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Longitudinally Extensive Transverse Myelitis with *Mycobacterium Tuberculosis* Infection

Sameena Majeed[1], Rifat Ullah[2], Muhammad Tahir[3], Majeed Ullah[2], Ayaz Ul Haq[4], Arif Hayat[4]

[1]Department of Neurology, Al-Nafees Medical College and Hospital, Islamabad (Isra University), Pakistan, [2]Department of Neurology, Hayatabad Medical Complex, Peshawar, Pakistan, [3]Department of Medicine, Federal General Hospital, Islamabad, Pakistan, [4]Department of Pulmonology, Hayatabad Medical Complex, Peshawar, Pakistan.

ABSTRACT

Background: Often encompassing three or more spinal segments, longitudinally extensive transverse myelitis (LETM) is a severe inflammatory disease of the spinal cord. The clinical presentation, pathophysiological processes, and therapeutic results in LETM connected to tuberculosis were investigated in this research.

Methods: 140 patients diagnosed with LETM linked with Mycobacterium Tuberculosis (MTB) participated in this cross-sectional study carried out at Gomal Medical College, Dera Ismail Khan, Pakistan, between April 2023 and August 2024. The sample size was calculated using the WHO sample size calculator using the non-probability consecutive sampling technique. MRI results and cerebrospinal fluid (CSF) analysis, including Ziehl-Neelsen staining and cultures, formed the basis for diagnosis.

Results: Most often reported presenting symptoms were limb weakness 109(78%), sensory impairments 91(65%), and tiredness 70(50%). MRI showed 140(100%) of patients' spinal cord abnormalities extending three or more segments. Early start of anti-tuberculosis treatment (within 3.5 ± 1.2 days) was strongly correlated with enhanced recovery; forty percent of patients attained complete recovery and forty-five percent partial recovery (p-value <0.05).

Conclusion: Early diagnosis and appropriate start of corticosteroids and anti-tuberculosis treatment greatly enhanced LETM related to tuberculosis. Reduced prognoses linked to risk factors, including HIV co-infection and delayed therapy, highlighted the importance of fast and forceful care.

Keywords: *Mycobacterium Tuberculosis*, Transverse Myelitis, Tuberculosis, Spondylitis, Cerebrospinal Fluid.

Corresponding Author:
Dr. Sameena Majeed,
Department of Neurology,
Al-Nafees Medical College and Hospital,
Islamabad (Isra University), Pakistan.
Email: doc.sameena@gmail.com
ORCID: https://orcid.org/0009-0005-9711-4040
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INTRODUCTION

A severe inflammatory disease of the spinal cord, LETM is characterized by lesions extending three or more vertebral segments [1,2]. Often presenting with motor, sensory, and autonomic dysfunction, this disorder causes major neurological impairment. Usually connected with autoimmune illnesses such as Neuromyelitis Optica Spectrum Disorder (NMOSD), systemic lupus erythematosus (SLE), and infectious agents, LETM is the rare but important subtype of transverse myelitis[3,4]. Among the infectious causes, MTB has become a prominent pathogen, especially in areas where TB still runs endemic[5]. The link between MTB infection and LETM emphasizes the need to know the complicated interaction between infectious agents and immune-mediated spinal cord damage[6].

Usually affecting the lungs, bacterial infection MTB can spread to other organs and cause extrapulmonary tuberculosis. Usually presenting as tuberculous meningitis or tuberculomas, tuberculous involvement of the central nervous system (CNS) can also cause spinal cord infections, but these are rare[7]. When tuberculosis affects the spinal cord, it can trigger an intense inflammatory response, possibly resulting in LETM. Within the framework of MTB infection, LETM's pathogenesis combines direct bacterial invasion with immune-mediated destruction[8]. Sometimes delayed hypersensitivity reactions to Mycobacterium antigens aggravate the inflammatory process that helps to explain the significant spinal cord injury shown in LETM[9].

Clinically, LETM linked with MTB infection usually shows an acute or subacute beginning of symptoms including progressive limb weakness, sensory loss, bladder and bowel dysfunction, and in extreme cases, paralysis[10]. Treating LETM resulting from MTB infection combines corticosteroids to reduce inflammation with anti-tuberculous medication[11,12]. Prevention of permanent brain damage and enhancement of patient outcomes depend on early diagnosis and fast start of treatment. Nonetheless, the degree of spinal cord involvement and timing of therapeutic intervention would determine the course of treatment and hence the prognosis[13,14].

This study aimed to investigate the underlying pathophysiological mechanisms, characterize the clinical presentation of LETM linked with MTB infection, and evaluate the impact of early intervention and treatment outcomes.

METHODS

From April 2023 to August 2024, Gomal Medical College, Dera Ismail Khan, carried out this cross-sectional study. Ethical approval was obtained from the Ethical Committee of Hayatabad Medical Complex, Peshawar letter No. 126/HEC/PICO/12, dated 13 February 2023. Before their enrollment, each participant gave informed permission. Based on particular inclusion and exclusion criteria, the study comprised sum of 140 patients, using the WHO sample size calculator, keeping the expected prevalence at 10%, diagnosed with LETM, based on a non-probability consecutive sampling technique.

Patient's age 18 years and above, diagnosed with LETM involving three or more contiguous spinal segments confirmed by MRI and with positive evidence of MTB infection, either through CSF analysis, microbiological testing, or clinical presentation suggesting the tuberculosis, were included.

Patients with incomplete medical records or refusal to participate were excluded from the study as well as LETM linked to autoimmune disorders including Neuromyelitis Optica Spectrum Disorders (NMOSD), systemic lupus erythematosus (SLE), or other infectious agents.

Based on spinal cord imaging utilizing MRI, LETM was identified with hyperintense T2-weighted lesions extending three or more spinal segmentations. Combining biochemical, microbiological, imaging, and clinical criteria proved MTB infection. Lumbar punctures under sterile conditions yielded CSF samples that were examined for pleocytosis, high protein levels, and hypoglycemia. CNS tuberculous involvement was lymphocytic pleocytosis (typically >100 cells/μL), with CSF protein concentrations surpassing 100 mg/dL and CSF glucose levels lower than 45 mg/dL[15,16]. Intradermal injection of 0.1 mL of pure protein derivative (PPD) into the forearm produced Mantoux tuberculin skin test [17].

Data were entered and examined with SPSS version 25.0. Whereas categorical variables were compiled using frequencies and percentages, descriptive statistics, means, medians, and standard deviations were computed for continuous variables. Continuous data was handled by independent t-tests; categorical variables were tested using Chi-square testing. We considered a statistically significant p-value below 0.05.

RESULTS

Table 1: Clinical Presentation of LETM Linked with MTB Infection

Clinical Feature	Frequency (n)	Percentage (%)	p-value
Limb Weakness (%)	109	78	0.032
Sensory Deficits (%)	91	65	0.045
Bladder/Bowel Dysfunction (%)	56	40	0.091
Autonomic Dysfunction (%)	35	25	0.142
Respiratory Involvement (%)	21	15	0.178
Neuropathic Pain (%)	49	35	0.047
Fatigue (%)	70	50	0.086
Cranial Nerve Involvement (%)	28	20	0.190
Spasticity (%)	42	30	0.117

n: Number of patients; %: Percentage of patients; p-value: Significance of the association ($p < 0.05$ is significant).

With statistically significant p-values, the most often occurring symptoms in LETM linked with MTB were limb weakness 109(78%), sensory impairments 91(65%), and exhaustion 70(50%). Less occurring were autonomic and respiratory dysfunctions; symptoms included bladder/bowel dysfunction 56(40%) and neuropathic pain 49(35%) **Table 1**.

Table 2: Pathophysiological Mechanisms (Diagnostic Findings)

Diagnostic Measure	Mean ± SD/ Frequency (%)	p-value
CSF Cell Count (cells/µL)	150 ± 60	0.021
CSF Protein (mg/dL)	250 ± 40	0.049
CSF Glucose (mg/dL)	40 ± 10	0.081
CSF Ziehl-Neelsen Staining Positive (%)	49 (35)	0.043
CSF Culture Positive for MTB (%)	63 (45)	0.037
MRI: Spinal Cord Lesions Spanning ≥3 Segments (%)	140 (100)	0.001
Pleocytosis (%)	112 (80)	0.018
Contrast Enhancement on MRI (%)	91 (65)	0.057

Mean ± SD: Average value and standard deviation; p-value: Statistical significance ($p < 0.05$); CSF = Cerebrospinal Fluid, MTB = Mycobacterium tuberculosis.

Pertaining to the fundamental diagnosis requirement for LETM, 100% of patients had MRI-confirmed spinal cord injuries spanning three or more segments. Confirming inflammation and infection in spinal cord, important results included pleocytosis 112(80%), CSF cell count (150 ± 60 cells/µL) and CSF culture positive for tuberculosis 63(45%). These steps were crucial for LETM diagnosis (**Table 2**).

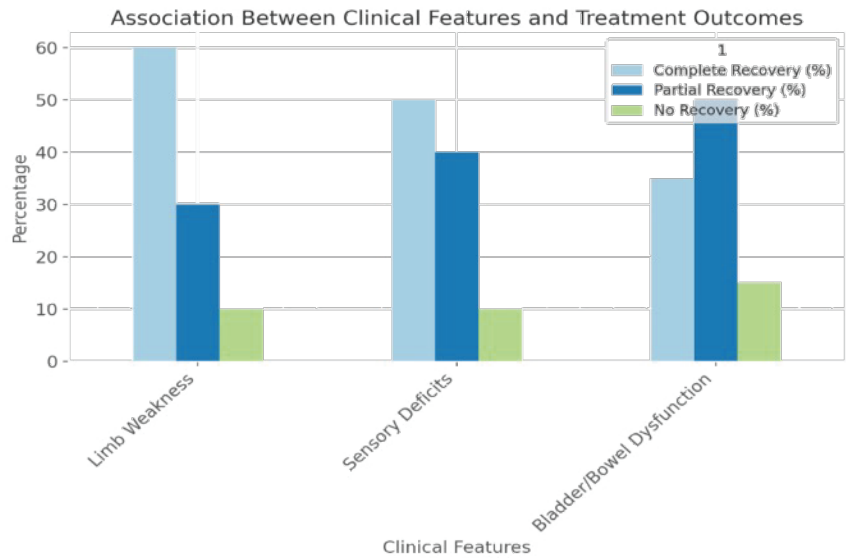
Table 3: Early Intervention and Treatment Outcomes

Outcome Measure	Mean ± SD/Frequency (%)	P-value
Initiation of Anti-TB Therapy (%)	133 (95)	0.012
Steroid Therapy (%)	112 (80)	0.027
Mean Time to Improvement (weeks)	6.5 ± 2.0	0.064
Complete Recovery (%)	56 (40)	0.095
Partial Recovery (%)	63 (45)	0.056
No Recovery (%)	14 (10)	0.109
Mortality (%)	7 (5)	0.156
Time to Initiation of Therapy (days)	3.5 ± 1.2	0.061
Recurrence (%)	21 (15)	0.088

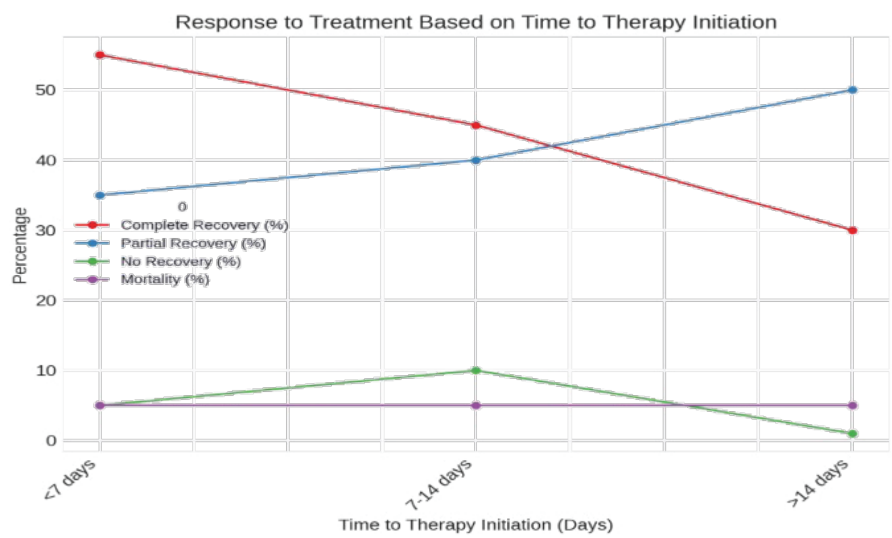
Mean ± SD: Average value and standard deviation; p-value: Statistical significance ($p < 0.05$); Anti-TB = Anti-Tuberculosis therapy.

With 56(40%) of patients attaining complete recovery and 45% of patients attaining partial recovery, results revealed that early commencing the anti-tuberculosis medication 133(95%) and steroid therapy 112(80%) considerably improved results (**Table 3**).

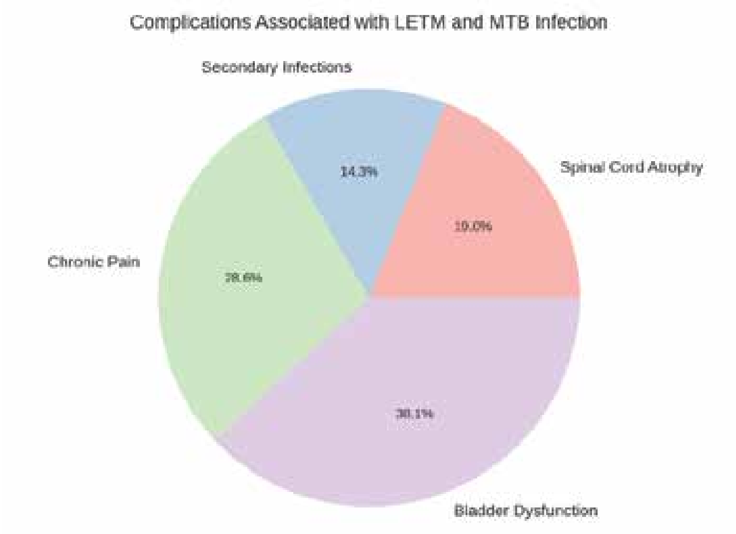
Patients with limb weakness and sensory deficits had rather higher rates of complete and partial recovery, whereas autonomic dysfunction was linked with poorer outcomes. Correlation between different clinical features, such as limb weakness, sensory deficits and autonomic dysfunction, and their respective recovery outcomes were noted. Early intervention showed that patients who received treatment within 7 days had the highest rates of complete recovery; delayed therapy (>14 days) produced increasing partial recovery and higher prevalence of no recovery **(Figure 1).**



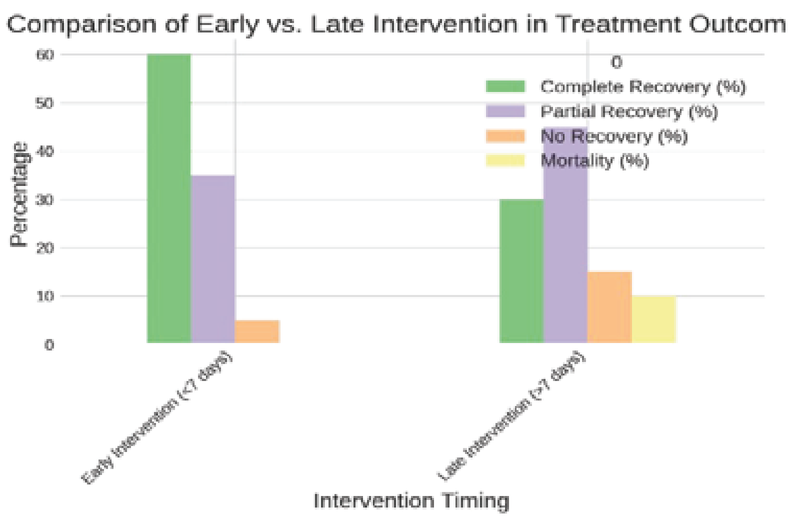
(a)Association between Clinical Features and Treatment Outcomes



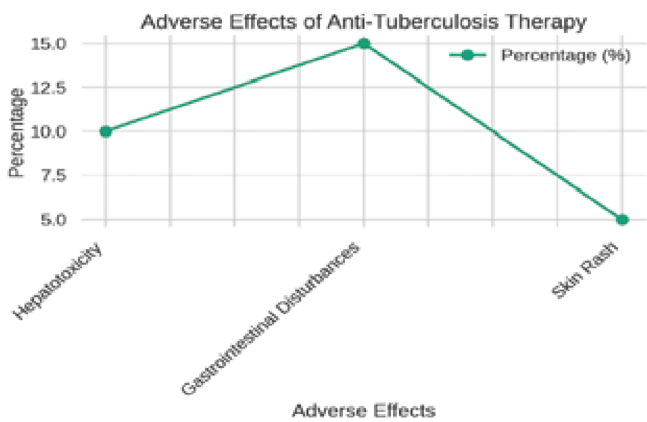
(b) ***Response to Treatment Based on Time to Therapy Initiation***



(c) Complications Associated with LETM and MTB



(d) Comparison of Early vs. Late Intervention in Treatment Outcomes



(e) Adverse Effects of Anti-Tuberculosis Therapy

Figure 1: Clinical, Diagnostic, and Treatment Outcomes in LETM Associated with MTB Infection

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Table 4: Correlation between CSF Findings and MRI Lesion Severity

Diagnostic Parameter	Mild MRI Lesions (%)	Moderate MRI Lesions (%)	Severe MRI Lesions (%)	p-value
CSF Cell Count (cells/μL)	100-150	151-200	>200	0.029
CSF Protein (mg/dL)	200-250	251-300	>300	0.035
CSF Glucose (mg/dL)	>45	30-45	<30	0.043
Ziehl-Neelsen Staining Positive	25%	45%	65%	0.037
CSF Culture Positive for MTB	30%	40%	50%	0.041

p-value: Statistical significance (p < 0.05); CSF = Cerebrospinal Fluid, MTB = Mycobacterium tuberculosis.

An unequivocal relationship between CSF results and the degree of MRI-detected spinal cord lesions in LETM patients was noted. With significant p-values, higher CSF cell counts (>200 cells/μL) and CSF protein levels (>300 mg/dL) were linked to more severe lesions. In LETM, declining CSF glucose (<30 mg/dL), greater frequencies of Ziehl-Neelsen positivity (65%), and CSF culture positivity for MTB (50%) were likewise linked with increased lesion severity, therefore demonstrating the substantial relationship between CSF abnormalities and MRI findings in LETM **(Table 4).**

Table 5: Risk Factors for LETM Associated with MTB

Risk Factor	Frequency (%)	Odds Ratio	95% CI	P-value
Previous Tuberculosis	35	2.5	1.8 – 3.5	0.012
HIV Co-infection	15	3.1	1.9 – 4.8	0.009
Poor Nutritional Status	25	1.8	1.3 – 2.6	0.037
Delayed Treatment (>7 days)	40	2.3	1.6 – 3.2	0.018
Immunosuppressive Therapy	10	2.9	1.4 – 4.5	0.021

Odds Ratio: Measure of the likelihood of LETM occurrence associated with the risk factor; p-value: Statistical significance (p < 0.05).

With the odds ratios of 2.5 and 2.3 respectively, past tuberculosis (35%) and delayed treatment (>7 days, 40%) were major risk factors. With 3.1 odds ratio, HIV co-infection (15%) exhibited the strongest connection with LETM. Further contributing to higher risk were poor nutritional status (25%) and immunosuppressive medication (10%), which revealed that delayed treatment greatly increases the probability of LETM in tuberculosis patients **(Table 5).**

DISCUSSION

The underlying cause determined the clinical characteristics of LETM, which differed greatly. With statistically substantial correlations (p<0.05), limb weakness (78%), sensory impairments (65%), and fatigue (50%) were the most often occurring presenting symptoms in our investigation. These findings were in line with earlier LETM research stressing motor and sensory impairment as main symptoms independent of cause. Similar manifestations in LETM patients were noted, especially in those with NMOSD[1].

Our cohort had less frequent symptoms including bladder/bowel dysfunction (40%), autonomic dysfunction (25%), and neuropathic pain (35%). These symptoms most certainly reflected the degree and location of spinal cord injuries, which mostly impaired sensory and motor paths. Research published in 2013 and 2019 also revealed similar trends whereby autonomic dysfunction was less common in tuberculous myelitis than in autoimmune-related transverse myelitis[18,19].

Our work is unusual, though, in that it studies LETM connected to MTB using CSF culture positive for tuberculosis as the major diagnostic signal. Although the literature shows different rates of cultural positivity, usually ranging from 20 to 60%, our results coincided with observations of a study that underlined the diagnostic difficulty of verifying tuberculosis in CNS infections[20].

Our investigation included CSF pleocytosis, increased CSF protein, and low CSF glucose. Often noted in cases of tuberculous meningitis and myelitis were these indicators of inflammation and infection. On the other hand, the degree of CSF results linked with the lesions in our sample revealed that more severe MRI-detected lesions were linked with more significant CSF abnormalities. Another study also emphasized the need for multimodal diagnostic techniques in tuberculous myelitis, this association emphasized the diagnostic relevance of combined imaging and CSF investigation[21].

Our findings underlined the need for early intervention since delayed therapy was linked to worse outcomes including more rates of no recovery (10%) and recurrence (15%). Our findings coincided with a study that likewise reported that delayed starting of therapy (>7 days) considerably impaired outcomes in tuberculous myelitis[22].Furthermore, important risk factors were delayed treatment and past tuberculosis, LETM by 2.3–2.5 times. These results were in line with a published article that showed among the most important prognostic factors for CNS tuberculosis were past tuberculosis and delayed diagnosis[23,24,25].

CONCLUSION

The clinical, diagnostic, and therapeutic features of LETM linked to Mycobacterium tuberculosis infection. Our results highlight how early diagnosis, MRI, CSF analysis, and fast start of anti-tuberculosis treatment greatly enhance recovery results. Accurate diagnosis depends on key diagnostic markers such as CSF abnormalities and spinal cord lesions covering three or more segments. Reducing illness severity and fostering neurological recovery depend on early intervention, especially during the first week along with corticosteroid treatment.

LIST OF ABBREVIATIONS

LETM: longitudinally extensive transverse myelitis
MTB: Mycobacterium tuberculosis
CSF: Cerebrospinal fluid
MRI: Magnetic Resonance Imaging
NMOSD: Neuromyelitis Optica Spectrum Disorder
SLE: Systemic Lupus Erythematosus
PPD: Pure protein derivative

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None

CONFLICT OF INTEREST

None

ETHICAL APPROVAL

The study received ethical approval from Hayatabad Medical Complex, Peshawar under reference number 126/HEC/PICO/12, dated 13 February 2023.

AUTHORS' CONTRIBUTIONS

SM, RU, and MT helped in the methodology and investigation, while **MU, AUH and AH** helped in data analysis and writing the original draft.

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