Patient Preference and Adherence

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ORIGINAL RESEARCH

# Adherence to Anti-Tuberculosis Treatment Among Pediatric Patients at Nekemte Specialized Hospital, Western Ethiopia

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**Background:** Non-adherence to tuberculosis treatment is the most challenging and hindering factor for successful tuberculosis therapy. The long duration of tuberculosis treatment and the undesirable effects of anti-tuberculosis drugs result in non-adherence to treatment among pediatric patients. Hence, this study was aimed to evaluate pediatrics adherence status among tuberculosis pediatric patients on anti-tuberculosis treatment at Nekemte Specialized Hospital.

**Methods:** A health facility-based cross-sectional study design was used to recruit pediatric TB patients who were receiving their treatment between February 15 and March 15, 2019. Adherence to tuberculosis therapy was evaluated using data obtained from face-to-face interviews of their respective caregivers. The collected data were entered into EPI-manager 4.0.2 software and analyzed using SPSS version 24. Logistic regression was used to analyze the variables and variables with p-value <0.05 had a statistically significant association with the adherence to anti TB treatment.

**Results:** Among 202 participants involved in the study, 120 (59.4%) of them were males and 119 (58.9%) were in the age category of 11–15 years. A total of 166 (82.2%) of the patients had extra-pulmonary tuberculosis and 174 (86.1%) of them were in the intensive phase. Of the pediatric tuberculosis patients, 48 (73.3%) of them have adhered to the treatment regimen. Female gender [AOR: 3.3, 95% CI: 1.52–7.2], younger age (0–5 years) [AOR: 5.96 95% CI: 1.81–19.6], living in urban area [AOR: 3.73, 95% CI: 1.67–8.36], and patients who did not experience side effect [AOR: 2.87, 95% CI: 1.41–5.81] were predictors of good adherence to tuberculosis treatment up on multivariable logistic regression analysis.

**Conclusion:** The level of adherence observed in our study area was low. Age, sex, residence, and side effect experience showed an association with tuberculosis treatment adherence. Therefore, health care providers should educate all patients with tuberculosis before the initiation of anti-tuberculosis treatment.

**Keywords:** adherence, pediatrics, tuberculosis, treatment, Ethiopia

## Background

Globally, tuberculosis (TB) becomes a public health concern due to the emerging drug-resistant tuberculosis.[1,2] It is the second cause of mortality after malaria, the third cause of hospital admissions, and the main reason for morbidity in Ethiopia.[3]

TB is the most common infectious disease in the pediatric population.[4] Less than half of the estimated 1 million children sick from TB were diagnosed and reported to the World Health Organization (WHO) in 2018.[5,6] An estimated

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230,000 children died of TB, among which 80% were younger than five years old. Ninety-six percent of child deaths from TB occur before the treatment is ever started.[7]

Among the world's 22 high-burden TB countries, Ethiopia ranked seventh. Approximately one million children are estimated to be infected by TB worldwide of which three fourth of them were found in the 22 high-burden countries including Ethiopia.[5] Therefore, to decrease the disease prevalence, compressive intervention should be undertaken by different responsible organizations and stakeholders.[8]

Adherence among Pediatrics TB patients is complex which is affected by the patients themselves and the health care system.[9] Non-adherences to TB treatment can increase TB prevalence and multi-drug resistant tuberculosis (MDR-TB) that in turn increases morbidity and mortality.[3,10-12] Mortality from MDR-TB and extensively drug-resistant TB (XDR TB) groups was 4.4% and 9.3%, respectively.[13]

Concurrent human immune virus (HIV) and TB infection can increase the complexity of TB therapy and it is estimated that 50%of TB patients are co-infected with HIV.[14] Both diseases place a big social, economic, and health burden. Patients with HIV and TB are likely to face more challenges because they have to get HIV care in addition to TB care. Because of their immune suppression, patients are more likely to get severe forms of TB.[15,16]

Non-adherence to tuberculosis treatment is the most challenging and hindering factor for successful tuberculosis therapy. Directly Observed Therapy (DOT) is introduced to ensure patient's adherence to the treatment by giving every dose under direct observation and has been related to decreased rate of treatment failure, relapse and drug resistance. Despite this, its influence on decreasing TB incidence has been inadequate which happens when patients do not turn-up for treatment at the health facility.[3,16-20]

Despite poor TB treatment outcomes of pediatric patients, few studies were reported regarding adherence in Africa.[9] Longer duration of anti TB drugs and their safety may add a particular challenge for non-adherence. However, individualized regimens for drug-resistant TB may help to overcome side effects and increase treatment success.[14,19,21] Anti-TB treatment among pediatric patients is challenging due to a lack of pediatrics drug formulations and difficulties in monitoring drug toxicity. Unlike adults, all children should be treated for latent TB infection if identified.[22]

Adherence to long term treatment is crucial to TB control. A comprehensive approach to TB determinants and enhanced disease awareness may increase treatment adherence.[4,14,18] Studying risk factors for non-adherence is also playing a paramount role to avoid MDR-TB.[19] Determining the contributing factors for non- adherence is indispensable to reduce the TB disease burden and poor outcomes. Hence, this study was aimed to evaluate pediatrics adherence status among tuberculosis pediatric patients on anti-tuberculosis treatment at Nekemte Specialized Hospital.

# Patients and Methods

## Study Setting, Design and Study Period

A health facility-based cross-sectional study design was used to determine the level of adherence to anti-TB treatment among pediatric TB patients on follow up from February 15 to March 15, 2019 at Nekemte Specialized Hospital (NSH). NSH is found in Nekemte town, which is located 330 km to the west of Addis Ababa, the capital city of Ethiopia. The hospital is a specialized hospital and gives health services for more than 10 million people living in western Ethiopia.

## Study Participants and Eligibility Criteria

Pediatric TB patients ≤15 years old who were on anti-TB treatment for at least 1 month and whose caregivers consented to participate in the study were included in the study. Patients who had transferred out to another health facility after treatment started and pediatric TB patients with incomplete data were excluded from the study.

## Study Variables and Outcome Endpoints

The primary outcome variable was adherence to anti-TB treatment whereas independent variables include socio-demographic factors (age, sex, weight, area of residence) and drug-related factors (treatment duration, prescribed medications other than anti-tuberculosis, previous exposure of side effect). The adherence to the drug was assessed based on the self-report of the caregivers. The proportion of adherence was calculated as the number of doses taken by the patients as prescribed by the clinician divided by the number of doses prescribed to the patients in the last 30 days. To calculate the percentage of adherence the ratio was multiplied by 100. Patients who took ≥90% of their medication as prescribed were said to be adherent whereas < 90% were considered as non-adherents.[19]

## Sample Size Determination and Sampling Technique

A total of 231 pediatric TB patients were receiving treatment at NSH from February 15 to March 15, 2019. But

202 Pediatric TB patients' fulfilling the inclusion criteria were included in the final analysis. Hence, the study participants were selected using a convenience sampling technique.

## Data Collection Process and Management

Data were collected using a semi-structured data collection tool which was developed after reviewing different previous pieces of literatures.[9,11,12,23-25] The data collection tool was translated to the area's local language (Afan Oromo and Amharic) and back-translated to English to ensure consistency of meaning. Data were collected by face-to-face interviews of the caregivers of the Pediatric Tb patients. Three nurses and two pharmacists who were working in the TB clinic were selected as data collectors. During the data collection, the completed questionnaires were reviewed and checked for completeness, accuracy, and consistency. Five percent of the sample was pre-tested at Wollega university referral hospital to check the consistency of the data collection tool before data collection was commenced.

## Data Processing and Analysis

EPI-manager 4.0.2 software was used to enter data and analysis was done using statistical software for social sciences (SPSS) version 24. Descriptive data were explained by proportion, means and standard deviations (SD). Multivariable logistic regression was used to analyze the variable and each variable was evaluated independently in bivariate analysis and association was determined using cross-tabulation and crude odds ratio (COR) with 95% confidence interval (CI). All variables that had p-value of less than or equal to 0.25 on the bivariate analysis were entered into multivariate logistic regression. Adjusted odds ratios (AOR) with 95% confidence intervals were computed and the variables with p-value of less than or equal to 0.05 had a statistically significant association with the adherence to anti TB treatment.

## Operational Definitions

Pediatrics: Children whose ages were ≤ 15 years.

Adherent: Patients who took > 90% of their expected medication doses.[3,19]

Non- adherent: Patients were considered non-adherent to treatment if they took < 90% of their expected medication doses.[3,19]

# Results

## Socio-Demographic Characteristics of Study Participants

Among 202 patients involved in the study, 120 (59.4%) of them were males and 119 (58.9%) were in the age category of 11–15 years. Regarding the weight of the participants, about 148 (73.3%) of them were more than 25kg weight and the majority of participants 126 (62.4%) were from rural residences (Table 1).

## Disease and Clinical Related Characteristics

The majority of 166 (82.2%) the patients had extrapulmonary TB and 192 (95%) of them were HIV negative. Regarding the treatment phase, 174 (86.1%) of them were in the intensive phase. Almost all of the patients who were in the intensive phase were taking two medications consisting of isoniazid and rifampin. About 126 (62.4%) of the study participants had experienced TB treatment-related side effects, of those the commonest reported were nausea, vomiting and diarrhea comprising of 55 (27.2%). A total of 15 (7.4%) of the participants reported as they were taking other medication besides TB treatment and of those taking additional treatment, about 10 (5.0%) were taking Highly Active Anti-Retroviral Therapy HAART regimen of Zidovudine + Lamivudine+ Efavirenz (Table 2).

## TB Treatment Adherence

About 148 (73.3%) of them had adhered to their treatment regimen, and the rest 54 (26.7%) had not adhered to their anti-TB drugs.

**Table 1** Socio-Demographic Characteristic of the Pediatrics TB Patients Attending NSH, 2019

| Variables | | Frequency (n) | Percent (%) |
|---|---|---|---|
| Age (years) | 0–5<br>6–10<br>11–15 | 43<br>40<br>119 | 21.3<br>19.8<br>58.9 |
| Gender | Male<br>Female | 120<br>82 | 59.4<br>40.6 |
| Weight (kg) | <25<br>≥25 | 54<br>148 | 26.7<br>73.3 |
| Residence | Urban<br>Rural | 76<br>126 | 37.6<br>62.4 |

**Table 2** Disease and Clinical Related Characteristics of TB Pediatrics Patients Attending NSH, 2019

| Variables | | Frequency (n) | Percent (%) |
|---|---|---|---|
| Side effect | Yes | 126 | 62.4 |
| | No | 76 | 37.6 |
| Type of side effect (n=126) | NVD | 55 | 27.2 |
| | Changed eye color | 27 | 13.4 |
| | Other | 44 | 21.8 |
| Disease classification | PTB-SM+ | 24 | 11.9 |
| | PTB-SM- | 12 | 5.9 |
| | EPTB | 166 | 82.2 |
| Pre-treatment Smear result | Smear positive | 64 | 31.7 |
| | Smear negative | 17 | 8.4 |
| | Not done | 121 | 59.9 |
| Treatment phase | Intensive | 174 | 86.1 |
| | Continuous | 28 | 13.9 |
| HIV status | Positive | 10 | 5 |
| | Negative | 192 | 95 |
| Medicines besides TB treatment | Yes | 15 | 7.4 |
| | No | 187 | 92.6 |
| | Total | 202 | 100 |
| Medicine was taking for (n=15) | HAART | 10 | 66.7 |
| | Multivitamins | 5 | 33.3 |

**Abbreviations:** HAART, highly active ant-retroviral therapy; NVD, nausea, vomiting, and diarrhea; EPTB, extrapulmonary tuberculosis; PTB-SM+, smear positive pulmonary tuberculosis; PTB-SM-, smear negative pulmonary tuberculosis.

## Association Between TB Treatment Adherence Level and Related Factors

In bivariate analysis, age, sex, weight, residence, treatment duration, taking other medication besides TB treatment and side effect experiences were associated with TB treatment adherence at p-value ≤0.25.

However, in the multivariate analysis age, sex, residence, and side effect experience showed an association with TB treatment adherence at p-value <0.05. In this study, patients who were in the age category of 0–5 years were about 6 times more likely to adhere to TB treatment than those in the age category of 11–15 years (AOR: 5.96 95% CI:1.81–19.6). Female patients were 3.3 times more likely to adhere to TB treatment than males (AOR: 3.3, 95% CI: 1.52–7.2). Patients from urban settings were 3.73 times more likely to adhere to TB treatment compared to rural residents. (AOR: 3.73, 95% CI: 1.67–8.36). Finally, patients who did not experience side effects were 2.87 times more likely to adhere to their TB treatment than those who experienced any side effects (AOR: 2.87, 95% CI: 1.41–5.81) (Table 3).

# Discussion

Drug resistance and treatment failure may happen as a result of non-adherence to anti-TB treatment.[12] Thus, the finding of this study plays a paramount role in achieving the TB treatment success rate by decreasing the occurrences of drug resistance.

The study revealed that the overall treatment adherence level was 73.3%, which was higher than study in north Portugal (63.9%)[4] and Mozambique (68.7%),[9] but lower than a systematic review and meta-analysis conducted by Zegeye et al (78.71%).[3] The differences in different findings could be due to variations in definitions of anti-TB non-adherence. No gold standard definition of adherence towards ant-TB treatment is yet available although quantity and timing of missed medication or hospital appointments were recommended by WHO. In our study, patients who missed 10% or more of their prescribed doses of anti-TB drugs were considered as non-adherents while others measured non-adherence if patients discontinued medication for 6 days.[26]

According to two African studies, younger age was associated with non-adherence.[27,28] On the contrary, in our study younger ages (0–5 years) were 5.96 times more likely to adhere to TB treatment than those in older ages (11–15 years). In our setting, pediatric populations did not face significant problems during TB treatment in comparison to the older age due to more support from their social network and caregivers. Hence, pediatric patients took their medication under the supervision of their family that increases the adherence level.

We found differences in adherence to anti-TB therapy between gender. Female patients were 3.3 times more likely to adhere to TB treatment than males. This finding was consistent with the study done in Argentina.[23] This might be because most females stay at home compared to males who are always busy with playing with their peers. Hence, females have less chance of missing their medications. However, the finding was different from the study done in Uganda, and Mozambique that revealed there was no significant difference between genders related to adherence status.[9,14]

Patients from urban were 3.73 times more likely adhere to TB treatment compared to rural residents. This was inconsistent with the finding at Alamata District, Northeast Ethiopia in which the adherence rate was similar among urban and rural residents.[1] Patients' lives in urban areas are more aware of the disease and easily access to nearby health facilities to deal with their treatments. Besides this, patients

**Table 3** Bivariate and Multivariate Analysis of Factors Associated with TB Treatment Adherence Among Pediatrics Patients Attending NSH, 2019

| Variables | | Adhered | Not Adhered | COR (95% CI) | AOR (95% CI) | p-value |
|---|---|---|---|---|---|---|
| Age (age) | 0–5<br>6–10<br>11–15 | 39 (90.7%)<br>30 (75%)<br>79 (66.4%) | 4 (9.3%)<br>10 (25%)<br>40 (33.6%) | 4.94 (1.65–14.78)*<br>1.52 (0.67–3.42)<br>1 | 5.96 (1.81–19.6)**<br>1.75 (0.7–4.36)<br>1 | 0.003<br>0.23 |
| Sex | Male<br>Female | 81 (67.5%)<br>67 (81.7%) | 39 (32.5%)<br>15 (18.3%) | 1<br>2.15 (1.09–4.24)* | 1<br>3.3 (1.52–7.2)** | <br>0.003 |
| Weight (kg) | ≥25<br><25 | 45 (83.3%)<br>103 (69.6%) | 9 (16.7%)<br>45 (30.4%) | 2.18 (0.98–4.85)*<br>1 | 0.74 (0.19–2.84)<br>1 | 0.6 |
| Residence | Urban<br>Rural | 52 (68.4%)<br>50 (39.7%) | 24 (31.6%)<br>76 (60.3%) | 3.29 (0.78–2.78)*<br>1 | 3.73 (1.67–8.36)**<br>1 | 0.001 |
| Treatment duration (months) | ≤2<br>>2 | 130 (74.7%)<br>18 (64.3%) | 44 (25.3%)<br>10 (35.7%) | 1.64 (0.7–3.82)*<br>1 | | |
| Treatment phase | Intensive<br>Continuous | 114 (91.2%)<br>11 (7.3%) | 60 (77.9%)<br>17 (22.1%) | 2.94 (0.93–8.24)<br>1 | | |
| Taking other medication | Yes<br>No | 10 (66.7%)<br>138 (73.8%) | 5 (33.3%)<br>49 (26.2%) | 1<br>1.41 (0.46–4.32)* | | |
| Experienced side effects | Yes<br>No | 81 (81%)<br>46 (60.5%) | 45 (19%)<br>30 (39.5%) | 1<br>2.76 (1.46–5.25)* | <br>2.87 (1.41–5.81)** | <br>0.013 |

**Notes:** *Shows significant at p-value 0.25, **Shows statistically significant at p-value 0.05.
**Abbreviations:** AOR, adjusted odds ratio; COR, crude odds ratio.

from rural areas miss their appointment due to low level of knowledge, lack of transportation, and other facilities.

Patients who did not experience side effects were 2.87 times more likely to adhere to TB treatment than those who experienced any side effects. This was consistent with the study conducted in Southern Ethiopia and Northern Ethiopia, in which side effects of the drugs is an important reason for non-adherence to anti TB drugs.[21,29] On the contrary, the study conducted in Uganda revealed that adverse effects did not have an association with non-adherence.[14] This might be due to clinical pharmacy service has fully applied in that area. When patients experience any side effects, they are fear taking their medications and develop a negative attitude toward the medications. If they are not convinced of the positive consequence of their medication, they start to interrupt to take the medications. Hence, during the provision of the medication and educating patients regarding common side effects helps to improve the adherence level.

## Strength and Limitations of the Study

As a strength, we tried to assess the level of TB treatment adherence in both pulmonary and extra-pulmonary TB patients who received their treatment in the study area. As a limitation, adherence was assessed based on retrospective data with incomplete information. Additionally, since it was a cross-sectional study, it is difficult to predict causality. We were also unable to assess all non-adherence risk factors investigated by other studies (like long wait times in the healthcare facility, distance from the health facility, cost of medications, forgetfulness, the use of herbal medication, social drug use, and co-infection with HIV) since that was operationally difficult at the time of data collection. Lastly, there might be a bias due to a self-reported assessment and was not recorded in any manner via a visual analog scale. Hence caution should be given to generalizing the finding for a large community.

## Conclusion

Compared to the previous studies, the level of adherence observed in our study area was low. Therefore, health care providers should educate all TB patients before the initiation of treatment focusing on the duration of treatment using locally used language. Additionally, clinical pharmacist plays a pivotal role in counseling the patients towards possible side effects of anti TB drugs and ways of management.

Furthermore, strengthening facility DOT for patients staying close to the health facility is needed. This would enable as many patients as possible to be observed by the health care professional when taking their drugs. For the patients living in rural areas, bringing the services closer to where they live is paramount in increasing their adherence status.

## Abbreviations

AOR, adjusted odds ratio; CI, confidence interval; COR, crude odds ratio; DOT, directly observed therapy; EPTB, extrapulmonary tuberculosis; HAART, highly active antiretroviral therapy; HIV, human immune deficiency virus; MDR-TB, multi-drug resistant tuberculosis NSH, Nekemte Specialized Hospital; PTB, pulmonary tuberculosis; SPSS, statistical package for social sciences; TB, tuberculosis; WHO, World Health Organization; XDR-TB, extensively drug-resistant TB.

## Data Sharing Statement

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

## Ethics Approval and Consent-to-Participate

Ethical clearance was obtained from the Institutional Review Board (IRB) of Wollega University. Permission was obtained from the medical director of the NSH to access TB patients and conducts the study. Informed consent was obtained from a parent or legal guardian of the participants. To ensure confidentiality, any identifiers of participants and health care professionals were not recorded on the data collection tool.

## Consent for Publication

Not applicable. No individual personal details, images, or videos are being used in this study.

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## Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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## Disclosure

No competing interests exist.

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