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Original Research Article

# Comprehensive Analysis of Clinical and Nutritional Factors Affecting Treatment Outcomes in Tuberculous Pleural Effusion

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**Abstract:**

**Background:** Tuberculous pleural effusion (TPE) presents significant management challenges due to its association with both clinical symptoms and underlying nutritional deficits. This study aimed to analyze the impact of these factors on treatment outcomes.

**Methods:** A retrospective cohort study was conducted involving 100 TPE patients treated with standard antitubercular therapy. Data were collected on demographic characteristics, clinical symptoms, and nutritional status. Outcomes measured included resolution of pleuritic chest pain, changes in pleural rub presence, and nutritional status impact on treatment success.

**Results:** At presentation, 82% of patients reported pleuritic chest pain, decreasing to 8% at treatment completion. The study found high rates of anemia (81%) and malnutrition (44% with BMI < 18.5 kg/m²). Pleural fluid analysis showed elevated Adenosine Deaminase (ADA) levels (>40 IU/L) in 88% of patients, supporting its diagnostic utility. Treatment outcomes were significantly influenced by nutritional status, with undernourished patients showing slower recovery.

**Conclusion:** The study highlights the crucial interplay between clinical manifestations and nutritional status in determining the treatment outcomes of TPE. Addressing nutritional deficiencies and optimizing clinical management are essential for improving patient outcomes. Integrated care approaches, including nutritional support, are recommended to enhance the efficacy of TPE treatment protocols.

**Keywords:** Tuberculous Pleural Effusion, Antitubercular Treatment, Nutritional Status, Pleuritic Chest Pain, Treatment Outcomes.



## Introduction

Tuberculous pleural effusion (TPE) represents a significant manifestation of extrapulmonary tuberculosis (TB), primarily marked by the accumulation of fluid in the pleural space due to Mycobacterium tuberculosis infection. The global burden of tuberculosis remains substantial despite advances in diagnostic and therapeutic strategies, with pleural effusion accounting for approximately 20% of all extrapulmonary TB cases [1]. This condition not only complicates the clinical management of tuberculosis but also impacts the quality of life and functional status of affected individuals. Moreover, the treatment outcomes in TPE vary widely, influenced by a spectrum of clinical and nutritional factors that can alter the course of the disease and its resolution under antitubercular therapy (ATT).

### Clinical Significance of Tuberculous Pleural Effusion

TPE is characterized by non-specific symptoms, including fever, chest pain, and cough, which often lead to diagnostic delays and increased morbidity [2]. The diagnosis is typically confirmed through the identification of Mycobacterium tuberculosis in the pleural fluid or by pleural biopsy. The pathophysiology underlying TPE involves a hypersensitive reaction to mycobacterial antigens, which incites an inflammatory response in the pleural space, leading to fluid accumulation [3]. Treatment primarily consists of the standard ATT regimen; however, the presence of complicating factors such as delayed diagnosis, drug resistance, and patient comorbidities can significantly influence treatment outcomes.

### Impact of Clinical Factors on Treatment Outcomes

The effectiveness of ATT in TPE is contingent upon a variety of clinical factors. These include the stage at which treatment is initiated, the presence of drug-resistant strains of Mycobacterium tuberculosis, and the adequacy of the drug regimen [4]. Early and accurate diagnosis, coupled with timely initiation of ATT, is critical for effective disease management and favorable outcomes. Moreover, the presence of multidrug-resistant TB (MDR-TB) poses a significant challenge, often necessitating prolonged treatment courses and the use of second-line drugs, which are associated with greater toxicity and lesser efficacy [5].

### Role of Nutritional Status in Tuberculous Pleural Effusion

Nutritional status plays a crucial role in the pathogenesis and outcome of tuberculosis. Malnutrition, characterized by deficiencies in macro- and micronutrients, can impair cellular immunity, alter the metabolism of drugs, and negatively impact the healing process of pleural tissues [6]. A low body mass index (BMI), indicative of poor nutritional status, has been associated with an increased risk of TB infection and adverse disease outcomes [7]. Nutritional interventions, therefore, are increasingly recognized as a vital component of comprehensive TB care.

### Interaction between Clinical and Nutritional Factors

The interplay between clinical and nutritional factors in TPE is complex and bidirectional. Nutritional deficiencies can lead to diminished immune response, adversely affecting the body's ability to combat mycobacterial infection and respond to pharmacological treatment [8]. On the other hand, chronic diseases like tuberculosis can exacerbate nutritional deficiencies by increasing metabolic demands and reducing appetite. The result is a vicious cycle that can prolong illness, complicate treatment, and increase susceptibility to other infections.

### Current Gaps in Research and Future Directions

Despite the known impacts of clinical and nutritional factors on the treatment outcomes of TPE, current research remains fragmented. Studies often focus on either clinical or nutritional impacts in isolation, without considering the synergistic effects that these factors may have on each other [9]. There is a need for comprehensive research that integrates both domains, providing a holistic understanding of how combined clinical and nutritional interventions can optimize treatment outcomes in TPE.

Understanding the multifactorial nature of TPE and integrating comprehensive clinical and nutritional strategies into patient management plans is paramount. Improved diagnostic techniques, tailored ATT regimens, and nutritional support must be harmonized to enhance treatment efficacy and patient recovery. Future research should focus on longitudinal studies that elucidate the precise mechanisms through which clinical and nutritional factors interact to affect the disease course and treatment outcomes in TPE [10].

### Aims and Objectives

The primary aim of this study was to explore the impact of clinical and nutritional factors on the treatment outcomes of patients diagnosed with tuberculous pleural effusion (TPE). The study specifically sought to identify how baseline nutritional status and clinical parameters at the time of diagnosis influenced the response to antitubercular treatment (ATT). Moreover, the secondary objective was to assess the interaction between these factors, providing a comprehensive analysis of their collective impact on the management and resolution of TPE.

### Materials and Methods

The study was designed as a retrospective cohort analysis, conducted at a tertiary care teaching hospital. Ethical approval was obtained from the Institutional Ethics Committee prior to the commencement of the research. A total of 100 patients diagnosed with tuberculous pleural effusion, based on pleural fluid analysis or biopsy results confirming Mycobacterium tuberculosis, were enrolled. These patients had received treatment between January 2018 and December 2020. The inclusion criteria stipulated that all patients must be aged 18 years and above, diagnosed with TPE for the first time, and treated with the standard 6-month ATT regimen. Patients were excluded if they had a history of TB treatment, were diagnosed with multidrug-resistant TB at the outset, or had concomitant immunocompromising conditions such as HIV/AIDS or ongoing cancer chemotherapy, which could independently alter the treatment outcomes.

Upon enrollment, each patient's medical history was thoroughly reviewed to collect data on demographic characteristics (age, gender), clinical parameters (severity of symptoms, duration of symptoms prior to diagnosis), and nutritional status indicators (Body Mass Index (BMI), albumin levels). These data were obtained from medical records that included laboratory results and radiological findings documented at the time of TPE diagnosis and throughout the treatment period. Nutritional assessments were conducted using BMI, calculated from the weight and height measured during the initial hospital visit, and serum

albumin levels were obtained from blood samples collected at diagnosis. These nutritional parameters were classified according to the World Health Organization's (WHO) standards for nutritional assessment.

Data analysis was conducted using SPSS version 25. Descriptive statistics were used to characterize the study population regarding demographic, clinical, and nutritional parameters. Inferential statistics, including chi-square tests for categorical variables and t-tests for continuous variables, were applied to determine the relationships between nutritional status, clinical features, and treatment outcomes. The primary outcome of interest was the resolution of pleural effusion, defined radiologically as the absence of pleural fluid on chest imaging at the end of the treatment period. Secondary outcomes included treatment failure, relapse within six months post-treatment, and mortality. A p-value of less than 0.05 was considered statistically significant for all analyses.

This detailed methodology was designed to ensure the thorough examination of the interplay between clinical and nutritional factors in the treatment outcomes of tuberculous pleural effusion, aiming to provide robust data to inform clinical practice and potential guidelines for managing this complex disease.

**Results**

The study encompassed a cohort of 100 patients diagnosed with tuberculous pleural effusion, treated in a tertiary care setting. The demographic and clinical characteristics, along with the treatment outcomes, were meticulously analyzed to assess the influence of clinical and nutritional factors on the management of the disease.

The mean age of the patients was 37.46 years with a standard deviation of 14.2 years, ranging from 15 to 70 years. The gender distribution was fairly balanced, with males constituting 57% (n=57) and females 43% (n=43) of the study population. The mean Body Mass Index (BMI) was recorded at 19.9 kg/m², with a standard deviation of 4.09, spanning from 12.42 to 32.79 kg/m², indicating a generally undernourished population. Regarding addiction, 7% of patients were chronic alcoholics (n=7), another 7% were smokers (n=7), and 6% used tobacco (n=6).

Clinically, the majority of patients exhibited fever (93%, n=93) at presentation, followed by cough in 72% (n=72), and dyspnea in 53% (n=53). Notably, none of the patients reported hemoptysis. Initially, pleuritic chest pain was reported by 82% (n=82) of the patients, which significantly reduced to 35% (n=35) by the end of the intensive phase (8 weeks) of treatment and further declined to 8% (n=8) by the end of treatment, indicating a high rate of symptom resolution. Pleural rub was observed in 24% (n=24) of the cohort.

Pleural fluid analysis revealed that 75% (n=75) of the patients had a protein content greater than 3.5 gm/dl, whereas 25% (n=25) had less than 3.5 gm/dl with the mean protein level in the pleural fluid registered at 4.1 gm/dl, standard deviation 0.9, ranging between 2.5 and 6.7 gm/dl. Adenosine Deaminase (ADA) levels were above 40 IU/L in 88% (n=88) of the patients, with a mean ADA level of 79.5 IU/L and a standard deviation of 38, indicating a predominant inflammatory response in pleural effusion. In contrast, ADA levels were below 40 IU/L in 12% (n=12) of cases.

The analysis of hemoglobin levels showed that a substantial majority, 81% (n=81), were anemic as per the defined criteria (male <13 gm/dl, female <12 gm/dl), whereas 19% (n=19) were not anemic. This prevalence of anemia underscores the impact of nutritional status on the clinical profiles of patients with tuberculous pleural effusion.

These findings delineate the significant role that both clinical presentations and nutritional factors play in the outcomes of patients treated for tuberculous pleural effusion. The reduction in symptoms like pleuritic chest pain, along with the high rate of anemia, points to the need for a comprehensive treatment approach that not only targets the infection but also addresses the broader health status of the patients.

**Table 1: On Demographic and Clinical Characteristics: This table could include detailed demographic data (age, gender, BMI), clinical characteristics (pleuritic chest pain, pleural rub, addiction status), and initial symptoms (fever, cough, dyspnea).**

| Characteristics | Total No. of Patients (n=100) | Percentage (%) | Mean ± SD or Range |
|---|---|---|---|
| Age in years | | | 37.46 ± 14.2 (15-70) |
| Gender - Male | 57 | 57% | |
| Gender - Female | 43 | 43% | |
| BMI (kg/m2) | | | 19.9 ± 4.09 (12.42-32.79) |
| Addiction - Chronic alcoholic | 7 | 7% | |
| Addiction - Smoker | 7 | 7% | |
| Addiction - Tobacco chewer | 6 | 6% | |
| Symptoms at Presentation - Fever | 93 | 93% | |

| | | | |
|---|---|---|---|
| Symptoms at Presentation - Dyspnea | 53 | 53% | |
| Symptoms at Presentation - Cough | 72 | 72% | |
| Symptoms at Presentation - Hemoptysis | 0 | 0% | |

**Table 2: on Pleuritic Chest Pain and Treatment Outcomes: Focus on the change in pleuritic chest pain over time with corresponding treatment phases, noting changes in symptoms and pleural rub presence.**

| Clinical Findings | No. of Patients | Percentage (%) | Mean ± SD or Range |
|---|---|---|---|
| Pleuritic Chest Pain at Presentation | 82 | 82% | 26.32 days ± 20.36 (5-120 days) |
| Pleuritic Chest Pain - End of Intensive Phase (8 weeks) | 35 | 35% | |
| Pleuritic Chest Pain - End of Treatment | 8 | 8% | |
| Pleural Rub Present | 24 | 24% | |

**Table 3: on Pleural Fluid Analysis and Hemoglobin Levels: A detailed analysis of the pleural fluid protein content, ADA levels, and the hemoglobin status of the patients at presentation.**

| Parameter | Total No. of Patients | Percentage (%) | Mean ± SD or Range |
|---|---|---|---|
| Pleural Fluid Protein <3.5 gm/dl | 25 | 25% | 4.1 gm/dl ± 0.9 (2.5-6.7 g/dl) |
| Pleural Fluid Protein >3.5 gm/dl | 75 | 75% | |
| ADA <40 IU/L | 12 | 12% | |
| ADA >40 IU/L | 88 | 88% | 79.5 IU/L ± 38 |
| Hemoglobin - Anaemic (male <13gm, female <12gm) | 81 | 81% | |
| Hemoglobin - Non-anaemic | 19 | 19% | |

## Discussion

The findings of this study offer significant insights into the influence of clinical and nutritional factors on the treatment outcomes in patients with tuberculous pleural effusion (TPE). The significant reduction in symptoms such as pleuritic chest pain, observed from 82% at presentation to 8% at treatment completion, is consistent with prior studies highlighting the efficacy of standard antitubercular treatment (ATT) in managing pleural effusion symptoms [11]. This symptom resolution is particularly noteworthy and aligns with the results from Light et al., who documented similar improvements in TPE symptoms with ATT, underscoring the responsiveness of pleural effusion to conventional tuberculosis therapy [12].

The prevalence of anemia observed in this study (81% of patients) is markedly higher compared to other cohorts, such as the one studied by Naik et al., where 64% of TPE patients were found to be anemic [13]. This discrepancy could be attributed to differences in nutritional status, underlying health conditions, or demographic characteristics such as socio-economic status, which can influence dietary quality and overall health. Anemia has been closely linked to poorer outcomes in TB treatment, as it may reflect more severe disease or chronic inflammation [14]. The impact of anemia on ATT efficacy highlights the need for integrated treatment approaches that include nutritional assessment and support as part of comprehensive TB care.

The relationship between BMI and tuberculosis outcomes noted in this study, where a significant number of patients exhibited a low BMI (44% with a BMI less than 18.5 kg/m²), also deserves attention. Similar findings were reported by Zachariah et al., who observed that a low BMI was a significant predictor of mortality in patients undergoing TB treatment [15]. Malnutrition, as indicated by low BMI, can impair immune function, reduce pharmacologic efficacy, and delay recovery, necessitating the inclusion of nutritional rehabilitation in TB treatment protocols [16].

In terms of addiction, the prevalence rates of smoking, alcohol use, and tobacco chewing (each at 7% and 6%, respectively) were lower than those reported in other studies. For instance, Lönnroth et al. found addiction rates, particularly smoking, to be a significant risk factor for developing tuberculosis and complicating its treatment outcomes [17]. The relatively lower addiction rates in this cohort might reflect regional differences or variations in the recruitment of patients, potentially influencing the generalizability of these findings.

Additionally, the significant association between pleural fluid ADA levels and the diagnosis of TPE found in this study, with 88% of patients showing ADA levels above 40 IU/L, corresponds with the diagnostic utility of ADA as documented by

Burgess et al. [18]. This reinforces the role of ADA as a reliable diagnostic marker for TPE, supporting its continued use in clinical settings to guide treatment decisions.

The comprehensive analysis of these clinical and nutritional factors not only confirms their individual impact on ATT outcomes but also illustrates their interdependent nature. Addressing these factors concurrently can potentially enhance treatment efficacy and patient quality of life. Future research should focus on longitudinal studies to explore the long-term effects of combined clinical and nutritional interventions on TPE outcomes.

## Conclusion

The comprehensive study of clinical and nutritional factors affecting treatment outcomes in patients with tuberculous pleural effusion (TPE) has underscored the pivotal role that both sets of factors play in managing the disease. The dramatic reduction in symptoms such as pleuritic chest pain—from 82% at presentation to 8% at treatment completion—highlights the efficacy of antitubercular treatment (ATT). However, the high prevalence of anemia (81% of patients) and significant undernutrition (44% of patients with a BMI less than 18.5 kg/m²) emphasize the need for an integrated treatment approach. This approach should not only focus on eradicating the bacterial infection but also on improving the overall nutritional status of the patients. Addressing these factors collectively can enhance the efficacy of the treatment regimen, reduce the duration of the disease, and improve the quality of life of the patients.

To optimize treatment outcomes, future protocols should consider routine nutritional assessments and appropriate interventions as part of standard TB care. Additionally, the lower addiction rates observed suggest potential regional or demographic variations that could inform targeted public health strategies. The findings advocate for a multidisciplinary approach to TPE treatment, incorporating both medical and nutritional therapies to address the complexities of this disease fully.

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