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Original Research Article

Association of nutritional status and respiratory muscle strength in patients with pulmonary tuberculosis - A cross-sectional study at a tertiary care hospital

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Abstract

Background: Pulmonary tuberculosis (PTB) dysfunction leads to fatigue, dyspnea, and poor quality of life (QOL), altering metabolism and muscle mass. This study aims to explore any association between nutritional status at the time of diagnosis and respiratory muscle strength after treatment in patients with PTB.
Materials and Methods: This cross-sectional study compared respiratory muscle strength in terms of maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP) among 52 subjects (26 cases and 26 controls) and serum albumin values as key outcome measures of newly diagnosed PTB and without a history of PTB.
Results: The MIP Median in the PTB group was 50 cm H_2O compared to the controls 79 cm H_2O. MEP Median in the PTB group was 57 cm H_2O compared to controls at 70 cm H_2O. There was a significant difference in MIP and MEP between PTB and controls at $p < 0.05$. A strong positive correlation (Pearsons) was seen between the serum albumin level and the MIP with a co-efficient of $p < 0.05$ and a moderate positive correlation with MEP.
Interpretation: There was an association between serum albumin level and respiratory muscle strength in PTB. A significant decrease in respiratory muscle strength was observed in individuals with PTB as compared to age-matched controls.

Keywords: Pulmonary tuberculosis, Serum albumin, Respiratory muscle strength

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1. Background

Tuberculosis is one of the world's deadliest infectious diseases, and according to WHO, almost 10.6 million cases of tuberculosis are expected to have been reported globally in 2022.[1-3] The incidence rate of tuberculosis (TB) increased by 3.6% from 2020 to 2021, India accounted for 28% of global TB cases (Global tuberculosis report 2022).[3] A history of pulmonary tuberculosis may put the individual at a lifelong risk of pulmonary impairment despite a microbiological cure.[1,2] The post-tuberculosis sequelae result from various processes, including pulmonary cavitation, fibrosis, and Bronchiectasis. These contribute to airflow obstruction, restrictive ventilatory defects, impaired gas exchange, decreased pulmonary functions, and release of inflammatory mediators. Extensive remaining lung lesions in pulmonary TB can be a sign of long-term impairment leading to respiratory failure.[4] Tuberculosis (TB) causes tissue wasting, altered metabolism, muscle proteolysis, and muscle weakness, leading to fatigue, exercise limitations, and breathlessness. It is linked to malnutrition, with many experiencing weight loss and vitamin and mineral deficiencies. Low BMI and inadequate weight gain increase the risk of death and re-infection.[5]

It has been proposed that low serum albumin in TB plays a vital role in contributing to a loss of muscle mass and

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strength. [6] Hypoalbuminemia is considered to represent poor nutritional status and chronic inflammation. However, there are very few studies reporting an association between hypoalbuminemia to loss of muscle mass and strength. Two longitudinal studies report a statistically significant association between low baseline measures of serum albumin and subsequent decline in muscle mass and grip strength (peripheral muscle) in the elderly.[6] However, there is very scarce literature on respiratory muscle strength being studied in persons with pulmonary tuberculosis.

Respiratory muscle weakness is one of the important manifestations in persons with PTB post- ATT and respiratory muscle strength is assessed by maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP). A reduced MIP is an independent risk factor for Myocardial Infarction and Cardiovascular Disease and a suggestion of an increased risk for stroke.[7] A low MIP may indicate poor respiratory muscle strength in general and therefore is considered a marker of generalized poor health. Reduced inspiratory and overall muscular strength has been linked to inflammation, malnourishment, mechanical stress, metabolic stress, oxidative stress, and medications.[7,8]

Malnutrition and reduced levels of MIP, MEP, and skeletal muscle strength were associated with lower levels of leptin and higher levels of TNFα in individuals with active tuberculosis.[9] However, there is very minimal literature that studied serum albumin levels and respiratory muscle strength. Therefore, there is a need to determine respiratory muscle strength (MIP and MEP) in persons with pulmonary tuberculosis and to find out if there exists an association with albumin levels. This result could probably be used to modify the treatment strategies in the direction of nutritional therapy and respiratory muscle strength training incorporated in pulmonary rehabilitation to improve exercise capacity and quality of life in these persons. Hence this study intends to check if there exists an association between nutritional status at the time of diagnosis and respiratory muscle strength after treatment in persons with pulmonary tuberculosis.

1.1. Research hypothesis

There is an association between serum albumin level at the time of diagnosis and respiratory muscle strength after completion of treatment in persons with pulmonary tuberculosis.

2. Materials and Methods

2.1. Study design

Cross-sectional study.

2.2. Study setting

People diagnosed with Pulmonary tuberculosis visiting the respiratory medicine and NTEP (National TB Elimination Program) center of a tertiary care hospital were recruited. Subjects without a history of pulmonary tuberculosis and other comorbidities were recruited for the control group.

2.3. Inclusion criteria

1. Adult persons, both males and females, more than or equal to 18 years of age
2. Newly diagnosed pulmonary tuberculosis (Drug susceptible), based on either Sputum for AFB- ZN Stain / LED Microscopy/ CBNAAT/ BAL and completed ATT treatment.
3. Persons willing to provide Informed consent.

2.4. Exclusion criteria

1. Persons with extrapulmonary tuberculosis, PTB with neuromuscular disease, and/or with hemodynamic instability.
2. Recent abdominal or thoracic surgery
3. Persons who are not able to comprehend commands making testing impossible.
4. Persons on active/ongoing treatment for malignancy.
5. Persons having CKD (chronic kidney disease), CLD (Chronic Liver Disease), or Chronic Lung disease.

2.4.1. Sampling method

Non-probabilistic convenience sampling method fulfilling the inclusion and exclusion criteria was used.

2.4.2. Sample Size

Considering 50% of the proportion of pulmonary tuberculosis persons had albumin value of less than 3.5 g/dl (q1 was set at 0.5), the hypothesis was set based on the effect size of 20 cm H_2O for MIP which was considered as the minimal clinically important difference, Standard deviation of 15, (α- (2tailed) = 0.05, β=0.10 (power of 90%), the sample size estimated was around 52 (26- case group; 26- normal group) using the statistical software samplesize.net.[10]

2.5. Outcome measures

2.5.1. Respiratory muscle strength

Respiratory muscle strength was measured in terms of maximal inspiratory pressure (MIP) and measured from the residual volume and maximal expiratory pressure (MEP) measured from total lung capacity.

2.5.2. Serum albumin level

Serum Albumin level (independent variable) in units of g/dl was documented by the investigator by reviewing the medical and investigation records of the patient at the time of diagnosis of PTB.

2.6. Statistical tests and data analysis

Age was represented as Mean and standard deviation. The outcome variables were expressed in terms of Median with inter-quartile range (IQR). The exposure variable (serum

albumin) was dichotomized, whereas the outcome variable (respiratory muscle strength) was considered a continuous variable. The association between the exposure variable (serum albumin level) and the outcome variable (Respiratory muscle strength) was analyzed using Pearson's correlation. A two-sided P-value of less than 0.05 was considered significant. Analysis was done using the latest version of SPSS.

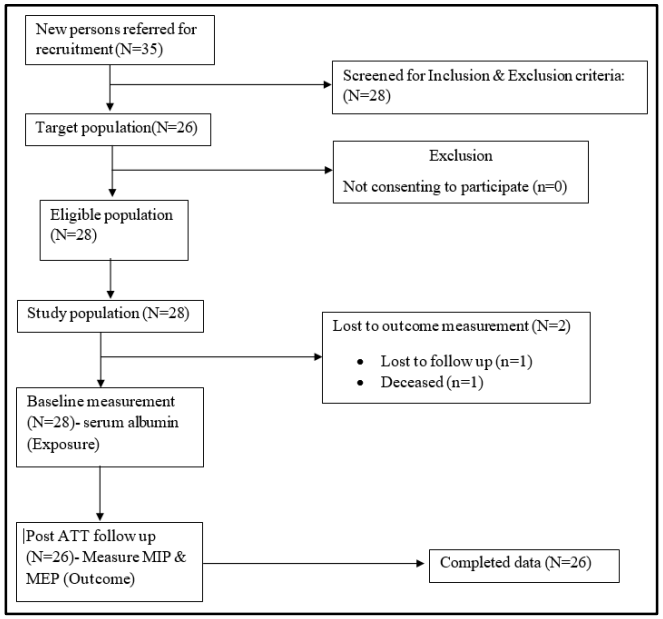

Figure 1: Study flow diagram

2.7. Method of data collection

After getting approved by the Institutional Ethical Committee, the study was registered in the Clinical Trial Registry of India. Newly diagnosed persons with PTB who visited the respiratory medicine department and other ambulatory/outpatient tuberculosis units were screened for Inclusion and Exclusion criteria and recruited into the study. After obtaining informed consent from the patient, the routine diagnostic tests, and investigations as per the PTB guidelines were done. Along with the demographic information such as age in years, height in cm, and weight in kg, the serum albumin and hemoglobin in g/dl values were obtained and documented. History in terms of duration of smoking, alcohol consumption, and food habits was recorded. The recruited PTB persons were followed up and contacted after they completed treatment (6 months) and were brought to the center for consultation with the Pulmonologist.

After doing the routine diagnostic tests and investigations as per the PTB guidelines, the repeat serum albumin values were measured in a standardized and accredited lab and documented. The other medical records, like Hemoglobin values, were reviewed and documented. At this point, the respiratory muscle strength in terms of cm H_2O was measured using the respiratory pressure meter, a standardized tool with good reliability and validity. The respiratory pressure meter was calibrated and checked at regular intervals using standard parameters. Disposable mouthpieces were used, and the valves were sterilized at CSSD. The measurements of MIP, MEP, and serum albumin levels were also taken from the age-matched control group (n=28). The collected data from both groups were interpreted and analyzed.(**Figure 1**)

2.7.1. Control group

After doing frequency matching and age and gender matching with the PTB group, participants for the control group were selected from the general community who had no history of respiratory illness or tuberculosis. Serum albumin levels were determined by blood tests following the acquisition of informed consent, and the respiratory muscle strength was then quantified in terms of MIP in cm of H_20 and MEP in cm of H_2O.

3. Results

The average mean age among PTB and controls was 42 years. MIP Median in the PTB group was 50 cm of H2O (46.75,56.50) compared to the Median in controls, which was 79 cm of H2O (69,100). MEP Median in the PTB group was 57 cm of H2O (54,60.50) compared to the Median in controls, which was 70 (61,96.50) cm of H2O.(**Table 1**) When comparing MIP and MEP between the groups, there was a statistically significant difference between PTB and controls at $p < 0.05$.

There is a weak linear correlation between Serum albumin and Hb. There is a moderate linear correlation between serum albumin and MIP, significant at $p< 0.05$. There is a weak linear correlation between Serum albumin and MEP. There is a weak linear correlation between Hb and BMI. There is a weak linear correlation between Hb and MEP. There is a moderate linear correlation between MIP and Hb. There is a strong linear relationship between MIP and MEP.(**Table 2**)

Table 1: MIP and MEP- Median & Interquartile range.

Outcome variables	PTB group Median (IQR)	Control group Median (IQR)
MIP (cm of H_2O)	50 (46.75, 56.50)	79 (69,100)
MEP(cm of H_2O)	57 (54, 60.50)	70 (61, 96.50)

The MIP and MEP values are significantly lower in terms of Median (IQR) in the PTB group than in the Control group.

Table 2: Correlation between variables of BMI, Hemoglobin, MIP, MEP, and Serum Albumin

	BMI	Serum Albumin	Hemoglobin	MIP	MEP
BMI (kg/m^2)	1.000	0.164	0.172	0.105	- 0.171
Serum Albumin (g/dl)	0.164	1.000	0.234	0.393*	0.244
Hemoglobin (g/dl)	0.172	0.234	1.000	0.308*	0.234
MIP (cm H_2O)	0.105	0.393*	0.308	1.000	0.655**
MEP (cm H_2O)	-0.171	0.244	0.234	0.655**	1.000

* Correlation is significant at $p < 0.05$ level, **Correlation is significant at $p < 0.01$ level (2-tailed), There is a weak linear correlation between BMI and serum albumin. There is a weak linear correlation between BMI and MIP. There is a negative correlation between BMI and MEP.

4. Discussion

This study evaluates the association between nutritional status and respiratory muscle strength in persons with pulmonary tuberculosis. The key findings of this study state that serum albumin levels were decreased in persons diagnosed with PTB, which could contribute to the reduced values of MIP and MEP. These results were similar to a study done by Aliae et.al in 2019, where they evaluated the effect of malnutrition on TB. It was seen that serum albumin was significantly lower in TB-positive persons than in persons who tested negative for TB. This could be attributed to the catabolic process that causes the wasting of both muscle and adipose tissue which usually begins before the patient is diagnosed with active TB, thus more is known about the nutritional status at the time of diagnosis than of the wasting process.[5] When the relationship between serum albumin levels and their clinical outcomes in persons with TB was investigated, it was observed that fluctuations in serum albumin levels during the early phases of anti-TB treatment can be used to identify TB persons who are at a high risk of therapeutic failure. Low albumin levels are associated with treatment failure in drug-resistant TB patients, which may be explained by the notion that serum albumin is one of the finest markers of a patient's nutritional state.[11]

A few animal studies have shown that hypoalbuminemia might change the absolute and relative numbers of total T-lymphocytes and several immune system cell groups, decreasing host defenses against MTB, and suggesting that malnutrition may also worsen the course of TB. According to these data, a weak immunological system combined with a low serum albumin level may lead to a subpar response to anti-TB medication.[11,12]

Malnutrition is a risk factor for progression from TB infection to active TB illness, and undernutrition at the time of diagnosis is a predictor of a greater risk of mortality and TB recurrence. Numerous studies have shown that people with TB have lower body weight. In comparison to controls, TB persons' body fat mass (percentage) and BMI dropped by up to 16% and 45%, respectively. Cell-mediated immunity is the most crucial TB defense. A person who is already malnourished is more likely to have TB, and a latent infection is more likely to progress to active TB. The phrase "Nutritionally acquired immunodeficiency" is used to characterize the condition's susceptibility to infections in part because of this immune weakness. Body mass and weight significantly decrease in TB persons.[5,12,13]

Along with the serum albumin levels, the results of this study show that there is a significant reduction in the MIP (Maximal Inspiratory Pressure) and MEP (Maximal Expiratory Pressure) in persons with pulmonary TB. Functional evaluation in persons with pulmonary tuberculosis sequelae was studied by Di Naso et al, 2011 it was seen that the MIP and MEP were reduced in Pulmonary TB who completed their treatment in six months, and it was much reduced in multidrug-resistant pulmonary TB,[4] A study that evaluated the functional assessment of persons with MDR-TB exhibited impaired pulmonary function, reduced respiratory muscle strength, functional capacity, and quality of life, warranting the need for a pulmonary rehabilitation program.[14] A previous study found that hospitalized PTB persons had lower leptin levels and higher TNF-alpha levels, while their body mass index, grip strength, MIP, and MEP were significantly lower. These results could be attributed to malnutrition, decreased body fat, and reduced muscle strength, leading to a sensation of fatigue and functional limitation.[9] Our results were similar to the findings in a study that evaluated the association of lung function disorders and the respiratory muscle strength in patients with tuberculosis and COPD, where the inspiratory muscles dysfunction was dominant in tuberculosis patients with COPD.[15]

4.1. Strengths

The findings of this study provide a base to start with relevant treatment plans that include respiratory muscle strength testing and training in the earlier course of the disease and pulmonary rehabilitation to enhance the quality of life and ability to exercise for people with pulmonary tuberculosis.

5. Limitations

A drawback of this study is that all the compositions of nutritional status were not explored. Also, detailed information on alcohol consumption and smoking history could not be sought.

6. Future Improvements

Discussing confounding variables using Adjustment models, to extend analysis to other markers of nutritional indices,

consider longitudinal follow up of outcome measures and a larger sample size.

7. Interpretation

Respiratory muscle weakness starts to occur much earlier in the course of the disease and hence respiratory muscle strength evaluation should be taken into consideration in the early stages of tuberculosis (TB) to rule out any persistent weakness in those individuals and, subsequently, enroll them in a long-term respiratory muscle training and pulmonary rehabilitation program for reducing symptoms and improving quality of life.

8. Conclusion

This study concludes that there is a moderate association between the serum albumin level and respiratory muscle strength, especially Maximal inspiratory pressure (MIP) in persons with pulmonary tuberculosis after completion of treatment. In addition, it was observed that there was a significant decline in respiratory muscle strength in persons with pulmonary tuberculosis compared to age and gender-matched controls.

9. Source of Funding

None.

10. Conflict of Interest

None.

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