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# LEVEL OF ADHERENCE TOWARDS ANTI TB REGIMEN AND ASSOCIATED FACTORS AMONG PEDIATRICS IN TIGRAY HEALTH INSTITUTIONS, ETHIOPIA, 2018.

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**ABSTRACT**

**Background:** Tuberculosis (TB) is a major public health problem throughout the world. It is a major problem of children in poor countries where it kills over 100,000 children each year. Almost 1.3 million cases and 450,000 deaths occur in children each year. Ethiopia is one of 22 high burden countries in which TB is the second leading cause of death. To the extent of my knowledge there are no studies conducted on the status of adherence towards anti TB drug and their related factors in children pediatrics in Tigray region.

**Objective:** To assess the level of adherence towards anti TB regimen and associated factors among pediatrics in Tigray health **i**nstitution'**s** 2018.

**Methods:** Institutional based cross-sectional study design was used. A total of 190 children who use anti TB drug were included consecutively from the selected health centers of Tigray in the data collection period. Structured interviewer administered questionnaire was used to the parents and to the children. Data on anti TB user children were reviewed from anti TB registration book. To describe the data percentages and frequency distribution were used binary logistic analysis was also employed. All factors with a p-value <0.25 in the bi-variate logistic regression analysis

was further entered into the multivariable model to control confounding effects then factors that are significant was declared at p-value <0.05. The result was presented using text, tables and figures.

**Result:** In this study the level of child adherence to wards anti TB drug among Tigray health institutions is 67.9%.Children who live in rural area (AOR=1.97; 95% CI: 1.35-10.9), ant-TB drug side effects (AOR=1.82; 95% CI: 1.91,3.33), parents used any method of reinforcement to give children's anti-TB medication (AOR=4.23; 95% CI: 1.66-10.7) and children with Comorbidity AOR=3.36(95% CI 1.21,9.31). were the factors significantly associated with anti TB drug adherence. Among the total rural residents, 37(60.7%) of children had poor adherence on anti TB drug and 24(39.3%) of urban residents also had poor adherence. One hundred seventy-four (91.6%) of respondents reported that there was always availability of ant-TB drug when they were arrived at health center

**Conclusion**: Anti-tuberculosis treatment Adherence is low among children in Tigray region. The study revealed that adherence of children to their medication is not only affected by patient taking medication as prescribed but also parents method used to take medication, drug side effect, presence or absence of other reasons like feeling better, forgetfulness and residence area. The health centers and woreda health office develop strong follow-up of children on anti-tuberculosis treatment to improve status of adherence with focus on rural children.

**Key words:** Anti TB drug, children, TB, adherence

## Background

TB 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 thus at risk of developing active disease. It is a major problem of children in poor countries where it kills over 100,000 children each year. **(1, 2).** Since 2000, significant progress has been made in reaching the World Health Organization's (WHO) global targets for tuberculosis (TB) prevention, care and control to ensure and improve the performance of national TB programme, regular external monitoring and evaluation are required. In 1998, WHO; issued guidance on carrying out reviews of TB program missed the context of DOTS implementation **(3, 4).**

Children with TB differ from adults in their response to the disease, and this has important implications for the prevention, diagnosis and treatment of TB in children. **(5).** It is one of the 10 major causes of childhood mortality with estimated annual death of 74,000_130,000. Ethiopia is one of 22 high burden countries in which TB is the second leading cause of death, it is estimated that children contribute to 16% of national TB burden **(6).**

The therapeutic regimens recommended by WHO have been shown to be highly effective for both preventing and treating TB. To treat TB disease and prevent acquired drug resistance, clinicians must ensure that their patients with TB disease follow the recommended course of treatment. However, ensuring that patients adhere to treatment can be difficult because patients are often unable or reluctant to take multiple medications for several months. Non adherence to treatment is a major problem in TB control **(7, 8).**

In low income countries childhood TB is associated with malnutrition, poverty, over-crowding, higher death rate and lower treatment success rate**(10).** it is estimated that children contribute to 16% of national TB burden. Childhood TB is indicator of recent transmission in population; moreover, children are the primary victims of poor TB control programs and TB is significant childhood morbidity and mortality in the country **(11).**

Adherence to long term therapy is a multidimensional phenomenon determined by the interplay of five set factors namely social and economic factor, health care team, conditional related factor, therapy and patient related factor poor adherence to treatment of chronic disease including TB The failure for cure increase the risk of development of drug resistance TB and further spread in community which in turn increase morbidity and mortality **(12).**

In sub-Saharan Africa there is high rate of loss to follow up of TB patient that range from 11.1% - 29%. Ethiopia is one of the seventh countries that reported lower rate of treatment success and patient who take TB treatment irregularly and unreliable way are at greatly increased risk of treatment failure **(13).** Surveillance of anti TB drug resistance during 1995-2007 among children from south Africa showed a significant increase in resistance to INH and RMP from 2.3%-6.7%. Drug-resistance among children has been documented in clinical trial of both pulmonary and extra pulmonary tuberculosis. Therefore, children under treatment for TB who default from treatment are at risk for clinical deterioration and complication and can continue to be infectious to other and at risk of premature death **(14, 15, 16).** Furthermore, mortality from tuberculosis is highest in early childhood due to children non-adherence to TB treatment. According to 2012 WHO report estimate, half of million children ill with tuberculosis in 2011 of which nearly 64000 children die of TB, even though there is effective medication. **(17, 18).**

In Ethiopia, even though TB drug are given free of fee TB continues to be major cause of TB related child hood death. In developing countries including our country large number of family have no balanced diet for their child normal growth? In these types of children when they are infected with mycobacterium tuberculosis with underlying malnutrition, they develop drug side effect such as drug intolerance and vomiting in intensive phase of the treatment which result in child non-adherence to their treatment. In this type of countries poor adherence is major concern of child hood TB treatment and usually less than one third of participant to the treatment program complete full course of poorly supervised treatment **(19, 20).**

As far as my knowledge little research has been done on level of adherence to anti tuberculosis drug treatment in pediatrics and none in the study area Tigray. The finding of this study also gives an insight to health professional about major factors affecting the pediatric adherence to their anti TB drug treatment schedule. If it is implemented it will improve children cure rate and minimize death from TB in pediatric. The finding may also be used to formulate strategies to improve quality of care for TB pediatric patient. The output of this study might be an input for policy makers in order to improve TB affected children adherence and prevent adherence associated factors.

# Methods and material

The research was conducted in Tigray, Tigray region is one of the nine regional states of the federal democratic republic of Ethiopia located on the northern part of the country. Total population of 5,055,999 (49.2% male and 50.8% female). The region consists of 237 health centers and all those health centers provide anti TB drug dispensing to pediatric patients 9026 health professional working in the health institutions **(28)**. Study was conducted from January - June, 2019. Health institutional based cross-sectional study was conducted. Source population, was all Children's who take/uses anti TB drugs and their parents in health centers of Tigray region. **Study population, was** Sampled Children's that uses anti TB drugs and their parents in selected health centers of Tigray region. We included All Children's who use anti TB drug currently employed in health centers of Tigray. We exclude those children's who are transferred or linked to other health institution during data collection pried. The sample size for the survey was determined using single proportion for population with 95% confidence interval, marginal error (d) of 5 % and the status of Adherence to anti TB in Children's at Adama, Oromia, Ethiopia which was 64.83% **(22)**. So, this proportion was used to determine the sample size. To compensate for non-response, 10% of the sample was added. The total number of children anti TB drug users recently in Tigray region in 2009 E.C yearly report is less than 10,000 [338children] therefore by using the correction formula n**=n/1+n/N= 354/1+354/338 n=354/2.047n=173**

So, the sample size is 173 then by considering 10% of non-response rate a total of 190 anti TB user children and parents will be selected for the study. To keep Data quality**,** Pretest was conducted at 5% of the anti TB children's users and parents necessary corrections were made. After data collection, each questionnaire was checked for completeness, then coded, entered, cleaned and analyzed using SPSS version 23 software package. Dependent variable was adherence to anti TB drug and Independent variables were Socio demographic data, Age, Sex, Residence, Educational level. Parents/Care giver factor, Parent's TB knowledge, Parent's relationship with provider Parent's educational status, Parent's occupation, Parent's income. Patient status factors, Type of TB, New to program, Co morbidity condition, Rx of Comorbidity. Drug related factors, Side effects, Types of side effect, Duration for which dose missed Tablet

load. Health facility related factors, Distance to Health facility, Waiting time, Availability of medication

## Sampling procedure

Sampling frame of the anti TB drug user children's and parents were attained from the 237 health centers TB registration book.

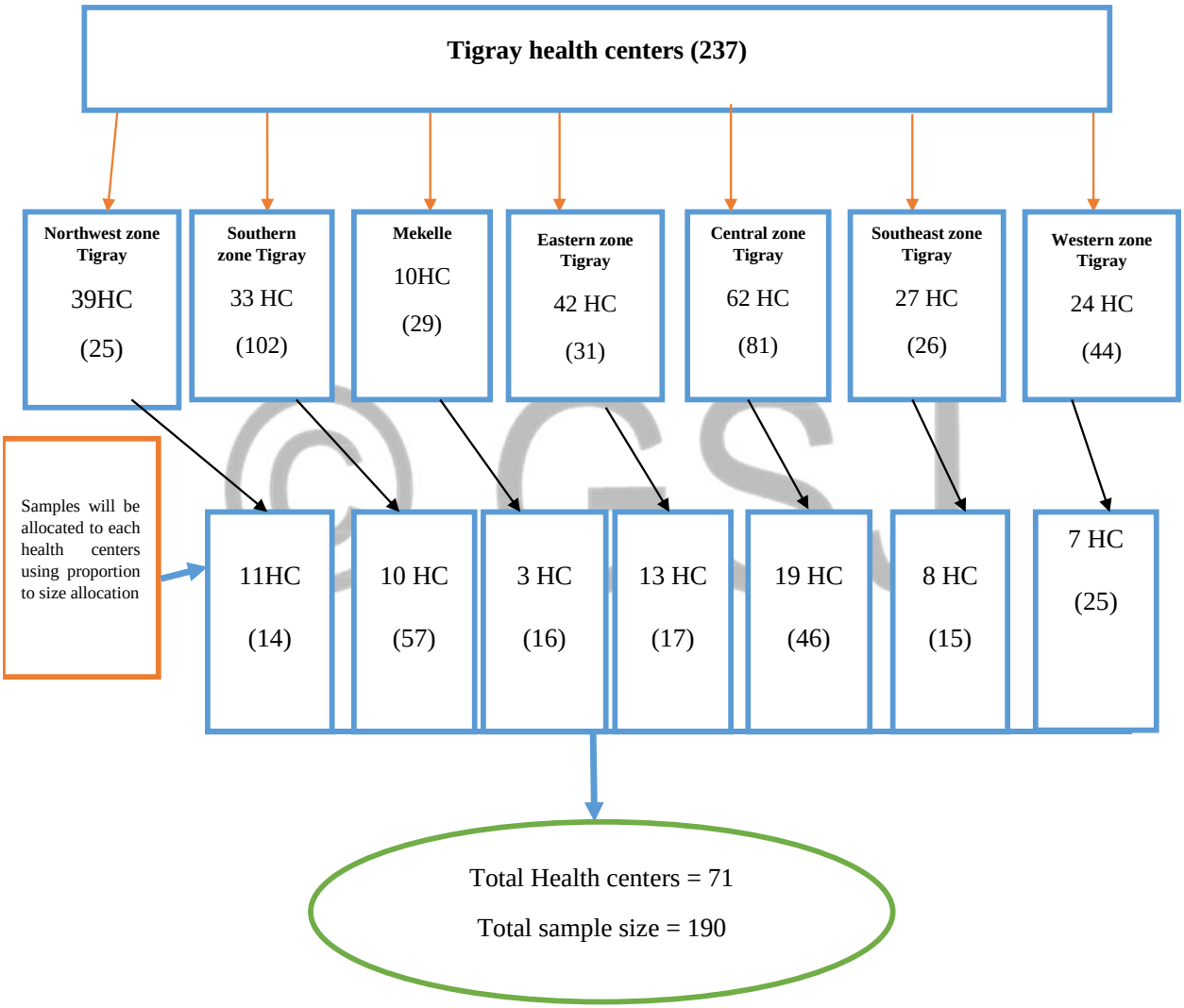


*Figure1 Schematic presentation of sampling procedure for selecting children from health centers, Tigray, Ethiopia, 2018.*

**Operational Definition**

- ✓ **Level of adherent** -Good adherence was defined as adherence rate of a child taking >90% the anti TB drug treatment whereas those who take ≤ 90 were considered as having poor adherence. (32)
- ✓ **Parent TB knowledge** – if parents answer the knowledge questions greater than or equals to 75% it is said to be good knowledge. If parents answers knowledge questions less than 75% it is said to be poor knowledge
- ✓ **Rural:** Inhabitants economic activities were mainly based on agriculture and lacks public facility like telephone, high school, health center, road and the like.
- ✓ **Urban**: for the purposes of this study urban was defined as inhabitant's economic activities were mainly based on non-agriculture and which have a minimum public services and facility like telephone, high school, and health center and year round road.

**Data collection Procedure and instrument**

The data was collected using structured interviewer administered questionnaire which was adapted from another study to the parents and to the children and document review checklist was used. Document on anti TB user children were reviewed from anti TB registration book **(29).** The children with any type of TB was identified after the registration book go through, then they were included consecutively. After provision of training for the data collectors and supervisors they were assigned to the selected study areas then primary data was collected using face to face interview of the care givers and children on anti-tuberculosis treatment. Secondary data was also collected using check list from the tuberculosis treatment register.

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**Ethical Consideration**

Ethical clearance was obtained from Institutional Review Board (IRB) of Mekelle University, College of Health Science. Support letters were obtained from department of nursing and official support letter was requested from Tigray regional health bureau and medical director office of the health centers. The purpose and significance of the study was explained to the study participants and they were assured that they had the right to withdraw from the study at any stage. Written consents for the parents and assent for the children 12≥17 years old were obtained before the data collection. Confidentiality of the study participants were maintained throughout

the study. Beneficence of this study enrolled in benefits of educating about anti TB drug adherence and their related consequences if missed once.

## Result

## Demographic characteristics of child

All the total 190 children sampled for the study, completed the interview yielding a response rate of 100 %. Among the total children participants, urban resident account for 100(52.6%). The mean (SD) age of the patients who participated in this study was (10±4.5) years. Male patients accounted for106 (55.8%) of the study participants

Among the total rural residents, 37(60.7%) of children had poor adherence on anti TB drug and 24(39.3%) of urban residents also had poor adherence. Thirty-three (54.1%) males had poor adherence and 21(34.4%) of the age between 9 -12 years had poor adherence. Thirty-seven (60.7%) of first cycle students had poor adherence of anti TB drug treatment (table1)

*Table 1.**Descrption of socio demographic characteristics with adherence level of children among Tigray health institutions, north Ethiopia, 2018.***

| Variable | | Status of Adherence | | |
|---|---|---|---|---|
| | | Poor | Good | Total |
| | | N(%) | N (%) | N(%) |
| Address of children | Rural | 37(60.7%) | 53(41.1%) | 90(47.4%) |
| | Urban | 24(39.3%) | 76(58.9%) | 100(52.6%) |
| Sex of children | Male | 33(54.1%) | 73(56.6%) | 106(55.8%) |
| | Female | 28(45.9%) | 56(43.4%) | 84(44.2%) |
| Age of children | 1 – 4 | 8(13.1%) | 17(13.2%) | 25(12.1) |
| | 5 – 8 | 20(32.8%) | 20(15.5%) | 40(21.1%) |
| | 9 -12 | 21(34.4%) | 36(27.9%) | 57(30%) |
| | 13 -17 | 12(19.7%) | 56(43.4%) | 68(35.8) |
| Educational status | Nursery | 6(9.8%) | 17(13.2%) | 23(12.1%) |
| | KG | 6(9.8%) | 13(10.1%) | 19(10%) |
| | First cycle | 37(60.7%) | 47(36.4%) | 84(44.2%) |
| | Second cycle | 7(11.5%) | 26(20.2%) | 33(17.4%) |
| | High school | 2(3.3%) | 22(17.1%) | 24(12.6%) |
| | Preparatory | 3(4.9%) | 4(3.1%) | 7(3.7%) |

## Parents' knowledge status

Among the total care giver respondents 59 (96.7%) knew sign and symptoms of TB and mode of transmission, TB curability 56 (91.8%) and important of finishing treatment 55 (90.2%) had poor adherence anti TB treatment and one hundred twenty seven (72.6%) parents did know the prevention of MDR TB (Table 2).

*Table 2.* ***Parent's knowledge status among Tigray health institution, north Ethiopia 2018.***

| Variable | | Status of adherence | | |
|---|---|---|---|---|
| | | Poor | Good | Total |
| | | N (%) | Count Column N% | N&% |
| Do you know cardinal signs and symptoms of TB? | Yes | 59 (96.7%) | 122 (94.6%) | 181(95%) |
| | No | 2 (3.3%) | 7(5.4%) | 9(4.7) |
| If yes cough greater than two weeks | Yes | 53 (89.8%) | 106 (86.9%) | 159(83.6) |
| | No | 6 (10.2%) | 16 (13.1%) | 22(11.5) |
| sweating at night time | Yes | 17 (28.8%) | 37 (30.3%) | 54(28.4) |
| | No | 42 (71.2%) | 85 (69.7%) | 127(66.8) |
| fever >2 weeks | Yes | 13 (22.0%) | 30 (24.6%) | 43(22.6) |
| | No | 46 (78.0%) | 92 (75.4%) | 138(72.6) |
| weight loss >2 weeks | Yes | 13 (22.0%) | 40 (32.8%) | 53(27.8) |
| | No | 46 (78.0%) | 82 ( 67.2%) | 128(67.3) |
| Do you know how it is transmitted? | Yes | 49 (80.3%) | 04 (80.6%) | 53(27.8) |
| | No | 12 (19.7%) | 25 (19.4%) | 37(19.4) |
| Does TB can cure? | Yes | 56 (91.8%) | 116 (89.9%) | 172(90.5) |
| | No | 5 (8.2%) | 13 (10.1%) | 18(9.5) |
| Do you know why it is important good adherence to treatment? | Yes | 55 (90.2%) | 117 (90.7%) | 172(90.5) |
| | No | 6 (9.8%) | 12 (9.3%) | 18(9.4) |

## Patient related factor

In this study pulmonary TB was the higher type of TB 101(53.2%) and among children's who had tuberculosis, 167(87.9%) were not previously treated on ant-TB drug (new) among them 47(77.%) poor adherence anti TB drug The total co morbid children were 35 (18.3%) among them 24(12.6%) were co morbid with HIV/AIDS and all of them were treated from their co morbid disease (HIV, DM) from those co morbid 22(11.5)were poor adherence anti TB treatment Among the total continuation phase 54(88.5%) of children's had poor adherence on anti TB drug (table3)

Table 3.**Patient related factor among Tigray health institution, north Ethiopia 2018.**

| Variable | | Status of adherences | |
|---|---|---|---|
| | | poor N % | Good N % |
| Have he/she ever been treated for TB before | Yes | 14(23.0%) | 9(7.0%) |
| | No | 47(77.0%) | 120(93.0%) |
| What is the type of Tuberculosis diagnosed on the child? | pulmonary tuberculosis | 47(77.0%) | 54(41.9%) |
| | Extra-pulmonary tuberculosis | 14(23.0%) | 75(58.1%) |
| phases in which RX | Intensive | 7(11.5%) | 59(45.7%) |
| | Continuation | 54(88.5%) | 70(54.3%) |
| Does the child have any Comorbidity illness disease? | Yes | 22(36.1%) | 13(10.1%) |
| | No | 39(63.9%) | 116(89.9%) |
| If yes what type of Comorbidity condition | HIV | 16(72.7%) | 8(61.5%) |
| | DM | 6(27.3%) | 5(38.4%) |



## Health facility and drug related factor

Among the total number of study participants,51(83.6%) poor adherence of the respondents were received information privately with their health professionals about treatment of TB and spent enough time with health care provider 46 (75.4%) poor adherence of anti TB drug.

One hundred seventy-four (91.6%) of respondents reported that there were always availability of ant-TB drug when they were arrived at health center and 175 (92.1%) respondents were suitable by space of ant TB clinic. One hundred two (53.7%) of children's were complained that they had anti TB drug side effects and the most common side effects were head ache , nausea and vomiting respectively. Sixty one (32.1%) of children's were *poor adherence* the ant-TB drug while they are on the treatment and the reason for this were; Forgetfulness of the drug, To decrease side effect of the drug, feeling better, religion factor and scarcity of medication; 28[45.95%], 14[23.0%], 11[18.0%], 4[6.6%] and 4[6.6%] respectively.

*Table 4.****Health facility and drug related factor among Tigray health institution, north Ethiopia 2018.***

| Variable | | Status of Adherence | | |
|---|---|---|---|---|
| | | Poor | Good | Total |
| | | N(%) | N (%) | N(%) |
| Do you get to privately speak to the health care provider at the clinic? | Yes | 51 (83.6%) | 97 (75.2%) | 148(77.8%) |
| | No | 10 (16.4%) | 32 (24.8%) | 42(22%) |
| Do you wait for long before you are attended to? | Yes | 29 (47.5%) | 35 (27.1%) | 64(33.6%) |
| | No | 32 (52.5%) | 94 (72.9%) | 126(66.3%) |
| Are the TB drugs always available when you go to pick them from the clinic? | Yes | 57(93.4%) | 117 (90.7%) | 174(91.5%) |
| | No | 4 (6.6%) | 12 (9.3%) | 16(8.4%) |
| Does the space of the clinic suitable for you? | Yes | 50 (82.0%) | 123 (95.3%) | 173(91% ) |
| | No | 11 (18.0%) | 6 (4.7%) | 17(8.9%) |
| Is the amount of time that you spend with the health care provider enough? | Yes | 46 (75.4%) | 114 (88.4%) | 160(84.2%) |
| | No | 15(24.6%) | 15 (11.6%) | 30(15.7) |
| Do you have side effects | Yes | 40(65.6%) | 62 (48.1%) | 102(53.6) |
| | No | 21(34.4%) | 67 (51.9%) | 88(46%) |

Among the total study participants 49% of them promised to reward their children to have good adherent to anti TB drugs (Fig 4).

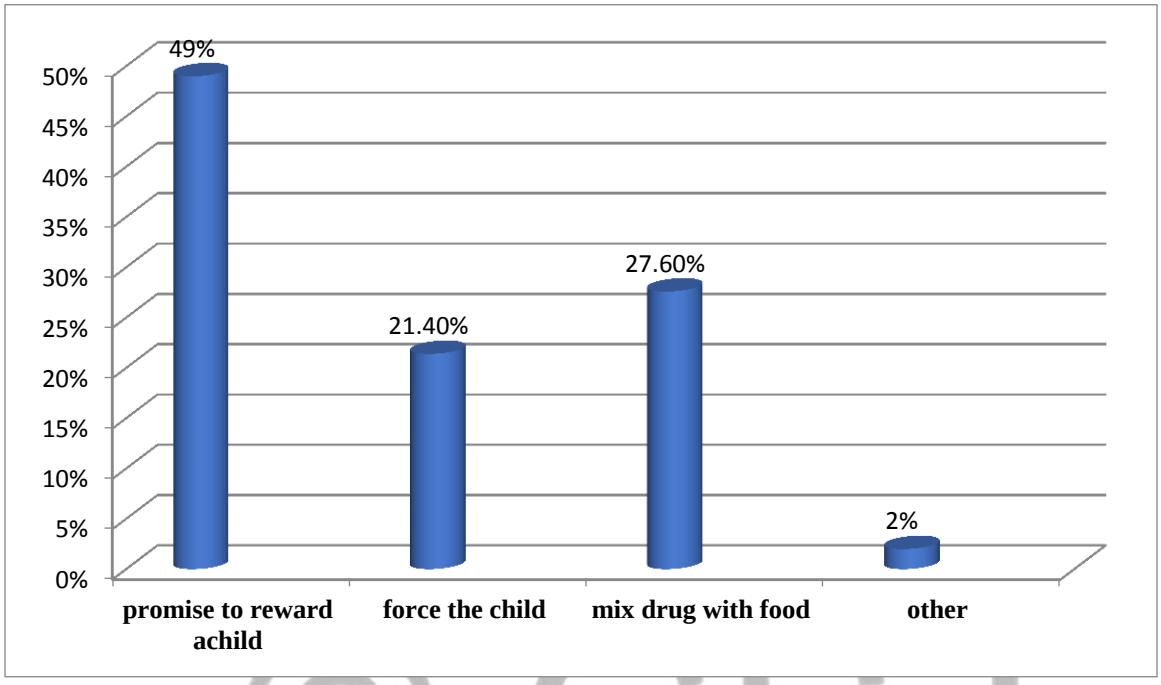


**Figure 4.Parent's method used to take their children's ant TB medication**

**Factors associated with Status of adherence towards anti TB drug among children.**

Bivariate logistic regression analysis was done to examine associations between children's adherence status and each of the determinant factors: care giver factor, drug related factor, health facility related factor, socio demographic factors. Among these all factors, resident, parent TB knowledge, parent educational status, parent income, side effect, and waiting time fulfilled the criteria (p <0.2 significant level).

Children's who live in rural area were 1.97(97%) times more likely to have good adherence than their counterparts **(AOR=1.97; 95% CI: 1.35, 10.9).** in addition**,** Children who complain ant-TB drug side effect were 1.82 times more likely to have poor adherence than who did not **(AOR=1.82; 95% CI: 1.31,3.33)**. Similarly, Care givers who did not use any method to take anti-TB medication were 4.23 times more likely to have poor adherence status than who did use **(AOR=4.23; 95% CI: 1.66, 10.7)**. in addition, Children with Comorbidity were 3 times more

likely to have poor adherence than who did not have Comorbidity **AOR=3.36(95% CI 1.21,9.31)**.

**Table 5. Associated factors with Anti-TB level of adherence among Tigray region health institution**

| Variable | Status of Adherence | | COR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|
| | Poor (% ) | good(% ) | | |
| **Child Address** | | | | |
| **Urban** | 24(12.6%) | 76(40.1%) | 1 | 1 |
| **Rural** | 37(19.5%) | 53(27.9%) | 2.21 (2.24-4.84) | 1.97(1.35-10.9) |
| **Comorbidity** | | | | |
| **Yes** | 22(11.6) | 13(6.8%) | 5.034(2.317,10.933) | 3.36(1.21,9.31) |
| **No** | 39(20.5%) | 116(61.1%) | 1 | 1 |
| **Amount of time spent with healthcare provider** | | | | |
| **Enough** | 32(16.8%) | 94(49.5%) | 1 | 1 |
| **Not enough** | 29(15.3 %) | 35(33.7%) | .41(.22- .77) | .54(.22- 1.32) |
| **Side effect** | | | | |
| **Yes** | 40(21.1%) | 62(32.6%) | 2.06(1.09- 3.77) | 1.82(1.31- 3.33) |
| **No** | 21(32.9%) | 67(76.1%) | 1 | 1 |
| **Method used to take medication** | | | | |
| **Yes** | 14(7.4%) | 37(19.5%) | 1 | 1 |
| **No** | 47(24.7%) | 92(48.4%) | 1.35(1.92- 7.19) | 4.23(1.66- 10.77) |

# Discussion

In this study adherence of children to anti tuberculosis regimen is 67.9% which is slightly lower than a study conducted on children registered for TB treatment at 6 health centers in Gondar which was 85% and a study conducted in urban Kenya showed that the rate of adherence to anti-TB medication was 91.8% (6,27). This could be due to the study conducted in this area were both in rural and urban which made this study to lower the adherence level.

The current study is almost similar study conducted in Adama, Mozambique and Uganda, 64.8%, 68.7%, 70.33%, respectively (17, 24, and31).

The result of this study showed that pulmonary TB was found to be more common in patients when compared with extra pulmonary TB, 101(53.1%) and 89(47.8%,) respectively. This result is similar with studies conducted in different countries (12, 13, 14, and 15). Furthermore, there was no statistically significant association (p = 0.76) between type of TB and patient adherence to their medication. This means that there is no difference in adherence to medication between the types of TB (15).

In this study, among study participants children who live in rural area were 1.97 times more likely to have poor adherence than urban children **(AOR=1.97; 95% CI: 1.35-10.9).** This not in line with study conducted in Kenya, Adama and Uganda **(**12, 22, 31**)**. The possible reason might be due to difference in residence area that is the other studies were conducted in urban area where as in this study both urban and rural were included. In this study children's whose residents from rural area were poorly adherence to anti TB treatment drug than urban residents because of the faraway of health institution from their home place.

As this study indicates Children who complain ant-TB drug side effect were 1.82 times more likely to poor adherence than who did not**(AOR=1.82; 95% CI: 1.31-3.33**). This result is similar with study conducted in Adama (22). This might be due similarity in knowledge of anti TB drug side effects on both communities and this could be due to the presence of drug side effect might bring the children's inability to take the treatment completely (18).

Among the children care giver who did not use any method to take anti-TB medication were 4.23 times more likely to poor adherence than who did use **(AOR=4.23; 95% CI: 1.66-10.7)**. This is

similar study finding in Kenya, (21). It could be due to similarity in educational status and knowledge of care givers and health care professional. Justified as different methods such as promising to reward a child and mix drug with different palatable food would enhance the child ability to take medication throughout the anti TB treatment

In this study there was no significant association between sex, age and patient's adherence to their anti TB medication. This result is also consistent with finding of the study conducted in Kenya, Adama, Nigeria (12, 22,30). Both studies concluded that there was no significant association between age, sex and patient adherence to medication. This could be due to the fact that in pediatric patients' adherence is highly dependent on care giver of the patients (22).

The finding of this study also showed that children with co morbidity like HIV, DM were more likely to have poor adherence than their counter part this is in line with studies done in in Adama, Uganda Nsambya. (17, 31,32).

**Conclusion and Recommendations**

Adherence to Anti-tuberculosis treatment is low among children in Tigray region, north Ethiopia. In the current study found that adherence of pediatric patients to their medication is not only affected by patient taking medication as prescribed but also parents method used to take medication, drug side effect, presence or absence of other reasons like feeling better, forgetfulness and residence area. As the finding of this study shows presence of underlying disease like HIV have effect on adherence of patient to anti TB drug. The parent monthly income also has no effect on adherence of the patient to anti TB medication.

Regional Health Bauru**,** should promote adherence of anti TB drugs through mass media and ensure constant supply of anti-tuberculosis drugs in all health centers**.** woreda health office Should conduct supportive supervision monthly and focus on how to create awareness about factor affecting adherence in the community. health professional Should give special consideration for parents of children who come from rural area and parents should be informed and made aware about TB because children's adherence to their medication is highly dependent on parent's TB knowledge. Health professionals must be sure as they gave all the necessary information's to the children as well as the care givers and Health status of children's patient

should be checked at every visit, Side effect and other reasons which account for missing the dose should be monitored early so that children's will adhere more to their medication.

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