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## Frequency of Tuberculous Lymphadenitis (TBLA) in Somalia: A Retrospective Study with GeneXpert PCR-Based Diagnosis

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### ABSTRACT

Tuberculous Lymphadenitis (TBLA) poses a significant public health burden globally, particularly in Somalia due to high tuberculosis prevalence. It often faces diagnostic challenges due to its nonspecific symptoms; making early treatment critical. Additionally, high HIV and MDR-TB burden can also exacerbate the scenario. Hence, this study aims to determine the rate of TBLA in Somali population using GeneXpert PCR assay. This retrospective observational study was conducted at NOVA Diagnostic and Research, a leading diagnostic center in Mogadishu, Somalia, from January 2024 to August 2024. A total of 499 suspected cases were included. Among the study participants, the male-to-female ratio was 0.98:1. 36.07% of individuals tested positive for TBLA. The disease was found to be more prevalent among younger participants, particularly those under the age of 40. A significant association was observed between the site of aspiration and TB positivity ( $p < 0.005$ ), with cervical lymph nodes being the most commonly affected site, accounting for 67.2% of positive cases. Additionally, TB was detected in multiple lymph node sites in 8.3% of the all specimens. In Somalia, the rate of TBLA continues to remain elevated, especially in younger population. More strategic approach is necessary to reduce the burden effectively. Rapid and accurate diagnosis of TBLA can be performed by GeneXpert real-time PCR, for early detection and treatment.

### INTRODUCTION

Tuberculous lymphadenitis (TBLA), earlier known as scrofula, is one of the most common manifestations of extra-pulmonary tuberculosis (EPTB) (Prasad *et al.*, 2024). TBLA is observed when the infection caused by tuberculous mycobacteria disseminates to the lymphatic system, generally to the cervical lymph nodes. This leads to granulomatous inflammation, caseous necrosis, and eventually the enlargement of the lymph nodes (Lucas, 2017). Symptom is typically associated with fever, night sweats, fatigue, and weight loss. Treatment typically involves a six-month regimen, with isoniazid, rifampin, ethambutol, and pyrazinamide for the initial two months, followed by isoniazid and rifampin for the next four months, as recommended by the WHO (Strategy, W.S.T., 2008). Due to its asymptomatic nature, TBLA often remains undiagnosed during its early stages. Hence, the severity of the disease is often overlooked on a global scale, resulting in delayed treatment. However, the regions with high disease burden such as Sub-Saharan Africa and Southeast Asia face substantial health crisis due to TBLA. Somalia, an East-African country, possesses a significant prevalence of TBLA cases in conjunction with high overall Tb burden. Risk factors such as the high prevalence of HIV in Somalia play a critical role in the development and spread of TB. As HIV weakens the immunity, it might result in individuals to become more susceptible to co-

infections like TBLA. Several studies have demonstrated a strong relation between TBLA and HIV co-infection, further complicating the disease management landscape (Tesfaye *et al.*, 2017; Gounden *et al.*, 2018; Perenboom *et al.*, 1994; Abebe *et al.*, 2012). Age and gender may also play as a critical contributor to the disease. Some studies have found that females are disproportionately affected with TBLA compared to males (Muluye, 2023; Fader *et al.*, 2010; Purohit *et al.*, 2009). On the contrary, no association between them was also observed in some studies (Mathiasen *et al.*, 2020). Moreover, the escalating prevalence of multidrug-resistant TB (MDR-TB) is a significant public threat, complicating the treatment of TBLA (Hassan *et al.*, 2024; Tukade *et al.*, 2024).

Over the decades, Somalia has continued to combat the TB epidemic, persistently working to eliminate it despite challenges. However, the Tb program management of the country has made remarkable improvements limiting the death rates by 14% in the last 14 years (WHO). Still, to eradicate the disease completely, it is crucial to improve surveillance, promote awareness, offer advanced and specialized diagnosis techniques, and effective treatment regime.

For identifying Tb more accurately and rapidly, molecular testing proves to be very effective, even from samples such as lymph node aspirates or biopsy. Techniques such as PCR or real-time PCR can immediately detect

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the presence of DNA of *Mycobacterium tuberculosis*, thereby providing quicker results than traditional culture methods. This is particularly efficient for determining TBLA, where the symptoms are often less specific (Mohamed *et al.*, 2023; Mirghani *et al.*, 2024). Molecular testing ensures timely treatment initiation, which is crucial in preventing further complications and transmission.

Given the circumstances, this research aims to determine the prevalence of TBLA among the patients of a hospital in Mogadishu, Somalia, using GeneXpert real-time PCR method. By leveraging real-time PCR, the study seeks to generate accurate and rapid diagnosis on the burden of TBLA in this region, which is necessary for advancing diagnostic accuracy, developing treatment strategies, and promoting public health interventions to address TBLA effectively in Somalia.

## MATERIALS AND METHODS

### Study Design, Period and Study Population

This retrospective observational study was conducted at NOVA Diagnostic and Research, a leading diagnostic center in Mogadishu, Somalia, from January 2024 to August 2024. The study enrolled participants with suspected cases of tuberculous lymphadenitis. Data were systematically extracted from the laboratory's registration logbook, and a total of 499 suspected cases were included. Records with incomplete demographic information were excluded to ensure data integrity and reliability.

### Sample Collection and Processing

Fine-needle aspiration cytology (FNAC) of lymph nodes was performed under aseptic conditions using a 20 mL disposable plastic syringe fitted with a 23-gauge needle. The obtained aspirates were analyzed using the GeneXpert assay. The diagnosis of tuberculous lymphadenitis (TBLA) was established based on cytological findings, which included the presence of chronic granulomatous inflammation, atypical hyperplasia, actinomycosis, secondary carcinoma, or secondary undifferentiated nasopharyngeal carcinoma, among other pathological features.

### Data Analysis

Data were analyzed using SPSS. The descriptive variables were described as frequency (percent). The association test between the categorical variables was analyzed using the Chi-square test. P-value <0.05 was considered statistically significant.

## RESULTS AND DISCUSSION

### Demographical Findings

The study examined the aspirates in a total of 499 suspected cases of tuberculous lymphadenitis (TBLA), with an almost equal gender distribution of 49.1% males and 50.9% females. The mean ( $\pm$ SD) age of the participants was  $27.71 \pm 17.53$  years. Participants were grouped into 10-year age intervals, with the largest proportion (26.7%) falling between 21 and 30 years,

while only a small percentage (2.6%) were over 70 years of age. When distributed regionally, the majority of participants (87.6%) were from Mogadishu, the capital city of Somalia. The remaining participants were across other regions, with 7.0% from Southern Somalia, 3.6% from the Central region, and 1.8% from the Northern region (Table 1).

Aspirates were collected from various lymph node sites, as shown in Figure 1. The most affected site was cervical lymph node with a proportion of 68.3% amongst all. Followed by were supraclavicular, submandibular, and axillary with 6.6%, 5.6%, and 5.2% respectively. Along with that, few participants were found with lymph node swelling at multiple sites (6.6%).

### GeneXpert Real-Time PCR findings

PCR findings showed in that, among the total participants, 180 (36.07%) had lymphadenopathy due to tuberculosis ( $p < 0.005$ ) (Figure 2). Male/female ratio did not have any significant difference (0.98:1). Based on age distribution, the highest rate of TBLA was found in age group 11-20 (41.7%), followed by 31-40 (39.2%) and 21-30 (38.3%) participants. Positivity rate was comparatively less in age group below 10 years and 41-50, with 26.3% and 21.6% respectively (Figure 3).

### PCR Findings Based on Sites of Aspiration

A diverse positivity rate of TBLA was observed in different aspirates depending on the site of lymph node involvement. The presence of the bacteria was observed in 35.5% cervical aspirates, accounting for 67.2% of all positive cases due to their high sample size. Higher positivity rates were observed in the supraclavicular (57.6%) and para-aortic (55.6%) lymph nodes as well, although the total number of aspirates from each site was relatively low.

### Discussion

Tuberculous Lymphadenitis (TBLA) is a significant health concern worldwide, particularly in the African region, which is facing a disproportionate burden due to high tuberculosis rates and associated risk factors. As a localized form of tuberculosis, TBLA is often characterized by swollen lymph nodes and can present diagnostic challenges due to its nonspecific symptoms, which may mimic other infectious or inflammatory conditions (Mathiasen *et al.*, 2020). In Somalia, where healthcare infrastructure is still developing and the population faces socioeconomic challenges, TBLA remains a critical public health issue. Hence, it underscores the need for enhanced diagnostic strategies, targeted public health interventions, and a better understanding of the epidemiological factors contributing to its spread. However, Mogadishu has initiated improved diagnostic approaches in association with WHO to mitigate the overall public health burden, particularly Tb and associated diseases. Therefore, the present study aimed to evaluate the rate of Tuberculous Lymphadenitis (TBLA) among patients with swollen lymph nodes.

In the present study, the prevalence of tuberculous lymphadenitis (TBLA) was found to be 36.07%, representing a substantial proportion and underscoring tuberculosis (TB) as a significant cause of lymphadenopathy in the study population. Comparable studies conducted in Ethiopia and Tanzania reported higher prevalence rates of 69.5% (Muluye, 2023). This discrepancy may be attributed to variations in sample size. Several factors contribute to the increased risk of tuberculosis (TB) progression in Somalia. These include the country's demographic profile, densely populated living-setting, nutritional deficiencies, and behaviors such as cigarette and khat consumption. These factors collectively worsen the susceptibility to TB by compromising the immune system and increasing exposure to potential infections. Regarding gender distribution, the male-to-female ratio in our study was 0.98:1, suggesting no association. This finding aligns with another study conducted in Ethiopia (Muluye, 2023). Along with demographical and genetic factors, addressing the interplay between behavioral factors like cigarette smoking and khat consumption is essential in understanding their combined impact on health. Khat is widely chewed traditionally and culturally in the Sub-Saharan countries by both males and females. Chronic khat consumption has been associated to weak immune system, impaired lymphocyte function, and accelerated inflammation, all of which can add the risk of TB infections (Kebede, 2002). The age distribution of TBLA cases revealed preponderance among younger individuals, with 11–20 years age group accounting for 41.7% of cases, followed by 31–40 years age group with 39.2%. These findings are consistent with earlier studies, which have also identified

that younger individuals are most commonly affected age group (Ali *et al.*, 2014; Mohamed *et al.*, 2023). This is possibly attributed to the fact that younger people are most likely to have a less developed immune system, which makes them more vulnerable to disease. Additionally, in densely populated areas, younger population may have greater exposure to Tb due to frequent interactions in schools, social gatherings, or crowded living-settings. While looking into the site of aspirates, the cervical lymph nodes were the most commonly affected site, accounting for 67.2% of positive cases. These nodes are the most common site for aspirates in the diagnosis of TBLA, due to its crucial role in the drainage of respiratory system. This finding is congruent with observations from the previous studies done in Ethiopia (47.5% and 74.2% respectively) where cervical regions were the most affected region (Muluye *et al.*, 2023; Bezabih *et al.*, 2002; Mathiasen *et al.*, 2020). Along with that, this study found that Tb was also detected in large proportion in supraclavicular, para-aortic and submandibular lymph nodes. Moreover, aspirates were collected from multiple sites, in which a high rate of Tb was observed (44.1%), highlighting the advancement of the disease. This is indicative of the requirement of intensive treatment, as the infection has disseminated to the bloodstream (Mathiasen *et al.*, 2020). The incidence of TBLA underscores a global, collaborative effort to focus on early diagnosis and treatment, and effective prevention strategies to eradicate tuberculosis (Le Roux & Vlok, 2021). In this study, the laboratory diagnosis of TBLA was performed by GeneXpert real-time PCR, which has proven to be a highly effective method for detecting the presence of TB early. This is because; PCR allows quick diagnosis and treatment, significantly

**Table 1:** Characteristics of the subjects

Variables	N (%)
<b>Gender</b>	
Male	245 (49.1)
Female	254 (50.9)
Mean age±SD [IQR]	27.71±17.53 [12.5-63.5]
<b>Age range</b>	
≤10	76 (15.2)
11-20	120 (24.0)
21-30	133 (26.7)
31-40	79 (15.8)
41-50	37 (7.4)
51-60	24 (4.8)
61-70	17 (3.4)
>70	13 (2.6)
<b>Region</b>	
Mogadishu (Capital)	437 (87.6)
Central	18 (3.6)
Northern	9 (1.8)
Southern	35 (7.0)

improving the accuracy of detection even in low-bacterial load samples. However, there were few limitations. As this is a retrograde study, a significant limitation was the absence of comprehensive patient records. Records of co-morbidity like HIV, lifestyle, and history of Tb could not be retrieved. HIV is highly prevalent in Somalia, and

may influence the risk of TB. Other limitation was lack of latest comprehensive research on the prevalence of TBLA in high-incidence countries like Somalia. The finding in the present study underscores the importance of considering TB as a primary differential diagnosis in regions or populations with high TB prevalence.

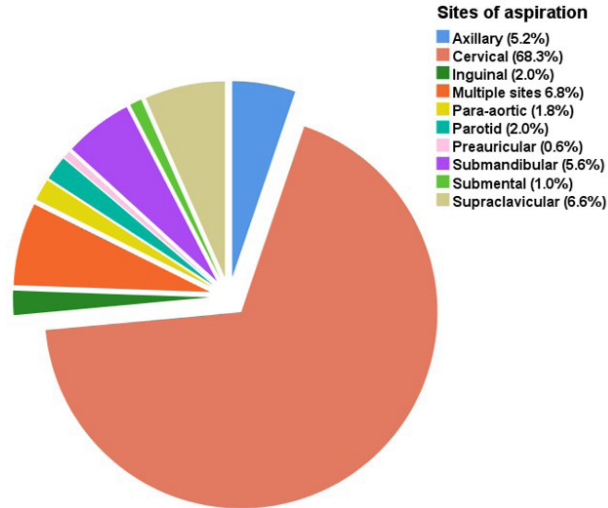


Figure 1: Distribution of sites of aspiration

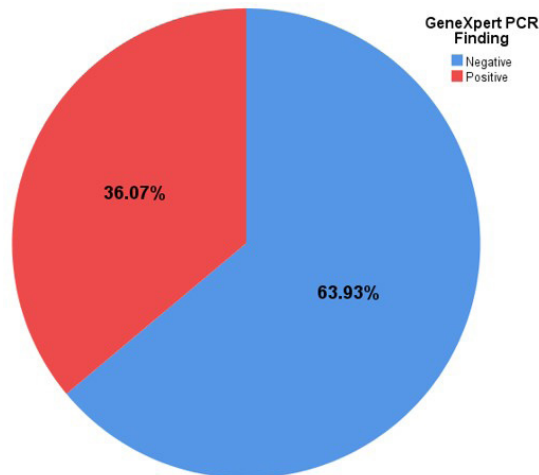


Figure 2: Incidence of TBLA

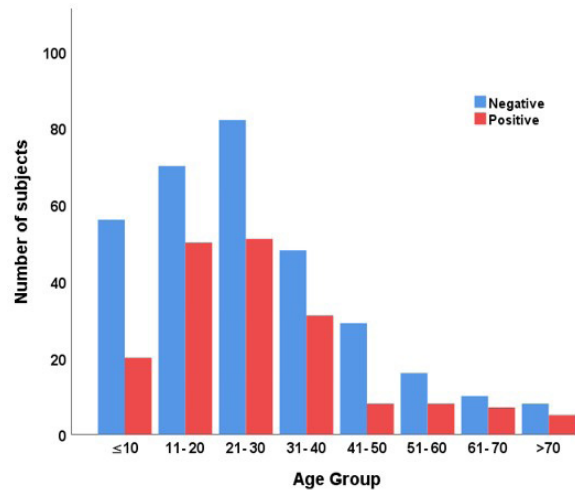


Figure 3: Incidence of TBLA based on age group

**Table 2:** PCR results based on sites of aspiration

Variables	Total N (%)	Positive N (%)	Negative N (%)	f/p value
<b>Site of aspirates</b>				
Axillary	26 (5.2)	7 (26.9)	19 (73.1)	0.032
Cervical	341 (68.3)	121 (35.5%)	220 (64.5)	
Inguinal	10 (2.0)	3 (30.0)	7 (70.0)	
Para-aortic	9 (1.8)	5 (55.6)	4 (44.4)	
Parotid	10 (2.0)	-	10 (100.0)	
Preauricular	3 (0.6)	-	3 (100.0)	
Submandibular	28 (5.6)	9 (32.4)	19 (67.9)	
Submental	5 (1.0)	1 (20.0)	4 (80.0)	
Supraclavicular	33 (6.6)	19 (57.6)	14 (42.4)	
Multiple sites	34 (6.8)	15 (44.1)	19 (55.9)	
<b>Number of lymph node</b>				
Single	466 (93.4)	165 (35.4)	301 (64.6)	0.245
Multiple	33 (6.6)	15 (45.5)	18 (54.5)	

Results are expressed as number (%). Chi-squared test was performed to calculate statistical difference. P-value <0.005 was considered as level of significance.

### CONCLUSION

Tuberculous Lymphadenitis (TBLA) remains a substantial burden in Somalia, despite public health initiatives and adherence to WHO-recommended treatment protocols. This study revealed that 36.07% of the participants were found with TBLA, reflecting significant concern due to tuberculosis in the region. Moreover, TB was detected from multiple lymph node sites, indicating systemic dissemination of the disease. Therefore, it strengthens the need for swift diagnosis and treatment to reduce the severity of disease and effective patient outcomes. The study also highlights the integration of molecular techniques such as PCR into routine diagnostics, as it allows early and accurate TBLA detection.

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