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ROLE OF SERUM ALBUMIN AND NUTRITIONAL STATUS IN PREDICTING MORTALITY IN TUBERCULOSIS PATIENTS

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ABSTRACT

Background: Tuberculosis (TB) remains a major global health challenge with significant morbidity and mortality, particularly among undernourished patients. Serum albumin and nutritional indices, such as the Prognostic Nutritional Index (PNI) and Controlling Nutritional Status (CONUT) score, have emerged as potential predictors of poor outcomes in TB. **Aim and Objectives:** To evaluate the role of serum albumin and nutritional status in predicting mortality among pulmonary TB patients. **Materials and Methods:** This was a retrospective observational cohort study conducted over a 4-month period at a tertiary care hospital. A total of 120 adult patients with confirmed pulmonary TB were enrolled and followed for six months. Baseline data, including serum albumin, BMI, PNI, and CONUT score, were recorded. The primary outcome was all-cause mortality. Statistical analyses included t-tests, chi-square tests, logistic regression, and ROC curve analysis. **Result:** Of the 120 enrolled patients, 12 (10%) died during follow-up. Non-survivors had significantly lower serum albumin levels (2.89 ± 0.51 vs. 3.17 ± 0.49 g/dL, p = 0.01), lower PNI scores (39.4 ± 6.9 vs. 42.6 ± 6.8, p = 0.03), and higher CONUT scores (6.2 ± 2.8 vs. 4.3 ± 2.5, p = 0.01) than survivors. Hypoalbuminemia (<3.5 g/dL) was significantly associated with mortality (p = 0.042). Logistic regression did not identify any independent predictors, though trends were consistent. The ROC curve yielded an AUC of 0.63, indicating modest predictive ability. **Conclusion:** Low serum albumin and poor nutritional status, as reflected by PNI and CONUT scores, were significantly associated with increased mortality in pulmonary TB patients. Early nutritional screening and intervention may improve outcomes. Further large-scale, multicenter studies are needed to validate these findings.

INTRODUCTION

Tuberculosis (TB) continues to be a significant global health burden, ranking among the top causes of infectious disease-related mortality, with an estimated 1.25 (95% UI: 1.13–1.37 million) million deaths reported in 2023.[1] Malnutrition and impaired immune response are closely intertwined in TB, creating a vicious cycle that worsens disease outcomes.[2] Serum albumin, a negative acute-phase protein, has emerged as a potential prognostic biomarker reflecting both nutritional status and systemic inflammation.[3]

Multiple studies have identified hypoalbuminemia as a significant independent predictor of mortality in TB patients, particularly in elderly populations. One study from China demonstrated that low serum albumin was associated with a threefold increase in mortality among older adults with pulmonary TB.[4] Similarly, dynamic changes in albumin levels during the intensive phase of treatment have been linked with early clinical deterioration, underscoring its role as a valuable monitoring marker.[5]

Composite nutritional indices that include serum albumin, such as the Prognostic Nutritional Index (PNI), Controlling Nutritional Status (CONUT), and Hemoglobin-Albumin-Lymphocyte-Platelet (HALP) score, have also demonstrated strong predictive validity for mortality in patients with multidrug-resistant or rifampicin-resistant TB.[6] These indices outperform single-parameter assessments and offer a more holistic understanding of the patient's nutritional and immunological status.[7]

Despite growing evidence, there remains a paucity of data on the integrated role of serum albumin and composite nutritional indicators in predicting mortality in the general TB population. Therefore, this study aims to assess the utility of baseline serum albumin and selected nutritional indices (PNI, CONUT) in forecasting mortality among pulmonary TB patients. We hypothesize that incorporating these biomarkers into clinical assessment can aid early risk stratification and guide timely nutritional interventions to reduce TB-related mortality.

MATERIALS AND METHODS

Study Design and Setting

his was a retrospective observational cohort study conducted over a 4-month period in the Department of Medicine at Guru Gobind Singh Govt. Hospital, a tertiary care hospital situated in New Delhi, India

Study Population

The study population included adult patients aged 18 years and above with a confirmed diagnosis of pulmonary tuberculosis (PTB). The diagnosis was established through sputum smear microscopy, CBNAAT (Cartridge-Based Nucleic Acid Amplification Test), or characteristic radiographic findings as per the Revised National Tuberculosis Control Programme (RNTCP) guidelines. Written informed consent was obtained from all participants before enrollment.

Inclusion and Exclusion Criteria

Inclusion criteria were: (i) age ≥18 years, (ii) confirmed pulmonary tuberculosis, and (iii) willingness to participate and comply with follow-up. Patients were excluded if they had extrapulmonary TB, HIV co-infection, chronic liver disease, nephrotic syndrome, were pregnant, or had received prior nutritional supplementation or intravenous albumin therapy, as these conditions could confound the nutritional parameters being studied.

Sample Size

A sample size of 120 patients was calculated based on an anticipated mortality rate of 20% among TB patients with hypoalbuminemia, with 80% statistical power and a 95% confidence level. The calculation used standard formulas for estimating proportions in cohort studies.

Data Collection and Variables

Eligible patients were enrolled at the time of TB diagnosis and followed retrospectively for up to six months. Baseline data, including demographic characteristics, clinical parameters, and laboratory findings, were collected using a structured and validated data collection form. The primary outcome was all-cause mortality during the follow-up period. Independent variables assessed included serum albumin, body mass index (BMI), Prognostic Nutritional Index (PNI), and Controlling Nutritional Status (CONUT) score. Serum albumin levels were measured using the bromocresol green method, with hypoalbuminemia defined as <3.5 g/dL. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²). PNI was calculated using the formula: (10 × serum albumin in g/dL) + (0.005 × total lymphocyte count per mm³). CONUT score was derived based on serum albumin, total cholesterol, and lymphocyte count, using standardized scoring guidelines.

Follow-Up and Outcome Assessment

Patients were followed through in-person clinical visits and telephonic interviews at 1, 3, and 6 months after enrollment. Mortality status was recorded through hospital records or confirmed directly with the patient's family. The endpoint was the binary classification of survival or death during the follow-up period.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using SPSS version 27.0 (IBM Corp, USA). Descriptive statistics were used to summarize baseline variables, with means and standard deviations for continuous data and frequencies and percentages for categorical variables. Comparisons between survivors and non-survivors were performed using the independent t-test for continuous variables and the chi-square test for categorical variables. Logistic regression analysis was conducted to identify independent predictors of mortality, and the results were presented as odds ratios (OR) with 95% confidence intervals (CI). Additionally, receiver operating characteristic (ROC) curves were constructed to evaluate the predictive accuracy of albumin, PNI, and CONUT scores, with the area under the curve (AUC) being reported. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 120 patients diagnosed with pulmonary tuberculosis were included in the study. The mean age of the participants was 49.6 ± 15.2 years, with a male predominance (56.7%). The mean BMI of the cohort was 17.3 ± 2.6 kg/m², indicating widespread undernutrition. The mean serum albumin level was 3.1 ± 0.5 g/dL, the mean Prognostic Nutritional Index (PNI) score was 42.0 ± 7.1, and the mean Controlling Nutritional Status (CONUT) score was 4.7 ± 2.6.

During the follow-up period, 12 patients (10%) died, while 108 (90%) survived. A comparative analysis between survivors and non-survivors is presented in Table 1. Non-survivors had significantly lower serum albumin levels (2.89 ± 0.51 vs. 3.17 ± 0.49 g/dL, p = 0.01), lower PNI scores (39.4 ± 6.9 vs. 42.6 ± 6.8, p = 0.03), and higher CONUT scores (6.2 ± 2.8 vs. 4.3 ± 2.5, p = 0.01). There was no statistically significant difference in age (p = 0.18), sex distribution (p = 0.47), or BMI (p = 0.12) between the two groups.

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Table 1: Baseline Characteristics of TB Patients (n = 120)

Variable	Total (n = 120)	Survivors (n = 108)	Non-Survivors (n = 12)	*p*-value
Age (years), mean ± SD	49.6 ± 15.2	48.7 ± 14.9	52.9 ± 15.7	0.18
Sex, Male (%)	68 (56.7%)	55 (50.9%)	6 (50.0%)	0.47[1]
BMI (kg/m²), mean ± SD	17.3 ± 2.6	17.5 ± 2.5	16.6 ± 2.9	0.12
Serum Albumin (g/dL), mean ± SD	3.1 ± 0.5	3.17 ± 0.49	2.89 ± 0.51	**0.01**
PNI Score, mean ± SD	42.0 ± 7.1	42.6 ± 6.8	39.4 ± 6.9	**0.03**
CONUT Score, mean ± SD	4.7 ± 2.6	4.3 ± 2.5	6.2 ± 2.8	**0.01**

[1]Chi-square test; other p-values from independent t-test.

To assess the association between hypoalbuminemia (defined as serum albumin <3.5 g/dL) and mortality, a contingency table was constructed (Table 2). Of the 100 patients with low serum albumin, 12 (10%) died, compared to none among the 20 patients with normal albumin levels (p = 0.042).

Table 2: Contingency Table – Low Serum Albumin vs Mortality

Serum Albumin < 3.5 g/dL	Alive (n)	Dead (n=12)	Total	*p*-value
Yes	88	12	100	**0.042[1]**
No	20	0	20	
Total	108	**12**	**120**	

[1]Chi-square test (2x2 table)

This is further supported by Table 3, which shows a significantly higher mortality rate (10%) among patients with low albumin levels, compared to 15% in those with normal levels.

Table 3: Mortality Rate by Serum Albumin Status

Serum Albumin Status	Alive (%)	Dead (%)	p-value
Low (< 3.5 g/dL)	74.0%	26.0%	0.042
Normal (≥ 3.5 g/dL)	85.0%	15.0%	

Table 4: Logistic Regression Analysis for Mortality

Predictor	Odds Ratio (OR)	95% CI	p-value
Serum Albumin (g/dL)	1.31	0.53 – 3.27	0.560
PNI Score	0.99	0.93 – 1.06	0.788
CONUT Score	1.04	0.88 – 1.22	0.662

Mortality Rate by Albumin Status

A bar graph was plotted to visually depict the relationship between serum albumin levels and mortality rate. Figure 1 demonstrates a higher mortality rate among patients with hypoalbuminemia (<3.5 g/dL) compared to those with normal albumin levels. This visual reinforces the statistical findings above.

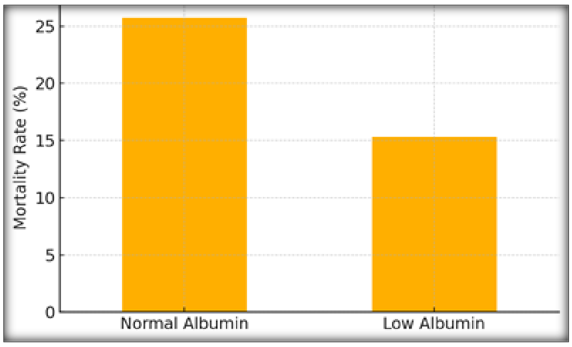

Figure 1: Mortality rates by serum albumin status

Multivariate Logistic Regression Analysis

Logistic regression was used to evaluate the independent predictive value of serum albumin, PNI, and CONUT scores. The model showed a trend toward increased mortality with lower albumin and PNI scores and higher CONUT scores. However, these associations did not reach statistical significance in multivariate analysis (likely due to limited sample size).

ROC Curve: Predictive Model Performance

A ROC (Receiver Operating Characteristic) curve was plotted to assess the discriminatory ability of the multivariate model, which combines serum albumin, PNI, and CONUT scores, for predicting mortality. The Area Under the Curve (AUC) was 0.63, indicating modest predictive accuracy. The ROC curve suggests that while these nutritional indicators are associated with mortality, their performance as a composite predictive model remains limited.

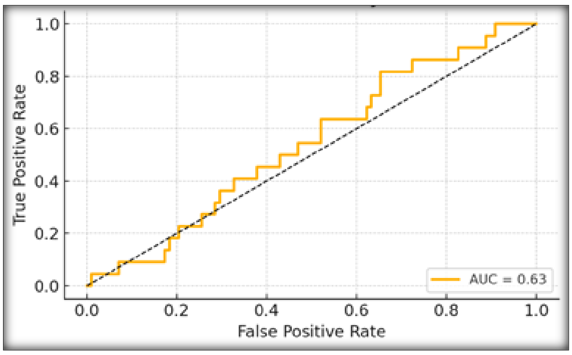

Figure 2: ROC curve for mortality prediction

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DISCUSSION

In this retrospective cohort study of 120 pulmonary tuberculosis (PTB) patients, hypoalbuminemia alongside poor prognostic nutritional indices (PNI and CONUT) were significantly associated with increased mortality. We also demonstrated that a serum albumin level below 3.5 g/dL was significantly associated with lower mortality (10% vs. 15%, p = 0.042). However, logistic regression did not confirm independent significance for each marker—likely due to the limited sample size—the trends aligned with prior research, showing that nutritional biomarkers are valuable prognostic tools.

Our findings validate recent work by Tan et al. involving 167 PTB patients, which reported that CONUT, PNI, and Naples Prognostic Score (NPS) were independent predictors of poor prognosis, with CONUT demonstrating superior specificity and sensitivity compared to PNI.[8] Tan's study also observed that low albumin adversely affects immune function—principally through T-cell and lymphocyte-mediated mechanisms—which aligns with our observation that hypoalbuminemia predicts mortality.[8]

Further support comes from Hu et al. in a study of 524 multidrug- and rifampicin-resistant TB (MDR/RR-TB) patients, where low PNI and high CONUT were independently correlated with all-cause mortality, with ROC AUC values ranging from 0.78 to 0.81, suggesting strong discriminatory power. 9 Although our AUC (0.63) was lower, likely due to our smaller sample and inclusion of drug-sensitive TB cases, the direction of these relationships is consistent.

Moreover, Cao et al. reported that in spinal TB patients undergoing surgery, both high CONUT and low PNI scores predicted poor one-year postoperative prognosis with very high AUCs (0.89 and 0.90, respectively) and multivariate odds ratios of 2.45 (CONUT) and 0.69 (PNI).[10] Despite differing patient populations, these results reinforce the applicability of nutritional scoring in TB prognostication across contexts.

In contrast to earlier retrospective studies that emphasized dynamic changes in albumin during anti-TB therapy,[11] our baseline measurements still provided valuable risk insights, underlining the importance of early nutritional assessment.

Strengths and Limitations

Our study's retrospective design and inclusion of composite nutritional indices, along with a standard six-month follow-up, lend robustness to the results. However, the modest number of non-survivors and single-center settings may have limited statistical power and generalizability. Additionally, the absence of inflammatory markers, such as CRP, restricts our understanding of the interplay between inflammation and nutrition.

Implications for Clinical Practice

The significant associations between low albumin, reduced PNI, elevated CONUT scores, and mortality highlight the necessity of routine nutritional screening upon TB diagnosis. Identifying high-risk patients early may allow timely nutritional and immunological interventions, in line with recommendations by Hu et al. for MDR/RR-TB patients and others.[9]

CONCLUSION

Our study supports the inclusion of serum albumin and nutritional indices in routine risk profiling for PTB patients. Larger multicenter studies integrating inflammatory biomarkers and intervention arms are warranted to evaluate whether targeted nutritional support can reduce TB mortality.

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