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Original Research Article

EVALUATION OF ANTITUBERCULOSIS TREATMENT RESPONSE IN PERIPHERAL TUBERCULOUS LYMPHADENOPATHY: INSIGHTS FROM A PROSPECTIVE COHORT

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ABSTRACT

Background: Peripheral tuberculous lymphadenopathy (PTL), a common extrapulmonary tuberculosis manifestation, particularly in endemic areas, presents diagnostic and therapeutic challenges. This study aimed to evaluate the efficacy of antituberculosis therapy for peripheral tuberculous lymphadenopathy.

Materials and Methods: This prospective study included 80 patients with cervical lymphadenitis. A structured proforma was maintained containing the basic characteristics of patients, including age, sex, occupation, personal history, symptoms, and investigations such as CBNAAT, FNAC, and Biopsy. After two months of the intensive phase, the patient's response to ATT was assessed. After the continuation phase of ATT, residual lymph nodes at the end of treatment (6 or 9 months) were assessed for treatment outcomes.

Results: The most affected age group was 21–30 years (33.8%), followed by 11–20 years (26.3%), with female predominance (62.5%). A history of TB contact was reported in only 8.8% of cases. Most patients (65%) did not exhibit any constitutional symptoms. Right-sided lymphadenopathy was observed in 51.3% of patients, with the upper jugular group being the most commonly involved (51.3%). Matted lymph nodes were observed in 22.5% of patients. After 9 months of ATT, 76.7% had complete resolution. Of 17 with persistent swelling, 3 had MDR-TB and 14 had drug-sensitive TB. New swelling developed in 4% of patients, 4% defaulted, 3% died during treatment unrelated to TB, and 1% received an alternative diagnosis after further evaluation.

Conclusion: Our study concluded that the treatment outcomes of PTL are suboptimal compared to those of pulmonary TB, with many patients showing incomplete lymph node resolution despite standard ATT.

Keywords: Peripheral tuberculous lymphadenopathy, cervical lymphadenitis, antituberculosis therapy, extrapulmonary tuberculosis, lymph node resolution, tuberculosis treatment outcome.

INTRODUCTION

Tuberculosis (TB) continues to pose a major global health challenge, with the World Health Organization (WHO) reporting an estimated 10.6 million new cases and 1.3 million deaths in 2022 alone.[1] While pulmonary tuberculosis accounts for the majority of cases, extrapulmonary tuberculosis (EPTB) constitutes about 15–20% of all TB cases in individuals with normal immune function, and a higher percentage in those with compromised immune systems.[2] Among the extrapulmonary forms, peripheral tuberculous lymphadenopathy (PTL) is the most common manifestation, especially in regions where TB is highly endemic.[3]

The PTL primarily targets the cervical lymph nodes, though it can also affect the axillary and inguinal nodes.[4] This condition is most common in children and young adults, often manifesting as painless lymph node enlargement accompanied by

constitutional symptoms such as fever, night sweats, and weight loss.[5] Diagnosis involves a combination of clinical suspicion, radiological imaging, histopathological evaluation, and microbiological confirmation through fine needle aspiration cytology (FNAC), excisional biopsy, or molecular assays like GeneXpert MTB/RIF.[6,7]

Standard antituberculosis therapy (ATT), as recommended by national and international guidelines, remains the cornerstone of PTL treatment. The standard treatment regimen includes a 6-month course beginning with an intensive phase using isoniazid, rifampicin, pyrazinamide, and ethambutol, followed by a continuation phase with isoniazid and rifampicin.[8] Despite following this standardised regimen, the therapeutic response in PTL cases can vary, with some patients experiencing paradoxical reactions, delayed lymph node resolution, or relapse. These outcomes raise significant concerns about the optimal treatment duration, early response predictors, and therapeutic endpoints.[9,10]

Although several studies have documented the clinical outcomes of ATT in pulmonary TB, there is limited high-quality evidence focused specifically on the efficacy of ATT in peripheral tuberculous lymphadenopathy.[9,11,12] Additionally, the variability in clinical presentations and therapeutic responses underscores the need for localised data to support evidence-based management in diverse populations. Therefore, this study was conducted to assess the effectiveness of antituberculosis therapy in patients with peripheral tuberculous lymphadenopathy, focusing on clinical resolution rates, time required for lymph node regression, incidence of treatment-related adverse effects, and recurrence after therapy. The findings of this study aim to assist clinicians in optimising therapeutic strategies and enhancing prognostic outcomes in PTL.

MATERIALS AND METHODS

This prospective study was conducted in 80 patients with cervical lymphadenitis at the Department of Thoracic Medicine, Tirunelveli Government Medical College, from January 2019 to June 2020, over 18 months. The Institutional Ethics Committee approved the study, and informed consent was obtained from all patients before the study initiation.

Inclusion and exclusion criteria

This study included all patients with cervical lymphadenitis and excluded those who were not willing to provide informed consent.

Methods

A structured proforma was maintained containing the basic characteristics of patients, including age, sex, occupation, personal history, symptoms, and investigations such as CBNAAT, FNAC, and Biopsy. After two months of the intensive phase, the patient's response to ATT was assessed. The continuation phase of ATT was initiated. After the continuation phase of ATT, residual lymph nodes at the end of treatment (6 or 9 months) were assessed for treatment outcomes. Data are presented as frequencies and percentages.

RESULTS

The highest proportion of patients (33.8%) were aged 21-30 years, followed by 11-20 years (26.3%) and 1-10 years (13.8%). Patients aged 31-40 comprised 10%, while those 41-50 years comprised 7.5%, 51-60 years comprised 6.3%, and 61-70 years comprised 2.5%. Females constituted 62.5% of patients, compared to 37.5% of males. Regarding TB contact history, 91.3% reported no contact, while 8.8% had known contact with a patient with TB [Table 1].

Table 1: Demographic characteristics of patients.

		N (%)
Age (in years)	1 to 10	11(13.8%)
	11 to 20	21(26.3%)
	21 to 30	27(33.8%)
	31 to 40	8(10%)
	41 to 50	6(7.5%)
	51 to 60	5(6.3%)
	61 to 70	2(2.5%)
Gender	Female	50(62.5%)
	Male	30(37.5%)
K/H/O contact with a TB patient	Yes	7(8.8%)
	No	73(91.3%)

In the age distribution, females were highest in the 21-30- and 11-20-year groups at 20% each, followed by 9% in 1-10 years. Both genders showed 5% in the 31-40 years. Males were 14% in the 21-30 years, with 6% in the 11-20 years and 5% in the 1-10 years. The 41-50 years group had 4% for both genders, while 51-60 years showed 4% males and 3% females. The 61-70 years group had only females at 3% [Table 2].

Table 2: Comparison of patient age with gender.

		Gender N (%)	
		Male	Female
Age (in years)	1 to 10	4(5%)	7(9%)
	11 to 20	5(6%)	16(20%)
	21 to 30	11(14%)	16(20%)
	31 to 40	4(5%)	4(5%)

	41 to 50	3(4%)	3(4%)
	51 to 60	3(4%)	2(3%)
	61 to 70	0(0%)	2(3%)

Among patients assessed for constitutional symptoms, 65% reported no symptoms. Of these, 25% experienced both loss of appetite and weight, whereas 6.25% reported either symptom alone. 3.75% of patients presented with fever only [Table 3].

Table 3: Distribution of patients based on associated or constitutional symptoms.

		N (%)
Associated/constitutional symptoms	Fever	3(3.75%)
	Loss of appetite/weight	5(6.25%)
	Both (LOA and LOW)	20(25%)
	No	52(65%)

The right side was more commonly involved in lymphadenopathy (51.3%) than the left side (40%). Bilateral involvement occurred in 7.5% of patients and anterior lymphadenopathy in 1.3% of patients. Group II (upper jugular) was the most frequently affected (51.3%), followed by group V (posterior triangle) at 48.8%. Groups III and IV (middle and lower jugular) were involved in 20% and 17.5% of cases, respectively. Group I (submental and submandibular) was affected in 7.5% of patients, and group VI (anterior compartment) in 2.5% of patients. Matted lymph nodes were present in 22.5% of the patients, whereas 77.5% had non-matted nodes [Table 4].

Table 4: Clinical characteristics of lymphadenopathy among patients.

		N (%)
Side of lymphadenopathy	Right	41(51.3%)
	Left	32(40%)
	Bilateral	6(7.5%)
	Anterior	1(1.3%)
Lymph node group	I (Submental and submandibular)	6(7.5%)
	11 (Upper jugular)	41(51.3%)
	III (Middle jugular)	16(20%)
	IV (Lower jugular)	14(17.5%)
	V (Posterior triangle)	39(48.8%)
	VI (anterior compartment)	2(2.5%)
Matted lymph node	Yes	18(22.5%)
	No	62(77.5%)

After 6 months of antituberculosis therapy, 59% of the patients showed complete symptom resolution. Partial resolution occurred in 33% of cases, 4% developed new swelling, and 4% defaulted. Of these, 3% died during treatment and 1% received an alternative diagnosis. After 9 months of ATT, 76.7% (56/73) of patients achieved complete resolution. Among 26 patients with initial residual swelling, only 9 showed further resolution, while 17 (23.3%) had persistent swelling and underwent excision biopsy. Of these, 3 patients (4.1%) had multidrug-resistant TB and 14 (19.2%) had drug-sensitive TB. [Table 5].

Table 5: Treatment Outcomes Following Completion of 6 Months of ATT.

		N (%)
After completion of 6 months of ATT	Complete resolution	47(59%)
	Partial resolution	26(33%)
	New swelling	3(4%)
	Defaulter	3(4%)
	Death	2(3%)
	Alternative diagnosis	1(1%)

DISCUSSION

In our study, the demographic profile revealed a higher prevalence of PTL among young adults, with the 21–30-year age group being the most affected (33.8%), followed by adolescents aged 11–20 years (26.3%). There was a female predominance, accounting for 62.5% of cases, and the ratio was 1:1.66 which is higher than that reported by Purohit et al. (1:1.2).[13] This is similar to the study by Fontanilla et al., who reported (1:1.4) while Bezabih et al. showed a male predominance, with a male-to-female ratio of 1.3:1 and a peak incidence at 20-40 years of age.[14,15]

Despite tuberculosis being contagious, only 8.8% of patients reported a history of TB contact, suggesting community-acquired or latent infection reactivation. This contrasts with the findings of Khan et al. (11.4%), and Iguchi et al. (14.3%).[16,17] Most patients (65%) were asymptomatic with no constitutional symptoms, while 25% experienced loss of appetite and weight loss. Fever alone was reported in 3.75% of cases, indicating that constitutional symptoms may not be reliable diagnostic cues. This is consistent with

Fontanilla et al. where 20 -50% of patients had fever.[14]

Regarding lymphadenopathy, cervical lymph nodes were predominantly involved on the right side (51.3%), followed by the left (40%) and bilateral cases (7.5%). This is consistent with Castro et al., who reported that 57 patients (71.25%) had involvement of a single group of lymph nodes.[18] This is consistent with Nidhi et al. where single lymph node enlargement is seen in 63.3% of patients and Aggarwal et al. had single lymph nodal enlargement in 48.6% of cases.[19,20]

The upper jugular group (group II) was the most frequently affected (51.3%), with involvement of the posterior triangle (48.8%). Matted lymph nodes were present in 22.5% of patients, suggesting chronic or advanced disease status. This is consistent with the findings of Agarwal et al., where matted lymph nodes were observed in 26.8% of patients.[20]

After 6 months of ATT, 59% of patients showed complete clinical resolution, while 33% showed partial resolution. 4% developed new lymph node swelling during therapy, and 4% defaulted from treatment. Mortality was observed in 3% of cases, and 1% of cases were reclassified with alternative diagnoses. The mortality observed in these patients was deemed unrelated to anti-tubercular therapy, based on clinical records and adverse event analysis.

Follow-up at 9 months revealed that an additional 11.25% of patients with partial resolution at 6 months achieved complete resolution, which is consistent with the observation by Jawahar et al. that continued clinical resolution can occur post-treatment completion. They showed 80% complete resolution after 2 months, and after 9 months of treatment.[21]

In our study, 11.25% showed complete resolution which is consistent with Jawahar et al. where 30% of patients had residual lymph nodes.[21] However, it is inconsistent with Jindal et al. who said that extension of treatment for an additional 3 months had no benefits in tuberculous lymphadenopathy.[11]

CONCLUSION

The treatment outcome of cervical tuberculous lymphadenopathy which is an extrapulmonary tuberculosis, is different from the treatment outcome of pulmonary tuberculosis. The problem of managing TB cervical lymphadenopathy starts from the diagnosis, where the patient needs to be subjected to invasive procedures. Even with these invasive procedures, the diagnosis of tuberculous lymphadenopathy is as difficult as the diagnosis of other extrapulmonary tuberculosis. After starting an appropriate treatment regimen, even when the patients are very compliant with the therapy, the response to treatment is not satisfactory. Many patients had residual swelling even after the completion of nine months of antituberculosis therapy. Some patients did not have a resolution of tuberculous lymphadenopathy even after completion of treatment. Unfortunately, almost all patients who had no resolution or residual swelling were drug-sensitive rather than drug-resistant. It is important to note that cases of multidrug-resistant tuberculous lymphadenitis have been associated with poorer treatment outcomes and higher relapse rates, often requiring extended regimens and second-line drugs. However, none of the cases in this study were identified as MDR-TB. Thus, the outcome of anti-tuberculous treatment in tuberculous cervical lymphadenopathy is not satisfactory when compared with pulmonary tuberculosis.

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