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Original Article

Tuberculosis lymphadenitis and its treatment outcome in Felege Hiwot Referral Hospital, Northwest Ethiopia: a retrospective study

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ABSTRACT

Background: In Ethiopia where there are limited diagnostic facilities and no strong surveillance system, the actual burden and treatment outcome of Tuberculosis lymphadenitis (TBL) is not well known. According to World Health Organization (WHO) treatment outcome is an important indicator of tuberculosis control strategy. Therefore, we conducted this study to describe the proportion and treatment outcome of TBL cases and identified risk factors associated with treatment outcome during treatment in Felege Hiwot Referral Hospital, northwest Ethiopia. **Methods:** We analyzed the records of 425 TBL patients registered at Felege Hiwot Referral Hospital from 2010 to 2012. Information was collected on the number of cases and the treatment outcome of patients was categorized according to the national tuberculosis control program guideline: cured, treatment completed, died, defaulted, failed and transferred out. Pearson's Chi-square test and Fisher exact tests were used to analyze the association between treatment outcome and potential predictor variables; $p < 0.05$ was considered to be significant. **Results:** 425 TBL patients were registered, 55 (12.9%) of whom were children. Of the total of TBL patients, 101 (23.5%) were HIV seropositive. A successful treatment outcome was achieved in 101 (24%) of the patients; the total death rate was 22 (5.2%). Two hundred eighty-nine (68%) patients were transferred to other clinics in the region and 13 (3.1%) were lost to follow-up (defaulted). There were no apparent treatment failures in the cohort. Significant predictors of TBL treatment outcome were: age above the mean (RR=1.65, 95%CI 1.168-2.317, $P = 0.005$) and rural residence (RR=8.65, 95%CI 3.604-20.755, $P = 0.000$). **Conclusion:** In the studied region, a rather high prevalence of TBL was documented. Unfortunately, successful TBL treatment outcomes (24%) in the Felege Hiwot Referral Hospital DOTS center were below the 85% threshold suggested by the World Health Organization. As this is a serious public health concern, it should be addressed urgently.

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1. Introduction

Tuberculosis (TB) is rising globally, with an estimated one-third of the world's population being infected with Mycobacterium

tuberculosis and 7 to 8 million new cases of tuberculosis occurring each year [1]. Developing countries, particularly Ethiopia, have experienced a major increase in the burden of TB, one of the most serious public health challenges. Ethiopia is highly affected by TB and it is ranked 7th among the 22 high TB burden countries by the WHO [2]. The WHO's 2009 Global TB report indicated that Ethiopia had an estimated 314,267 TB cases in 2007, with an incidence rate of 378 cases per 100,000 individuals/year and with prevalence and mortality rates estimated to be 579 and 92 per 100,000 individuals/year, respectively [3]. Thirty-six percent of the cases

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were extrapulmonary tuberculosis (EPTB) with TBL as the most common form, accounting for 80% [4].

EPTB is usually due to dissemination of the bacteria soon after primary infection of the lungs via the lymphohematogenous route to different tissues in the body. EPTB has made a profound contribution to the burden of TB, particularly since the advent of human immunodeficiency virus (HIV) infection [5]. Although previously considered a disease of childhood, TBL now has a peak onset age of 20 to 40 years [6]. According to the Ministry of Health's (MOH) information on TB cases in Ethiopia, the proportion of TBL among newly diagnosed TB cases has increased to 36% [7]. This contrasts with the proportion of EPTB in other high-burden countries in Asia, such as India (14.9%), China (4%), Indonesia (2.5%), and in Africa such as South Africa (17.5%), Nigeria (4.3%) or Kenya (16.6%) [8]. According to the 2008 WHO report [9], Ethiopia is ranked 3rd in terms of the number of EPTB cases globally, most of which are TBL, after India and South Africa but exceeding those of China [8].

Lymphadenopathy is a common clinical problem in Ethiopia and is difficult to diagnose in most rural health centers, because they do not provide culture and cytology/histology services. The diagnosis is usually made by employing conventional microscopy for acid-fast bacilli (AFB). This technique is simple and fast, but it lacks sensitivity, whereas culture is more sensitive and specific, but takes several weeks to produce the results [10]. A fluorescent stain (FS) has been proven to be superior to the Ziehl Neelsen's (ZN) stain [11]. The limited diagnostic capacity for TBL in the country remains a challenge to improving case detection rates.

In Ethiopia, a standardized TB control program using DOTS was started in 1992 and it has been subsequently scaled up in the country and implemented at national level. A DOTS center was introduced in 2000 as part of the strategy for the tuberculosis prevention and control program at Felege Hiwot Referral Hospital. Currently the DOTS geographic coverage in the country is at 95%. However with the population increasing at an annual rate of 2.7%, the country has an increasing demand for the expansion of health services. Physical health service coverage has increased to 87% [8]. The treatment success rate in all forms of tuberculosis is close to the 85%-target set by the WHO. After falling from 80% in 2000 to 70% in 2003, it rose up to 84% in 2007 [12]. The level of TBL and its treatment outcomes has not been assessed in northwest Ethiopia. Therefore, the purpose of this study was to assess the proportion and treatment outcomes of TBL at Felege Hiwot Referral Hospital, northwest Ethiopia.

2. Materials and Methods

The study was conducted at Felege Hiwot Referral Hospital in Bahir Dar, which is the capital city of Amhara National Regional State; 565 km away from Addis Ababa. The hospital is a tertiary health care level hospital serving the population of Bahir Dar town and remote areas of northwest Ethiopia. The total population

served by the hospital is about 12 million. In the hospital DOTS clinic is operating under the National Tuberculosis and Leprosy Program (NTLCP) of Ethiopia, under which the diagnosis of TBL is followed by pathological investigations. In brief a pathologist collected fine needle aspirates of the affected nodes using a 22-gauge needle attached to a 10-cc syringe. The aspirate was macroscopically evaluated for caseation. Freshly purchased reagents were used and air dried smears per patient were prepared and stained with Wright stain for cytological diagnosis. TBL diagnosis by cytology was visualized with the presence of sheets of epitheloid cell granulomas and caseous necrosis with or without multinucleated giant cells. Patients are referred to the DOTS clinic where they are registered and treated according to the NTLCP [13].

Study design and data collection

A two-year retrospective descriptive analysis to assess the prevalence of TBL and treatment outcomes of 425 TBL patients who were registered from January 2010 to January 2012 was carried out in the Felege Hiwot Referral Hospital's DOTS clinic. All of the 425 TBL patients registered at the DOTS clinic were followed up during their course of treatment in order to assess treatment outcome. Socio-demographic data such as patient's age, sex, address as well as, patients HIV serostatus, and treatment outcome were included in the registration form.

Patients' treatment outcomes were evaluated in accordance with the NTLCP [9] and classified as: cured (finished treatment with negative bacteriology result at the end of the treatment), treatment completed (finished treatment but without bacteriology result at the end of their treatment), defaulted (patients who interrupted their treatment for two consecutive months or more after registration), treatment failure (remaining smear-positive at five months despite correct intake of medication), died (patients who died from any cause during the course of treatment), transferred out (patients whose treatment result is unknown due to transfer to another health facility), and successfully treated (a patient who was cured or completed treatment). Patients were provided with free TB medications for a period of 6 to 8 months by the DOTS clinic in the hospital. Patients were followed up regularly until completion of their treatment.

Statistical analysis

Data were entered, cleared, and analyzed using the SPSS statistical software package, Version 15. For categorical data, we used proportions with 95% confidence intervals, differences in proportions were evaluated by Pearson's Chi-square test and Fisher exact tests; $p < 0.05$ was considered to be significant. Institutional ethical clearance was obtained from the Research and Publication Committee Ethical Review Board of the Bahir Dar University.

3. Results

Demographic characteristics and treatment outcome of patients

The study included 425 TBL patients out of which 239 (56%) were males and 186 (44%) were females. Their ages ranged from 1 to 80 years, with a mean age of 24 years. Of the 425 registered TBL patients in the DOTS clinic, 55 (13%) were pediatric and 370 (87%) were adults. The majority of them, 349 (81.9%), belonged to the economically productive age group [Figure 1]. The distribution of TBL patients by sex and age are summarized in Table 1. Among the study subjects, 101 (23.5%) were HIV seropositive. Of the HIV seropositive patients, 51 (12%) were males and 49 (12%) were females. Eighty one (19%) of them were from urban areas and 37 (9%) were in the age group of 25-34 [Table 3].

Table1: Distribution of TBL patients by age, sex and residence (n=425), Northwest Ethiopia, 2010- 2012.

	Male		Female		Urban		Rural	
	N	%	N	%	N	%	N	%
≤14	27	6.4	23	5.4	31	7.3	19	4.5
15-24	87	20.5	46	10.8	95	22.4	38	8.9
25-34	59	13.9	47	11.1	74	17.4	32	7.5
35-44	26	6.1	27	6.4	38	8.9	15	3.5
45-54	27	6.4	30	7.1	37	8.7	20	4.7
55-64	10	2.4	11	2.6	15	3.5	6	1.4
>64	3	0.7	2	0.5	3	0.7	2	0.5

Table 2: HIV Serostatus of study subjects (n=425) by age, sex, and residence, Northwest Ethiopia, 2010- 2012.

Characteristics	HIV Serostatus					
	Positive		Negative		Total	
	N	%	N	%	N	%
Sex						
Male	51	12.0	189	44.5	239	56.2
Female	50	11.5	134	31.8	186	43.8
Residence						
Urban	81	18.8	212	50.1	293	68.9
Rural	20	4.7	112	26.4	132	31.1
Age in years						
≤14	10	2.4	40	9.4	50	11.8
15-24	13	3.1	120	28.2	133	31.3
25-34	38	8.7	68	16.2	106	24.9
35-44	21	4.9	32	7.5	53	12.5
45-54	14	3.3	43	10.1	57	13.4
55-64	3	0.7	18	4.2	21	4.9
>64	1	0.2	4	0.9	5	1.2

We also analyzed the treatment outcome of TBL patients registered at the Felege Hiwot Referral Hospital DOTS clinic during the study period. Treatment outcome of 425 TBL patients is shown in Table 4. A successful treatment outcome was achieved in 101 (24%) of the cases in the study clinic. However, the total defaulter count was 13 (3%), total death count was 22 (5.2%), and 289 (68%) of the patients were transferred out to other clinics in the same region. In these TBL patients it is impossible to know if they are cured or completed their treatment. There were no apparent treatment failures in the cohort. The death rate was high (5%, n=19)

in patients from rural sites as compared to urban dwellers (1%, n = 3). Pearson's Chi-square test and Fisher exact tests analysis showing the association between treatment outcome and potential predictor variables among TBL patients is presented in Table 5. Patients in the age group ≤ 24 had a significantly higher treatment success rate compared to other age groups (RR=1.65, 95%CI 1.168-2.317, P =0.005). On the other hand, patients from rural areas had a significantly lower treatment success rate compared to cases from urban locations (RR=8.65, 95%CI 3.604-20.755, P=0.000).

Table3: Treatment outcome of TBL patients by sex, age, residence, and HIV serostatus (n=425), Northwest Ethiopia, 2010- 2012.

Characteristics	Rx outcome							
	Rx completed		Died		Defaulted		TO	
	N	%	N	%	N	%	N	%
Sex								
Male	54	12.7	11	2.6	5	1.2	169	39.8
Female	47	11.1	11	2.6	8	1.9	120	28.2
Residence								
Urban	96	22.6	3	0.7	5	1.2	173	40.7
Rural	5	1.2	19	4.8	8	1.9	116	27.3
Age in years								
≤14	10	2.4	2	0.5	1	0.2	37	8.7
15-24	46	10.8	1	0.2	4	0.9	82	19.3
25-34	23	5.4	6	1.4	4	0.9	73	17.2
35-44	11	2.6	8	1.9	-	-	34	8.0
45-54	6	1.4	3	0.7	3	0.7	45	10.6
55-64	5	1.2	1	0.2	1	0.2	14	3.3
>64	-	-	1	0.2	-	-	4	0.9
HIV serostatus								
Positive	21	4.9	10	2.4	-	-	70	16.5
Negative	80	18.8	12	2.8	-	-	233	54.8

Rx-Treatment, TO- Transferred out

Table 4: Association between different factors which may affect treatment outcome among TBL patients (n= 425), Northwest Ethiopia, 2010 - 2012.

Variables	Successful Rx=101 (23.5%) N (%)	Unsuccessful Rx=324(76.5%) N (%)	Total (N=425)	RR (Riskratio95%CI)	P-value
Sex					
Male	54(12.7)	185(43.5)	239(56.2)	1.00	0.566
Female	47(11.1)	139(32.7)	186(43.8)	0.89(0.635-1.257)	
Age					
≤ 24	56(13.2)	127(29.9)	183(43.1)	1.00	0.005
> 24	45(10.6)	197(46.4)	242(56.9)	1.65(1.168-2.317)	
Residence					
Urban	96(22.6)	197(46.3)	293(68.9)	1.00	0.000
Rural	5(1.2)	127(29.9)	132(31.1)	8.65(3.604-20.755)	
HIV serostatus					
Positive	21(4.9)	80(18.8)	101(23.7)	1.00	0.503
Negative	80(18.8)	245(57.5)	325(76.3)	0.84(0.551-1.292)	

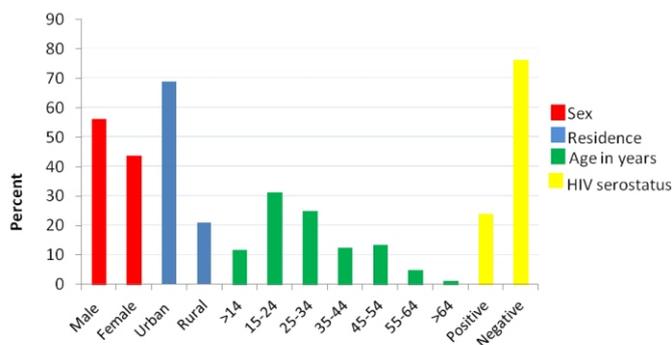


Figure 1: Percent of TBL (n=425), by sex, age, residence, and HIV serostatus, Northwest Ethiopia, 2010- 2012.

4. Discussion

TB remains a major public health problem all over the world and especially in Ethiopia. The proportion of EPTB among newly diagnosed TB cases in Ethiopia is increasing. TBL is the most common presentation of EPTB. The reasons for the increased frequency of TBL in Ethiopia are unknown. There was no information about the proportion and treatment outcome of TBL in Felege Hiwot Referral Hospital, northwest Ethiopia. In this study the proportion of TBL patients was 56.2%. This can be contrasted to the national estimate of EPTB which is 34%. This proportion of TBL is higher than the proportions found in studies conducted in Gondar 28.3% [14], Tigray and Amhara 39% [15], southeast Ethiopia 19.5% [16], the Afar region 28% [6], and Shashemene 54% [15]. However, our finding is comparable to the rate found in a study conducted in Butajira, (a part of rural Ethiopia): out of 72 patients with a clinical diagnosis of EPTB, 40 (56%) were TBL [17]. Rahel et al. [18] also reported the occurrence of high proportion of TBL (78%) in the country in 2009.

Yet another study conducted in Butajira also showed that out of 147 patients, 107 (73%) were confirmed TBL [19]. This variation might be due to the underestimation of TBL in most rural health centers in Ethiopia where there is lack of expertise and laboratory facilities. In addition, the design of the studies, including factors such as sample size and study subjects, geographical differences, hospital organization, and differences in policies of infection prevention and control may be other reasons for the discrepancies in the study results. Furthermore, other studies in different areas of the country also reported the occurrence of high proportions of TBL at 74.4% and 68.6% [20, 21], respectively. Delayed diagnosis of pulmonary tuberculosis, incomplete treatment of TB, HIV co-infection, and other underlying diseases may increase the TBL manifestations of TB. The most common age group affected in this study was 15-24 years, followed by 25-34 years. This is in agreement with the study conducted in the Afar region [6]. Also, in the USA and UK, the highest incidence of TBL is found in patients between 25 and 50 years of age [22]. The ratio of males to females in this study was 1.3:1, which is in contrast to that found by Mengstu et al. (1:1.4) [6] and Subrahmanyam (1:1.3) [23].

In our two-year national cohort of pathologically-confirmed TBL cases in Felege Hiwot Referral Hospital DOTS clinic, we observed a successful outcome of treatment in 24% of patients, far less than the target level presented by the WHO for successful outcomes. This is unsatisfactory. The proportion of successful treatment outcomes in our study was lower than for all forms of pulmonary tuberculosis reported in Gondar (29.5%) [14], the southern part of Ethiopia (70%) [16], and by the NTLCP in Ethiopia (78%) [13].

In a study combining outcomes from pulmonary and extrapulmonary cases, the proportion with successful treatment outcomes was 82% [24], but it is not comparable to our current figures. The present study shows that the death rate (5.2%) was similar to other studies conducted in southeast Ethiopia (5.3%) [16]. The defaulter rate in this study (3.1%) was lower than in other studies conducted elsewhere in the country which yielded 36.4%, 11.3%, 6%, and 20% [14, 16, 19, and 25] defaulters, respectively. This lower defaulter rate in this study might be due to the proper supervision and health education that occurred in the cohort. According to a WHO report [26], the treatment failure rates are low, i.e., in Zimbabwe 0.1% and in other high TB burden countries approximately 1.5%. Belay et al. in 2009 [14], also reported only 0.2% treatment failure rate and there were no apparent treatment failures in the patients of our study group. In this study, the patients from rural areas had a significantly lower treatment success rate compared to cases from urban areas ($P=0.000$). The main reason for this difference may be lower awareness of TB treatment and the long distance between their homes and the treatment center. Close monitoring and health education for rural patients is very necessary. The patients in the age groups > 24 had significantly lower treatment success rates compared to other age groups ($P=0.005$); advanced age has been reported to be a risk factor for death, partly due to co-infection and general physiological deterioration with age. Thus it is vital to exercise close monitoring of TB treatment in older patients [14].

The large number of TBL cases in this study might be TB-HIV co-infection. In the present study, the prevalence of HIV among TBL patients was 23.5% of which the most affected age group was 25-34 years. This is much higher than the national average HIV infection rate of 7.5% [22]. However, it is similar to that found by Yassin et al. (22.5%) [19], it is much higher than found in a study done in Butajira, a rural town (11%) [18], and it is markedly lower if compared with other reports by Rahel et al. (28%) [18], and from countries in sub-Saharan Africa where the HIV co-infectivity rate among TBL was greater than 80% [26]. In 2007, Afework et al. [27] reported 34.4% of TB-HIV co-infection in EPTB patients. According to a WHO report [9], the prevalence of co-infection in all forms of TB was 11% which is much lower than the present finding. Thus, our results indicate the necessity of strengthening interventions to reduce TB-HIV co-infection in the study region. In this study, the treatment success rate for HIV negative patients (18.8%, $n = 80$) was higher than for HIV positive TBL patients (4.9%, $n = 21$), indicating that HIV testing before treatment is important.

5. Conclusion

The current study has provided an insight into the dynamics of TBL in northwest Ethiopia, Bahir Dar. The proportion of TBL in the study area is 56.2%. However, the actual risk factors for contracting TBL remain to be assessed in future studies. In addition, the proportion of favorable outcomes for TBL patients treated at the Felege Hiwot Referral Hospital DOTS center was far below the goal set by the WHO. Assessment of the outcome of TB patients' treatment in general and TBL patients' treatment in particular is an important step in achieving the WHO treatment success target. To improve the treatment outcomes of tuberculosis patients, we suggest that enhanced supervision, follow-up, counseling during their treatment phases, and health education is crucial. Separate reporting of treatment outcome in pulmonary and extrapulmonary tuberculosis should be also considered.

Competing interests

We authors declare that we have no competing interests.

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