other health care facilities .

- ✓ Stunting, underweight and wasting is defined as if the child has either of one Height/age< -2, or Weight/age<-2 or weight/Height <-2 standard deviation respectively according to WHO 2006 curve.
- ✓ Normal nutrition is defined as if the child has either of one Height/age> -2, or Weight/age>-2 or weight/Height >-2 standard deviation respectively according to WHO 2006 curve.

4.10. Data collection process and procedures

4.10.1. Data collection instrument

The data extraction tool was developed from the format of WHO standardized ART entry and follow up form currently used by the ART clinics. Data collectors were use the data collection tool to collect the information from patients' cards. Necessary data was extracted by reviewing patients ART cards. Death was confirmed by reviewing medical registration in the hospital, or registration by ART adherence supporter through calling using the registered phone number. The tool contains four part which include socio demographic factors ,nutritional factor, clinical factors and treatment factors. The most recent laboratory test results before starting ART was used as a baseline value. If there is no pre-ART laboratory test registered, results obtained within one month of ART initiation was used as a baseline. If the two results were obtained within one month, the mean value was used.

4.10.2. Data quality control

Three BSC Nurses from Adama referral hospital and medical college, who were trained on comprehensive HIV care and currently involved in patient follow up care were employed to collect the data. Both principal investigator and supervisors in hospital were closely supervised the entire data collection process. One-day training was given concerning the data extraction tool and data collection process for both data collectors and supervisors. 5% Pre-test was under taken in Adama health center before data collection and some modification was made accordingly. Data quality was assured by designing a proper data extraction tool and through continuous supervision. All collected data was examined for completeness and consistency during the data management, storage and analysis. Consistency was examined through random selection of cards by the principal investigator.

4.10.3. Data processing and analysis

Data was entered using Epi-data version 4.2.0.0 and analysis was done using STATA 14.1statistical software. ENA2011 for smart software's was used to generate Z score (WAZ, HAZ and WHZ) to define nutritional status. Before analysis, data was cleaned and edited. Cox-proportional hazard regression model assumption was checked using schoenfeld, residual test and variables having P-value >0.1 was considered as fulfilling the assumption. Patients' cohort characteristics of continuous data was described in terms of central tendency (mean or median), dispersion (standard deviation) and in frequency distribution for categorical data.

Finally, the outcome of each participants was dichotomized into censored or incidence of TB. The Kaplan Meier survival curves was used to estimate time of TB occurrence among HIV positive children, and log rank tests was used to compare survival curves. Bivariate Cox-proportional hazards regression model was fitted for each explanatory variable. Moreover, those variables having p-value ≤ 0.25 in the bivariate analysis were fitted to the multivariable Cox-proportional hazards regression model. Hazard ratio with 95% confidence interval and p-values was used to measure the strength of association and to identify statistical significant results. On multivariate analysis variables having P-value,< 0.05 was considered as predictors of incidence of tuberculosis after enrolled to HIV chronic care.

4.10.4. Ethical considerations

Ethical clearance was obtained from Institutional review committee of school of nursing and mid-wifery, college of medicine and health sciences, Addis Ababa University. Permission letter was obtained from hospital administration. As this is a retrospective study, informed consent from individual patients was not requested. Since, the study was done through reviewing of medical records, the individual patients might not be subjected to harm as much as the confidentiality was kept. To keep the confidentiality all collected data was coded and locked in a separate room before entered into the computer. After entered to the computer the data was locked by password, names and unique ART numbers was not included in the data collection format and the data was not disclosed to any person other than principal investigator.

5. RESULTS

5.1. Socio-demographic characteristics of the study participants

Among 466 HIV positive children's records reviewed, 428 (91.8%) records were included in the final analysis and 38(8.2%) records were not analyzed due missing of data file. The median age f the cohort at the time of diagnosed of HIV was 6 years with IQR[3-10]. The finding revealed that about half 222(51.87%) of the study participants were males and more than half of them are above five years of age 245(57.25%). Out of total study subject more than two third 293(68.46%) are live in urban area, more than half of them 242(56.54) live with family size three to four and majority of them 375(87.62%)get care from their parents respectively (Table 2).

Table 2:Baseline socio-demographic characteristics of children living with HIV in Adama referral hospital and medical college, East Shoa Ethiopia, 2018.(n=428)

Variables	Frequency	Percent
Sex		
Male	222	51.87
Female	206	48.13
Age		
<=5 years	183	42.76
6 - 10 years	153	35.75
>=11 years	92	21.50
Residence		
Urban	293	68.46
Rural	135	31.54
Family size		
≤2	84	19.63
3-4	242	56.54
≥5	102	23.83
Care giver of the child		
Parents	375	87.62
Sibling	12	2.8
Grandparent	26	6.07
Guardians	13	3.04
Orphanage centers	2	0.47

Regarding the parental status of HIV positive children living with HIV/AIDS nearly two third 268(63%) both parent alive and only 25(6%) are double orphan(Figure 2).

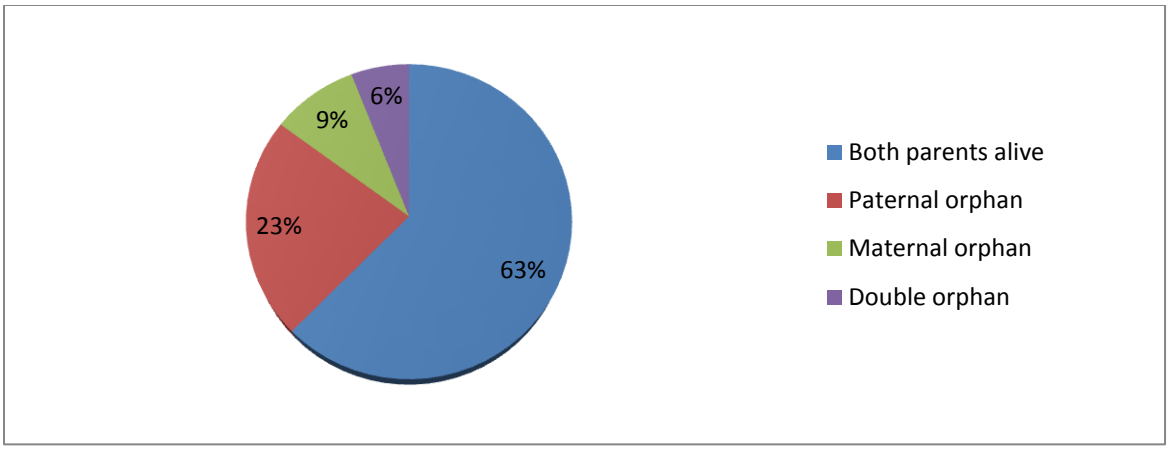

Figure 2:Parental status of HIV positive children living with HIV/AIDS in Adama hospitals referral and medical college, East Shoa Ethiopia, 2018.(n=428)

5.2. Baseline clinical, laboratory and ART information

The eligibility criteria for initiation of ART were mainly with both CD4 count and WHO clinical stage 171(39.95%). More than half 237(55.37%) of them were at WHO clinical stage 1 & 2 and 124(28.97%) had a CD4 count below the threshold for severe immunodeficiency during ART initiation. Nearly half of the children were in ambulatory functional status 134(49.63%) and more than half of children were in delayed developmental history status 84(53.16%) at baseline respectively . Nearly three fourth of children were 313(73.13%) had less than 10 Hg level. During the follow up period most of children 339(93.65%) had taken CPT but only 154(42.45%) had taken IPT and 55(82.09%) TB patients presented with pulmonary TB, followed by 12(17.91%) extra pulmonary TB. 48 (71.64%) patients developed TB for the first time during the PRE ART period and 19(28.36%) developed TB during on ART period (Table 3).

Table 3: Baseline clinical, laboratory and ART information of children living with HIV/AIDS in Adama referral hospitals and medical college, East Shoa Ethiopia, 2018.(n=428)

Variables	Frequency	Percent
Functional status (age >=5year) (N= 270)		
Working	123	45.56
Ambulatory	134	49.63
Bedridden	13	4.81
Developmental history (age <5year) (N=158)		
Appropriate	65	41.14
Delayed	84	53.16
Regressive	9	5.70
WHO clinical stage		
Stage I and II	237	55.37
Stage III and IV	191	44.63
CD4 count or percent		
Below the threshold	124	28.97
Above the threshold	304	71.02
Hemoglobin level		
<10 gm/dl	298	69.63
≥10 gm/dl	130	30.37
ART eligibility criteria		
CD4 cell count	121	28.27
WHO clinical stage	50	11.68
Both	171	39.95
Not recorded	86	20.09
Cotrimoxazole preventive therapy(n=362)		
Yes	339	93.65
No	23	6.35
Isoniazide preventive therapy(n=362)		
Yes	154	42.54
No	208	57.46
Types of TB(n=67)		
PTB	55	82.09
EPTB	12	17.91
Time TB developed(n=67)		
PEART	48	71.64
ART	19	28.36

Regarding ART regimen given for HIV positive children, the predominant regimens initially prescribed were a combination of Zidovudine, Lamivudine and Nevarapin (4c=3TC-TDF-NVP) 195 (45.56%), followed by Zidovudine,Lamivudine and Efavirenz (4d=AZT-3TC-EFV) 152 (35.51%). (Figure 3).

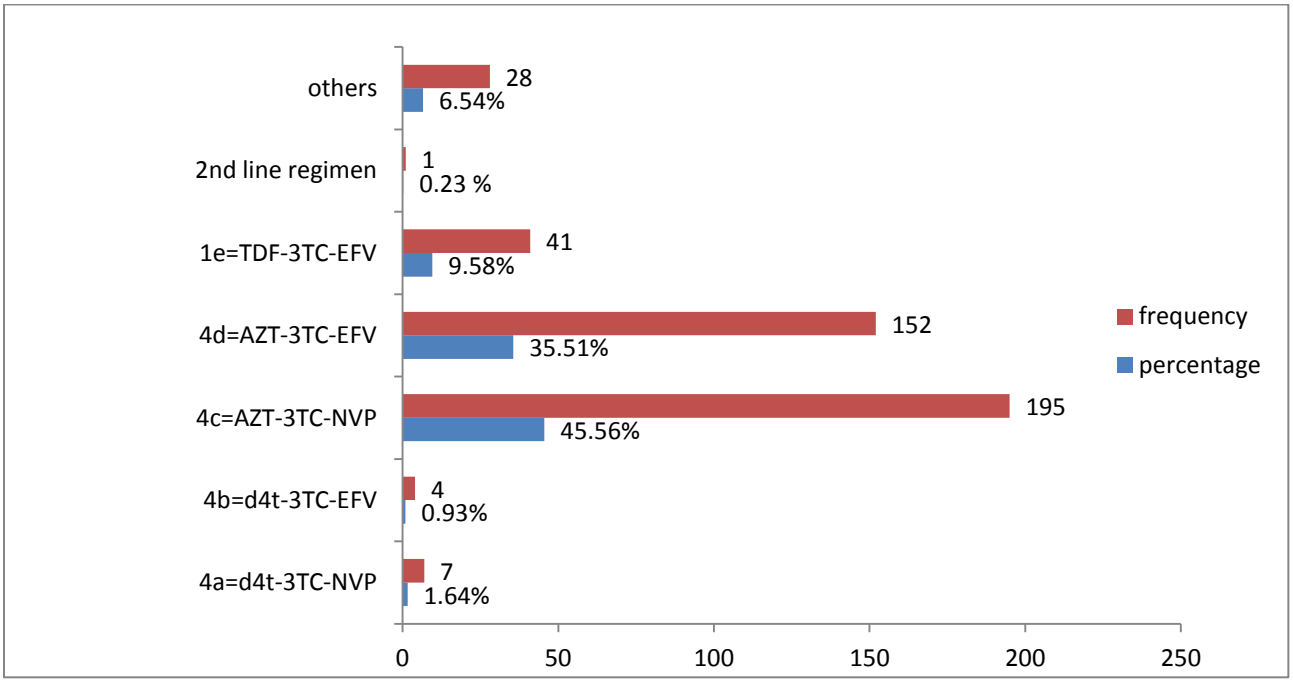

Figure 3:ART regimen given for HIV positive children during follow up in Adama referral hospitals and medical college, East Shoa Ethiopia, 2018(n=428).

Regarding Vaccination status of HIV positive children more than half children had vaccinated for their age 226(52.80)%) and 68(15.89%) their vaccination status were not recorded(Figure 4).

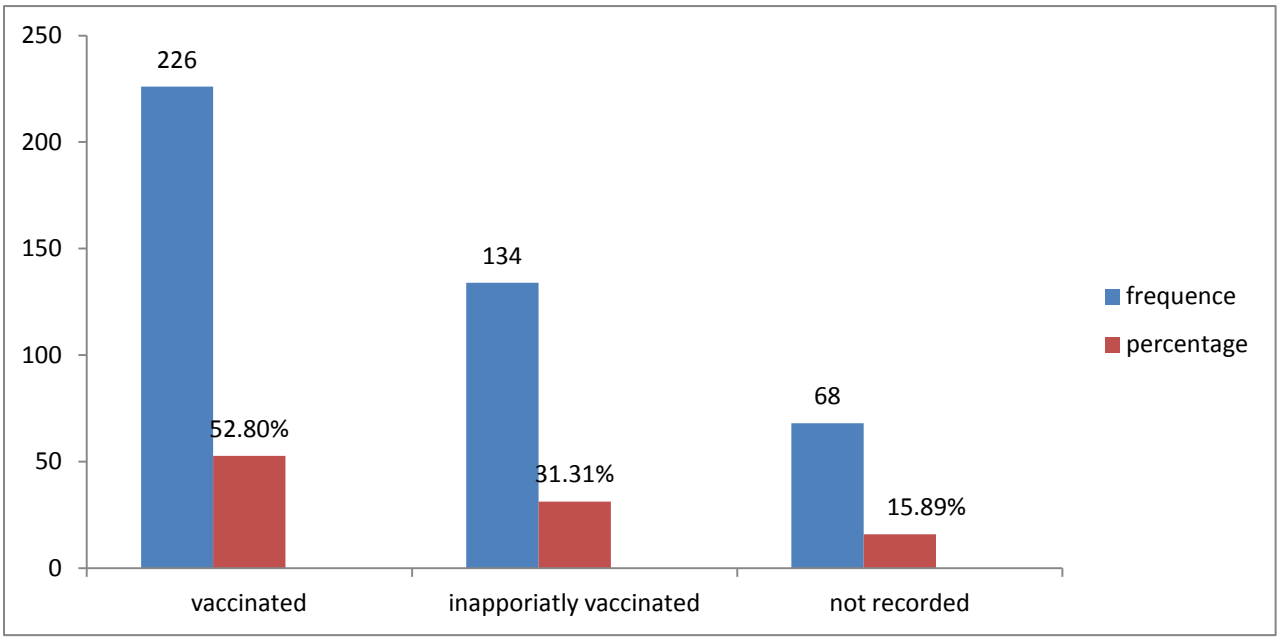

Figure 4: Vaccination status of HIV positive children in Adama referral hospitals and medical college, East Shoa Ethiopia, 2018(n=428).

5.3. Nutritional characteristics

Regarding nutritional status of HIV positive children categorized by age about less than one third 112(26.16%) were underweight followed by 73(17.05%) were wasted and 67(15.65%) were stunted respectively(Table 4).

Table 4: Baseline nutritional status of HIV/AIDS positive children categorized by age at Adama referral hospital and medical college, 2018(n=428).

Nutritional parameter	Age category			
	≤5(n=183)	6-10(n=153)	≥11(n=92	Tot(n=428)
Normal WFA	144	125	47	316
Moderate underweight(<-2)	30	17	39	86
Severe underweight (<-3)	9	11	6	26
Normal HFA	162	131	68	361
Moderate stunting (<-2)	13	13	20	46
Severe stunting(<-3)	8	9	4	21
Normal WFH	146	119	90	355
Moderate wasting (<-2)	23	28	2	53
Sever wasting (<-3)	14	6	0	20

5.4. Incidence of Tuberculosis occurrence after HIV confirmed

A total of 428 children started confirmed HIV/AIDS have been followed from 0 to 60months. The median follow up duration was 32.5 with IQR[12.30, 50.13] months, the minimum and the maximum follow up time was 0.63 and 60 months respectively. Out of total observation 275 (64.25%) were alive, 69 (16.12 %) were died, 60 (14.02%) were lost to follow up, and 24 (5.61%) were transferred out. The incidence rate in this cohort was found to be 6.03 per 100 child-years observation. There were 67 new TB cases observed during follow-up. The cumulative probabilities of survival at 6, 12, 18,36 and 60 months date confirmed of HIV status were found to be 0.96, 0.93, 0.91, 0.84 and 0.75 respectively. The mean survival time of the

entire cohort was found to be 31.10 months with (95% CI: 29.20 ,33.01) and the cohort contributed to a total of (13314.63) person-months of follow up(Figure 5).

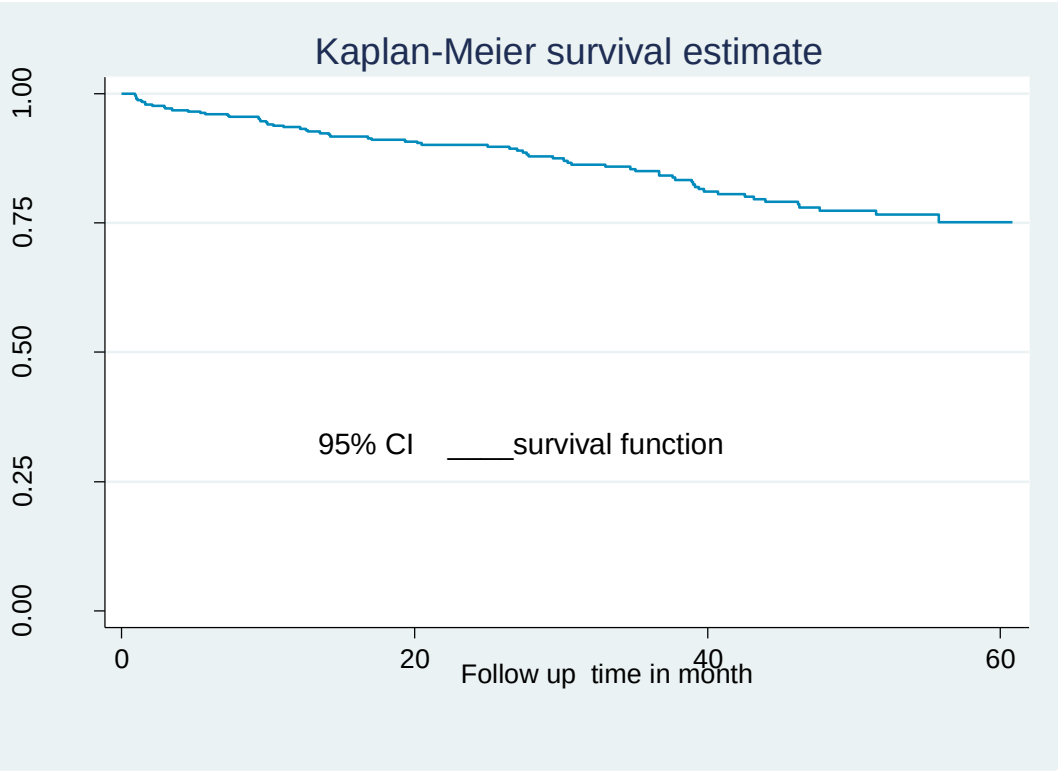

Figure 5:The overall Kaplan-Meier survival curve with 95% confidence intervals of TB-free survival proportion for Children on Chronic HIV care at Adama referral hospital and medical college, East Shoa Ethiopia, 2018(n=428).

5.5. Survival function for different categorical variables

To test equality of survival curves of different categorical explanatory variables Cochran-Mantel Haenszel Log rank test was performed. The test statistics showed that there is a significant difference in survival function for different categorical variables. These variables include: residence (urban and rural), those who are taking CPT and those who did not take cotrimoxazole preventive therapy and those who are taking INH at baseline and who did not INH at baseline.

In this historical cohort those study participants who are living in an urban area have lower survival time as compared to those who are living in rural area ($P < 0.006$).

The median survival time for those who were living rural was found to be 55.92 month with SD ± 1.32 month as compared to those who were living in the urban with a mean survival time of 50.76 months with SD ± 1.20 months. This difference is statistically significant with p-value= 0.006 (Figure 6).(n=428)

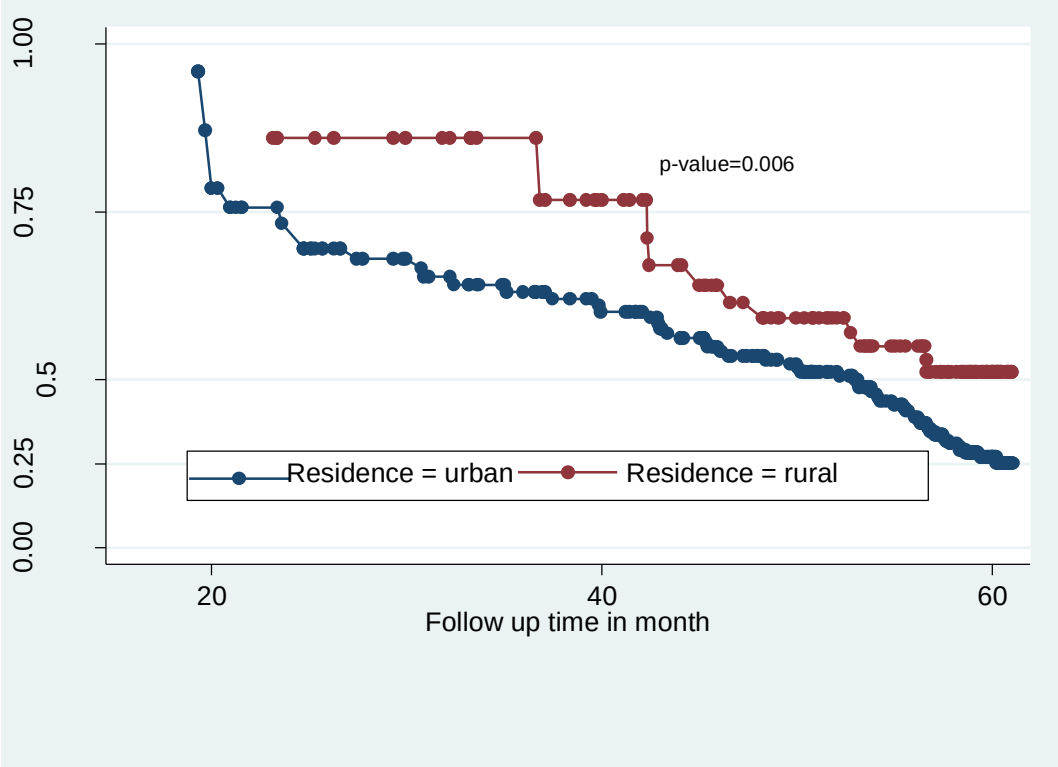

Figure 6:The Kaplan-Meier survival curve of TB -free survival proportion based on residence among children on chronic HIV care at Adama referral hospitals and medical college, East Shoa Ethiopia, 2018(n=428).

In this historical cohort those study participants who had a low hemoglobin level (<10gm/dl) have lower survival time as compared to those who had a high hemoglobin level (>=10gm/dl) (P < 0.001).

The mean survival time for those who have hemoglobin level >10 g/dl was found to be 57.00months with SD ± 1.19 month as compared to those who have hemoglobin level ≤10 with a mean survival time of 50.36 months with SD ± 1.20 months. This difference is statistically significant with p-value= 0.001(Figure 7).

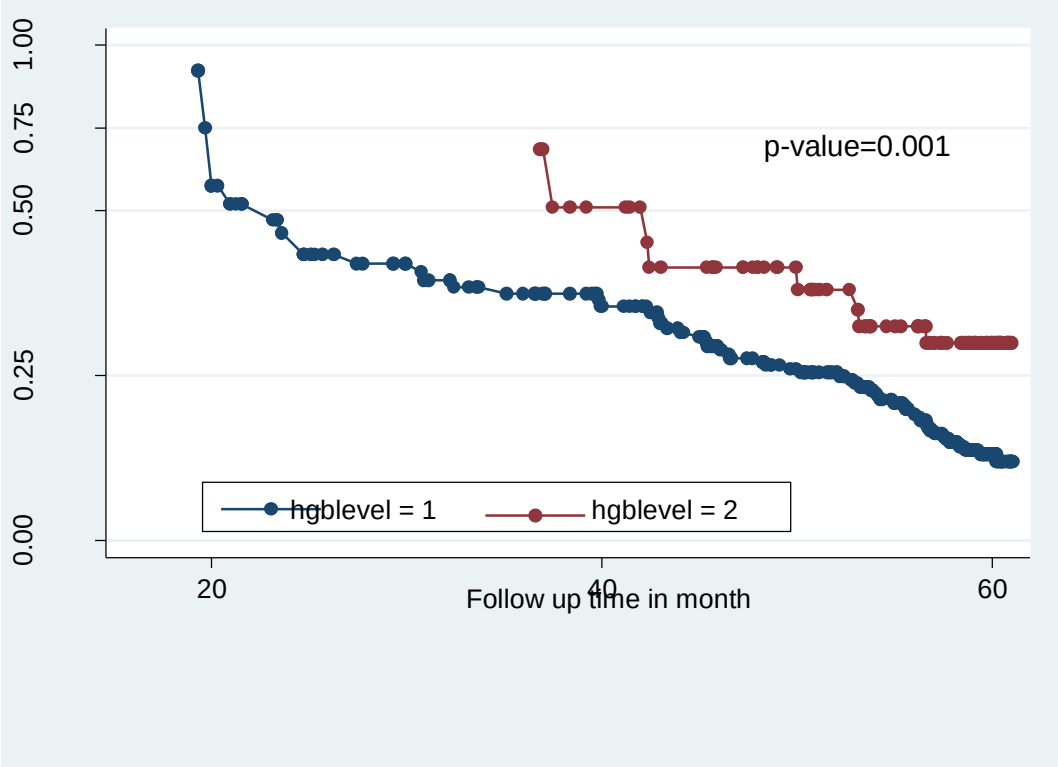

Figure 7: The Kaplan-Meier survival curve of TB -free survival proportion based on hemoglobin level among children on chronic HIV care at Adama referral hospitals and medical college, East Ethiopia, 2018.(n=428)

In this historical cohort those study participants who had not taken cotrimoxazole preventive therapy have lower survival time as compared to those who had taken cotrimoxazole preventive therapy ($P < 0.000$).

The mean survival time for those who have been taking cotrimoxazole preventive therapy (CPT) was found to be 55.10 months with SD $\pm$ 0.90 month as compared to those who were not taking cotrimoxazole preventive therapy with a mean survival time of 34.91months with SD $\pm$ 4.18 months. This difference is statistically significant with p-value= 0.000 (Figure 8).

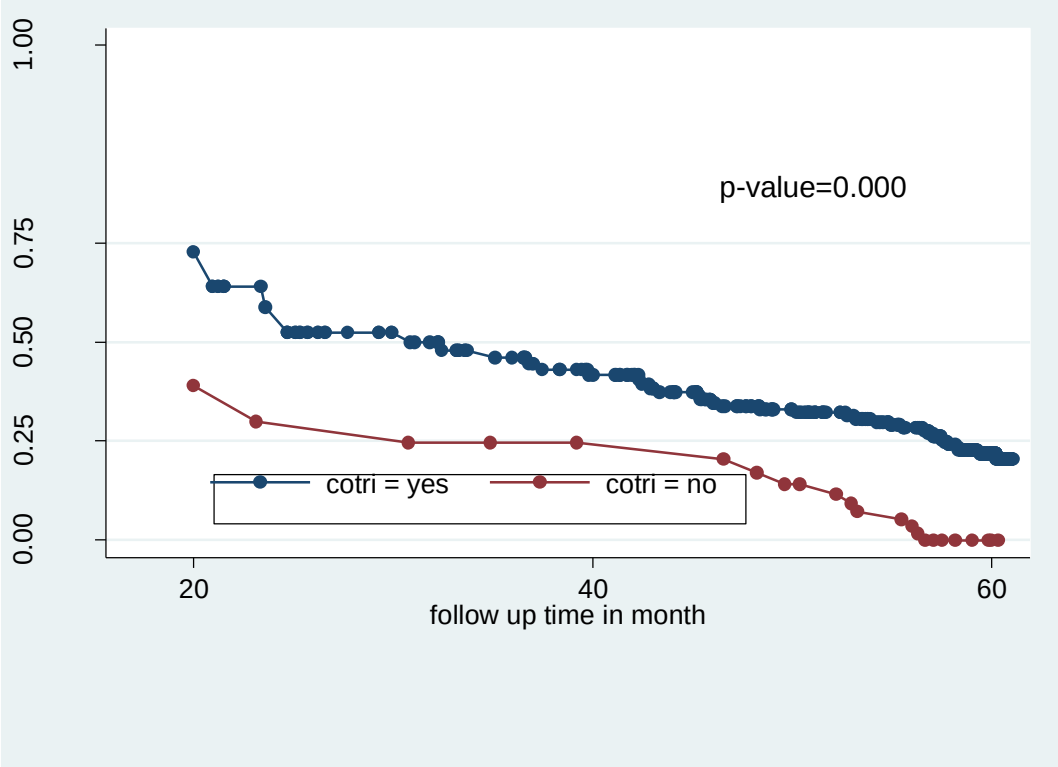

Figure 8: The Kaplan-Meier survival curve of TB -free survival proportion based on Cotrimoxazole preventive therapy among children on chronic HIV care at Adama referral hospitals and medical college, East Shoa Ethiopia, 2018(n=362).

5.6. Predictors of tuberculosis occurrence

The relationship between the baseline variables and the incidence of tuberculosis was analyzed using bivariate Cox proportional Hazard regression model. The result of bivariate analysis showed that, factors including being age ≥ 6 years, living in urban, having family size ≥3,Hgb level <10 g/dl, being ambulatory and bedridden functional status, being WHO clinical stage (III&IV), underweight (moderate and severe), stunting (moderate) ,wasting (moderate and severe), not taking cotrimoxazole and INH as well as not appropriately vaccinated were found to have association with incidence of tuberculosis occurrence.

In multivariate Cox proportional hazards model, only six variables were associated with incidence of tuberculosis. The result of multivariate analysis revealed that children who had not took cotrimoxazole at baseline were 2.41 times more likely to develop tuberculosis as compared to those who had took cotrimoxazole at baseline (AHR: 2.41,95% CI: 1.07, 5.45). Children who had not take INH are 8.23 times more likely to develop tuberculosis as compared to those with

WHO had took INH (AHR: 8.23, 95%CI: 2.11, 32.06). Those children who were not appropriately vaccinated were 3.73 times more likely to develop tuberculosis as compared to those children who were vaccinated (AHR: 3.73,95%CI:1.59,8.76).

Children having a hemoglobin level less than 10 gm/dl were 7.04 times more likely to develope tuberculosis as compared to those having hemoglobin level greater than or equal to 10 gm/dl (AHR: 7.04, 95% CI: 1.03-48.15). Children those who are being moderately underweight at the beginning of ART were 5.19 times more likely to develop tuberculosis as compared to those who are not being underweight (AHR: 5.19, 95% CI: 1.89,14.21). Furthermore, children who are moderately wasted were 2.86times more likely to die as compared to those who are not wasted (AHR: 2.86, 95% CI: 1.02, 7.99) (Table 5).

Table 5: The bivariate and multivariate Cox regression proportional Hazard regression analysis of predictors of incidence of TB among HIV infected children at Adama referral hospital and medical college, East Shoa Ethiopia, 2018(n=428).

Variables	Survival status		CHR (95%CI)	AHR (95%CI)	p-value
	CensoredN(%)	EventN (%)			
Residence					
Urban	237 (55.37)	56 (13.08)	1	1	
Rural	124 (28.97)	11 (2.57)	0.40(0.21,0.76)	0.84(0.27,2.55)	0.78
Family size					
≤2	77(17.99)	7(1.7)	1		
3-4	202(47.19)	40(9.34)	2.41(1.07, 5.39)	2.74(0.72 , 10.44)	0.14
≥5	82(19.15)	20(4.67)	2.37(1.00, 5.62)	2.36(0.54, 10.15)	0.25
Functional status					
Working	113(26.40)	10(2.33)	1		
Ambulatory	91 (5.61)	43(10.04)	3.35(1.68, 6.67)	1.02(0.39, 2.68)	0.95
Bedridden	8(1.86)	5(1.16)	5.82(1.98 , 17.05)	3.01(0.51, 17.71)	0.22
WHO clinical staging					
Stage I and II	202 (47.19)	35 (8.17)	1		
Stage III and IV	159 (37.14)	32 (7.47)	1.35(0.83, 2.19)	1.30(0.67, 2.51)	0.43
Hemoglobin level					
<10 gm/dl	**239(60.04)**	**59 (13.08)**	**3.48(1.66, 7.29)**	**7.04(1.03,48.15)***	**0.04**
≥10 gm/dl	122 (24.29)	8 (2.57)	1	1	
CPT					
Yes	303(70.79)	36(8.41)	1		
No	**10(2.33)**	**13(3.03)**	**6(3.17, 11.36)**	**2.41(1.07-5.45)***	**0.03**
IPT					
Yes	149(34.81)	5(1.16)	1		
No	**164(38.31)**	**44(10.28)**	**8.48(3.36, 21.44)**	**8.23(2.11,32.06)***	**0.002**
Vaccination status					
Vaccinated	211(49.29)	15(3.50)	1		
Inappropriately vaccinated	**86(20.09)**	**48(11.21)**	**6.70(3.74,11.98)**	**3.73(1.59,8.76)***	**0.002**
Not recorded	64(14.95)	4(0.93)	1.13(0.37, 3.42)	1.40(0.26-7.34)	0.69
Underweight(WFA)					
Normal	290(67.75)	26(6.07)	1		
Moderate underweight	**49(11.44)**	**37(8.64)**	**7.50(4.52, 12.45)**	**5.19(1.89,14.21)***	**0.001**
Severe underweight	22(5.14)	4(0.9)	3.52(1.22, 10.12)	0	1
Wasting(WFH)					
Normal	303(70.79)	52(12.14)	1		
Moderate Wasting	**39(6.45)**	**14(3.27)**	**2.32(1.23, 4.04)**	**2.86(1.02-7.99)***	**0.04**
Severe wasting	19(4.43)	1(0.2)	0.31(0.04, 2.29)	2.39(0.22-25.19)	0.47

CHR=crudehazard ratio AHR=adjusted Hazard ratio CI=confidence Interval

6. DISCUSSION

In this historical cohort study, the aim was to determine the incidence of tuberculosis and its predictors among HIV positive children. At the end of follow up, about 275 (64.25%) were alive, 69 (16.12 %) were died, 60 (14.02%) were lost to follow up, and 24 (5.61%) were transferred out. In this study the incidence of TB in children living with HIV was 6.03per 100child-years with. The TB incidence rate observed in this study is consistent with a study conducted in Northern Ethiopia and Gondar hospital which observed an incidence of 4.2 and 4.9 per 100child years(26, 43) and in Tanzania 5.2 per 100 child-years respectively**(33)**. However it is higher than the findings of a study conducted in china , Kenya, cote d'Ivoire and Nigeria which described an incidence of 0.83 ,1.34 ,1.4 and 1.4 per 100 child-years respectively(31, 38, 41, 42). This gap might be due to different reasons. The discrepancies in incidence rate may be due to the difference in follow-up period of the studies and the difference in the overall burden of TB in the general population. Another reason was it could be due to the fact that this study consider both PRE-ART and ART follow up care unlike other study which consider after ART initiation follow up care. The other possible explanation might be the characteristics of the population included under the follow up.

In this study, HIV positive children with baseline anemia had 7.04 times higher risk of developing TB as compared to non anemic children. This finding is similar to the study done in Northern Ethiopia**(26, 43)**and Tanzania **(33)**. This could be due to the fact that children were affected by infections when their Hemoglobin level is lower than 10 mg/dL. The reason for anemia to be the predictor of incidence TB in our study might be due to the fact that 81.07 % of study participants have been taking the drug of 4c (AZT-3TC-EFV) or 4d (AZT-3TC-NVP) during follow up time which AZT is one of the most common causes of anemia (megaloblastic anemia) among patient living with HIV as a result, they become at higher risk for TB.

Finding revealed that no prophylaxis preventive therapy initiation at baseline was another important predictor of incidence tuberculosis. Children who had not taken cotrimoxazole preventive therapy at baseline were 2.41 times more likely to develop tuberculosis as compared to those who had took cotrimoxazole preventive therapy . This finding is similar to the study done in Northern Ethiopia(43).This could be due to Cotrimoxazole preventive therapy significantly reduces HIV related morbidity and mortality and another reason could be due to study setting **(46)**.

Children who had not taken INH preventive therapy were 8.23 times more likely to develop tuberculosis as compared to those with who had took INH preventive therapy. This finding is similar to the study done in Northern Ethiopia **(43)**. This could be due to the fact that IPT decreases mycobacterium load and reduces progression of latent bacilli to active TB**(47)**. In a situation where prevalence of latent TB infection is high, guideline for pediatric HIV/AIDS care and treatment in Ethiopia recommends IPT for HIV positive children in whom active TB has been excluded **(48)**.

In this study, not-appropriately vaccinated found to be a strong predictor of incidence tuberculosis among HIV positive children. Children who were not appropriately vaccinated were higher risk of developing tuberculosis ,3.73 times as compared to children who were vaccinated This finding is similar to the study done in Northern Ethiopia and Tanzania. This could be due to the fact that BCG scar was associated with a reduced risk of TB, as research showed BCG vaccination considerably reduced the risk of TB, both among individuals with and without HIV infection**(26, 49)**.

In this study, moderate underweight was found as an independent predictor of incidence TB occurrence. Children with moderate underweight at the time of HIV confirmed were 5.19 times more likely to develop TB as compared to those who were not with underweight. This finding is consistence with study done in Kenya**(42)** and Democratic republic of Congo **(41)**.
Furthermore this study, children with moderate wasted were 2.86 times more likely to develop tuberculosis compared to those who were not with wasted .This finding is similar to the study done Tanzania. This could be due to large sample size**(33)**.

7. STRENGTH AND LIMITATIONS

Strength

Long follow up period (around five years).

This study considers time to event for analysis which enables us to consider contribution of censored study subject.

Limitation

Use of retrospective nature of the cohort study design. Some of data (TB contact history) were incomplete and inconsistent so it wasn't analyzed.

Narrow scope of the study setting and population being only one hospital set up and population from specific area.

In this study it was not possible to measure some data such as house hold income, housing condition, viral loads and others which might be important predictors.

8.CONCLUSION

In conclusion, there was high rate of early Incidence of tuberculosis among children living with HIV especially in the first year of enrollment to chronic HIV care. Incidence of tuberculosis was high in Pre ART groups. Baseline malnutrition in the form of moderate underweight and moderate wasting, not taking prophylaxis's(Cotrimoxazole and Isoniazide),in appropriate vaccination and anemia (Hgb≤10mg/dl) count found to be the independent predictor of tuberculosis occurrence among HIV positive children.

9. RECOMMENDATIONS

1. To governmental and nongovernmental organizations

Tuberculosis/HIV collaborative long term surveillance program need to be strengthening at Chronic HIV care clinic.

Tuberculosis prevention strategies need to be strengthened with early initiation of HAART and prophylaxis preventive therapy as recommended in national guideline

2. To Health care providers

Close follow-up and screening of Children for tuberculosis is important especially with in the first year of enrollment to the chronic HIV care.

It would be better to give special attention for Under nutrition(underweight and wasting), early initiation of prophylaxis preventive therapy(Cotrimoxazole and Isoniazide),inappropriate vaccination and Children with low hemoglobin level (≤10g/dl) to prevent and treat Tuberculosis early.

3. For the patients

Early seek of health care; enrolled to chronic HIV care , taking HAART and early initiation of prophylaxis have great importance to reduce the risk of Tuberculosis.

4. To Researchers

Further prospective follow up study should be conducted by incorporating important predictors of tuberculosis occurrence like viral load .

Survival after tuberculosis diagnosis among Children living with HIV needs to be studied .

The impact of income ,contact of tuberculosis history and viral loads on tuberculosis needed to be studied which was not included in this studies due to incomplete data file.

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10. ANNEX

Annex 1 - Information Sheet

Title of the Research Project: Incidence of Tuberculosis and Predictors among HIV infected children attending HIV care clinic in Adama referral hospital and medical college, Ethiopia.

Name of Investigator: Masino Tessu(Bsc in Generic nursing)

Name of the Organization: Adama Hospital and Medical College

Name of the Sponsor: AAU

Introduction: This information sheet is prepared for in Adama Referral Hospital and Medical College administration and Hospital HIV care clinic coordinating office. The aim of the form is to make the above concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: To determine incidence of Tuberculosis and its Predictors among children living with HIV attending children HIV care clinic in Adama Hospital and Medical College.

Procedure: In order to achieve the above objective, information which is necessary for the study was taken from HIV care medical record follow up forms.

Risk and /or Discomfort: Since the study was conducted by taking appropriate information from medical chart, it would not inflict any harm on the patients. The name or any other identifying information was not recorded on the questionnaire and all information taken from the chart was kept strictly confidential and in a safe place. The information retrieved was only be used for the study purpose.

Benefits: The research have no direct benefit for one whose document/ record is included in this research. But the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing predicted plan there is a benefit for clients in the program of getting appropriate care and treatment services. Of all, the research work has a paramount direct benefit for health care planners and managers, especially for those on HIV/TB collaborative program planning and management.

Confidentiality: To reassure confidentiality the data on the chart was collected by those individuals who are working on the HIV care clinic in the facility and information was collected without the name of the clients. The information collected from this research project was kept confidential and will be stored in a file. In addition, it will not be revealed to anyone except the investigator and it will be kept in key and locked system with computer password.

Person to contact: This research project was reviewed and approved by the institutional review board of College of Medicine and Health Science, AAU. If you want to know more information, you can contact the committee through the address below. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you may ask at any time you want.

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Annex 2- Data collection tool and check list

This tool is prepared for the collection of socio-demographic, clinical, laboratory, treatment and outcome related information that are important for the assessment of incidence of Tuberculosis and Predictors among children living with HIV attending children HIV care clinic in Adama Referral Hospital and Medical College,2018. All this information was retrieved from the clients ART and pre-ART registration book and from individual patient card without mentioning the name of clients. This information was collected by health care providers (BSc Nurses) possibly working in the ART clinic of the hospitals.

Contact information :-Masino Tessu Cell phone: +251-0920000658, Aklil Hailu Cell phone: +251-09 14 73 12 28, Tefera Mulugeta Cell phone: +251-09 10 36 04 95

Data collection date----------month----------Year----------

Name of the Hospital ----------

Name of data collector---------- signature----------

Name of supervisor----------signature----------

Code No._____

S.N	Part I: Socio demographic characteristics	
101	Date of enrolment	/ / / DD/MM/YY
102	Age at enrolment	Year
103	Sex	1. Male 2. Female
104	Residence	1. urban 2.rural
105	Parental status	1. Both parents alive 4.Double orphan 2.Paternal orphan 5.Not recorded 3.Maternal orphan
106	Family size	1.<2 2.3-4 3.≥5
107	Care givers	1. Parents 4.Guardians 2.Sibling 5.Orphanage centers 3.Grand parents

Part II: Base line clinical, laboratory and ART information

201	Weight at base line	(----------) kg
202	Height/length at base line	(----------) cm

203	Nutritional status at base line	1.Normal …….. 2.Under-nutrition (wasting, stunting) 3.underweight(severe underweight)
204	Functional status at baseline for age ≥ 5 years	1. working 2. Ambulatory 3. Bedridden
205	WHO clinical staging at baseline	Stage I 3. Stage III Stage II 4. Stage IV
206	Did the patient had past TB treatment history	1. Yes 3. Not recorded 2. No
207	Is the treatment completed?	1. Yes 2. No
208	Number of house hold	_____persons
209	CD4 count or CD4% at baseline	(---------) date----------/-------/------
210	Hgb count at base line	----------
211	If CD4 count or CD4% is lower at base line when become normal?	_____months
	Part III: HIV care/ ART follow up and other medication	
301	Date confirmed HIV+	/ / (DD/MM/YY)
302	ART Eligible date	/ / (DD/MM/YY)
303	Eligible criteria	1. CD4 cell count 3. Both 2. WHO clinical stage 4.Not recorded
304	Date ART started	/ / (DD/MM/YY)
305	Initial Regimen	1. 4a=d4t-3TC-NVP 4. 4d=AZT-3TC-EFV 2. 4b=d4t-3TC-EFV 5. 2nd line regimens 3. 4c=AZT-3TC-NVP 6. Others specify(-----)
306	OI prophylaxis given	1.Not given 3.INH 2.Cotrimoxazole 4.other specify(------)
307	Vaccination status	1.Vaccinated 2.Not appropriately vaccinated 3.Not recorded
401	Did the patient develop TB during F/up	1.yes 2.no
402	When was it developed?	/ / DD/MM/YY
403	During what was it developed?	1. Pre ART 2. ART
404	What type of TB was it?	1.PTB 2. EPTB