

ORIGINAL ARTICLE

Serum albumin, creatinine and urinary protein-creatinine index in patients of tuberculosis: A cross-sectional study

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Background: Tuberculosis (TB) is one of the most important infectious diseases throughout the world. India is a highly populated country, and a significant amount of mortality and morbidity is caused by TB, especially pulmonary TB. **Aim:** The aim is to evaluate serum albumin, creatinine, and urinary protein-creatinine index in patients with TB. **Objectives:** To estimate the levels of serum albumin, creatinine, urinary protein, and creatinine in patients with TB and compare them with those of apparently healthy subjects. **Materials and Methods:** This was a cross-sectional study. A total of 168 subjects were included in this study. Among them, 84 were smear-positive PTB patients, denoted as the case group, and 84 were apparently healthy individuals, denoted as the control group. Biochemical tests were carried out in the Department of Biochemistry at Rohilkhand Medical College and Hospital. All the statistical analysis was performed using SPSS version 23.0. Results were evaluated using an unpaired Student's t-test and Pearson correlation. A $P < 0.05$ was considered statistically significant. **Results:** The study revealed that mean values of serum albumin were 3.55 ± 0.89 gm/dL and 3.27 ± 0.83 gm/dL in the case and control groups, respectively, and the difference between the two groups was not significant ($P > 0.001$). The mean serum creatinine level was higher in the case group when compared to the control group. The mean values of serum creatinine were 1.93 ± 1.60 mg/dL and 1.01 ± 0.86 mg/dL in case and control groups, respectively, and the difference between the two groups was highly significant ($P < 0.001$). The mean value of the urinary protein-creatinine index was 0.663 ± 0.982 and 0.147 ± 0.110 in the case and control groups, respectively. The analysis showed that the difference in mean UPCI levels between the two groups was highly significant ($P < 0.001$). **Conclusion:** The protein-creatinine index in random urine is a convenient, quick, and reliable method of estimation of proteinuria for the diagnosis and monitoring of renal disease in TB patients.

KEY WORDS: Serum albumin, serum creatinine, tuberculosis, UPCI

INTRODUCTION

India stands in second position all over the world in terms of tuberculosis (TB) cases. TB is a chronic condition that causes

both pulmonary and systemic diseases.^[1] TB is caused by *Mycobacterium tuberculosis*, which primarily affects the lungs but can also affect other parts of the body. The disease is spread through the air when an infected person coughs, sneezes, or talks. It is estimated that one-third of the world's population is infected with TB. The symptoms of TB include coughing, chest pain, fatigue, weight loss, and fever. If left untreated, TB can be fatal.^[2] Albumin is the major plasma protein with a high molecular weight. Serum albumin plays important role as a biochemical marker of the nutritional status of pulmonary TB patients, and considerable changes take place in serum albumin levels.^[1] Creatine and creatine phosphate cyclize slowly and

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spontaneously at a constant rate to form creatinine (anhydride of creatine), which is excreted in urine. Creatinine is synthesized from creatine and excreted through the kidneys; creatinine is produced from creatine phosphate in skeletal muscle. The estimation of creatinine levels in serum and urine serves as a reliable indicator to assess kidney function.^[3] Serum creatinine is a very important parameter; urine creatinine evacuation depends on muscle mass, and it has been predictable that 1 g (9 mmol) of creatinine is derived from 17kg of skeletal muscle.^[4] A urine protein creatinine index test gives information about how the kidneys are working. It measures the levels of proteins and creatinine in urine. This urine test helps the provider diagnose kidney disease and monitor conditions that can damage the kidneys during TB treatment.^[5]

Serum albumin, creatinine, and urinary protein-creatinine index have previously been identified as candidate biomarkers in TB patients, but there is inconclusive data regarding these markers, with few studies documented and also not extensively investigated in TB patients around the Rohilkhand region. Keeping these points in mind, the present study was conducted to evaluate the association between serum albumin, creatinine, and urinary protein-creatinine index in patients with TB.

METHODOLOGY

Place of Study

The present study was carried out in the department of biochemistry in collaboration with the Department of Respiratory Medicine at Rohilkhand Medical College and Hospital, Bareilly.

Study Population

All TB patients attending OPD and admitted to the respiratory medicine department of Rohilkhand Medical College and Hospital, Bareilly. Subjects in the age range of 18–65 years^[1] were included by the purposive (non-random) sampling technique, among which the case group (group-1) consisted of 84 smear-positive TB subjects and the control group (group-2) of 84 age- and sex-matched healthy subjects without any history of TB.

Inclusion Criteria

- All newly diagnosed pulmonary TB patients (positive tuberculin skin test or positive interferon-gamma release and assay and clinical, chest radiology, smear microscopy, nucleic acid amplification, or culture evidence of TB)^[3] from the Respiratory Medicine Department of the Rohilkhand Medical College and Hospital, Bareilly.
- Age group: 18–65 years.^[1]

Exclusion Criteria

1. Multidrug-resistant TB
2. Any history of long-term steroid or cytotoxic drug therapy
3. Pregnancy/lactation
4. Alcoholism (drinking of seven or more standard drinks by

males and five or more standard drinks by females within a single day).^[6]

5. Other systemic disorders-
 - a. Acute and chronic liver diseases
 - b. Renal or cardiac diseases
 - c. Asthma
 - d. Diabetes mellitus
 - e. Malignancies.

Data Collection with Ethical Concern

The study was conducted for a duration of 1 year, from August 2022 to July 2023, after obtaining ethical clearance from the Institutional Ethics Committee with vide reference number IEC/RMCH/89/2022/AUG and registered on CTRI with registration number CTRI/2022/12/048051. Informed and written consent was taken from all subjects included in the study. Data were collected from the subjects and entered in the patient information sheet.

Collection of Samples

- Under all aseptic conditions, 4 mL of venous blood was collected from the subjects in a serum-separating tube. Venostasis was avoided during specimen collection to avoid hemoconcentration.
- Blood was allowed to clot for 30 min at 37°C and then centrifuged at 2000 rpm for 10 min. The obtained serum was stored at 2–8°C for further analysis for a maximum period of 7 days.
- A first-morning urine sample was collected in a separate sterile container, which was analyzed immediately to estimate the urine protein and urine creatinine in TB patients.

Test Parameters

Patients will be investigated for the following parameters:

- S. Albumin- by Bromo Cresol Green Dye binding method.
- S. Creatinine—by Jaffe's method
- Urine Protein—by Pyrogallol Red Method
- Urine Creatinine—by Jaffe's Method

Statistical Analysis

The data was processed and analyzed using Microsoft Excel 2021 and Statistical Package for Social Science software version 23.0. All the values of the analyzed parameters were expressed as the mean \pm S.D. (standard deviation). Unpaired Student's t-test was used to compare two groups, and Pearson correlation was used to correlate different parameters of TB patients. A probability of $P < 0.05$ was considered statistically significant.

RESULTS

The study was done from August 2022 to July 2023 that included 84 newly diagnosed pulmonary TB patients and 84 apparently healthy subjects. We observed that the TB group has 68 males and 16 females, and the healthy subjects group has fifty males and thirty-four females with an age range of 18–65 years.

Table 1 shows that a total of 84 people with TB were studied; 68 (80%) were males and 16 (20%) were females. The mean age of the TB patients was 49.17 years.

Table 2 shows that TB and healthy subjects were distributed according to age into three groups. Age group between 18 and 35 years in TB patients percentage is less than compared to age group between 36 and 50 or 51–65 years of TB patients. It shows that those who have an age group of 18–35 years have less effect on TB infection compare to those aged 36–50 and 51–65.

Table 3 shows serum albumin and urinary creatinine were not statistically significant. Serum creatinine, urinary protein, and urinary protein-creatinine index were highly statistically significant in TB patients as compared to healthy subjects ($P < 0.05$) Graph 1a-c.

Table 1: Age distribution among both subjects

Subjects	Age (Mean±SD) (Years)
Tuberculosis	49.17±12.82
Healthy subjects	41.69±15.17

Table 2: Age group distribution among tuberculosis and healthy subjects

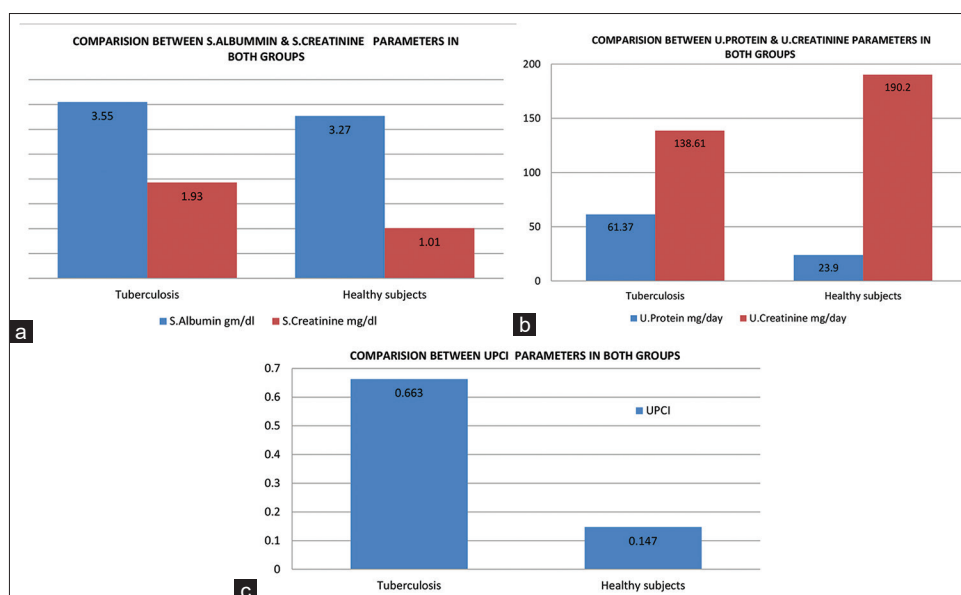
Age group (18–65)	Tuberculosis (n=84)		Healthy subjects (n=84)	
	No of subjects	Percentage	No of subjects	Percentage
18–35	14	16.66	33	39.28
36–50	29	34.52	24	28.57
51–65	41	48.80	27	32.14

Table 4 shows serum albumin, serum creatinine, urinary protein, and urinary protein creatinine index levels that were found to be increased in male and female TB patients as compared to male and female healthy subjects. The urinary creatinine level was decreased in both groups of TB patients as compared to healthy subjects.

Table 5 shows an excellent correlation was found between serum albumin and urinary creatinine. The correlation coefficient of serum albumin with urinary creatinine ($r = 0.32$) was significant ($P < 0.01$). The high correlation suggests that urinary creatinine provides an accurate and valid assessment of serum albumin, and a correlation was found urinary protein-creatinine index with urinary protein and urinary creatinine. The correlation coefficient of UPCI with urine protein ($r = 0.23$) and urine creatinine ($r = 0.34$) was significant ($P < 0.01$). Graphs 2-4 The high correlation suggests that the urine protein and urine creatinine provide an accurate and valid assessment of UPCI.

DISCUSSION

In the present study, serum albumin levels increased in TB patients when compared to healthy subjects. The mean value of serum albumin was 3.55 ± 0.89 gm/dL in TB patients and 3.27 ± 0.83 gm/dL in healthy subjects. Biswas *et al.*^[1] and Batra *et al.*^[7] revealed that the mean serum albumin level was lower in TB patients when compared to healthy subjects. There was a significant ($P < 0.001$) decrease in serum albumin level in TB patients when compared to healthy subjects. Elevation of serum albumin concentration occurs due to some reasons, like sample size being very small, dehydrated patients, and taking a high-protein diet. So, the differences in mean serum albumin levels between the two groups were not significant.



Graph 1: (a) Distribution of serum albumin and serum creatinine parameters among Tuberculosis and Healthy subjects [Table 3], (b) Distribution of urine protein and urine creatinine parameters among Tuberculosis and Healthy subjects [Table 3], (c) Distribution of Urinary protein-creatinine index among tuberculosis and healthy subjects [Table 3]

Table 3: Distribution of parameters among tuberculosis and healthy subjects

Parameter	TB subjects Mean±SD	Healthy subjects Mean±SD	t-test	P-value
Serum albumin (gm/dL)	3.55±0.89	3.27±0.83	0.05	0.159
Serum creatinine (mg/dl)	1.93±1.60	1.01±0.86	4.61	<0.01*
Urinary protein (mg/day)	61.37±50.56	23.90±9.45	6.67	<0.01*
Urinary creatinine (mg/day)	138.61±83.11	190.2±76.31	5.02	0.343
Urinary protein creatinine index	0.663±0.982	0.147±0.110	4.78	<0.01*

*P-value <0.05 (Statistically significant)

Table 4: Comparison of parameters based on gender in tuberculosis and healthy subjects

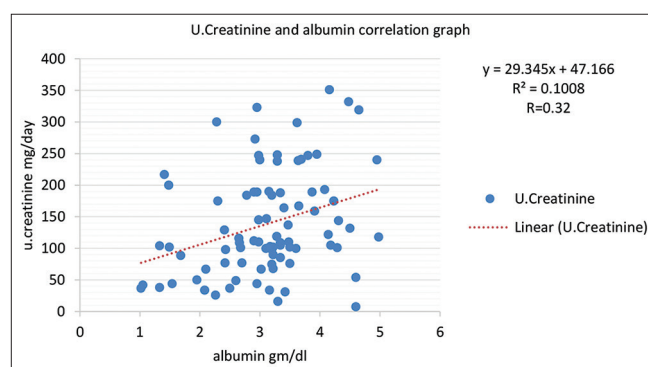
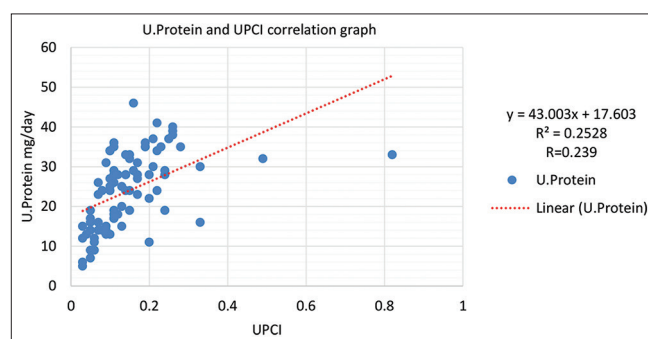
Parameters	Male tuberculosis Mean±SD n=68	Male healthy subjects Mean±SD n=50	Female Tuberculosis Mean±SD n=16	Female healthy subjects Mean±SD n=34
Serum albumin (gm/dL)	3.55±0.88	3.22±0.77	3.64±0.92	2.96±0.69
Serum creatinine (mg/dL)	1.83±1.56	1.05±1.09	2.37±1.66	0.95±0.39
Urinary protein (mg/day)	56.75±29.98	25.04±8.56	81.00±94.70	22.24±10.29
Urinary creatinine (mg/day)	149.37±85.54	191.74±83.51	92.92±46.51	188.00±62.87
Urinary protein creatinine index	0.63±1.00	0.16±0.12	0.80±0.84	0.13±0.09

Table 5: Correlation among parameter in tuberculosis patients

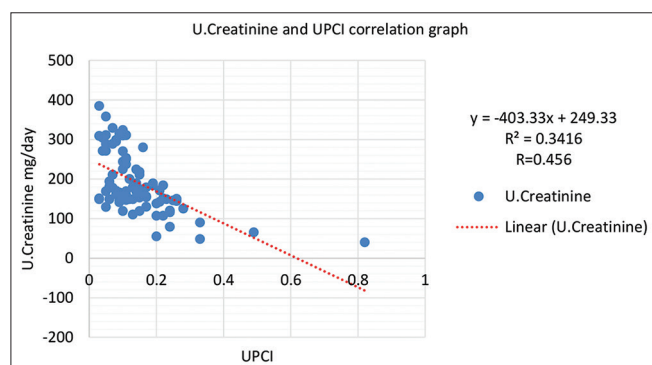
Parameters	Serum albumin		UPCI	
	R-value	P-value	R-value	P-value
Serum creatinine	-0.11	0.36	-0.067	0.59
Urinary protein	0.01	0.92	0.239	0.03*
Urinary Creatinine	0.32	0.004*	0.456	<0.01*
UPCI	-0.09	0.0079	-	-
Serum Albumin	-	-	-0.09	0.47

Serum creatinine levels increased in TB patients when compared to healthy subjects. The mean value of serum creatinine was 1.93 ± 1.60 mg/dL in TB patients and 1.01 ± 0.86 mg/dL in healthy subjects. The analysis showed that the difference in mean serum creatinine levels between the two groups was significant ($P < 0.001$). Serum creatinine in pulmonary TB changes significantly ($P \leq 0.01$). This observation could be due to a number of reasons: One may be the changes in renal dynamics as a result of the drug-induced hyperuricemia associated with anti-TB drug medication. A very few studies have been done on serum creatinine in TB patients. Till now, sufficient data are not available for drawing a definite conclusion.

Urinary protein creatinine index levels increased in TB patients when compared to healthy subjects. The mean value of UPCI was 0.66 ± 0.98 in TB patients and 0.147 ± 0.110 in healthy subjects. The analysis showed that the difference in mean urinary protein-creatinine index level between the two groups was significant ($P < 0.001$). Khan *et al.*^[8] explained that the protein-creatinine index and ratio were more than 140 and 0.18, respectively, in a random urine sample, indicating pathological proteinuria. An excellent correlation ($r = 0.96$) was found between random

**Graph 2:** Positive Pearson's correlation between serum albumin and urinary creatinine in tuberculosis patients**Graph 3:** Positive Pearson's correlation between urinary protein-creatinine index and urinary protein in tuberculosis patients

urine protein, creatinine index/ratio, and standard 24 h urinary protein excretion in these patients ($P < 0.001$). Future studies need to investigate the urinary protein-creatinine index as a non-invasive tool to monitor treatment success early on and to serve as a predictor of treatment failure and relapse, particularly in patients infected with *M. tuberculosis*.



Graph 4: Negative Pearson's correlation between urinary protein-creatinine index and urinary creatinine in tuberculosis patients

CONCLUSION

TB patients showed a wide range of protein excretion rates in this series. A significant correlation was found between the protein creatinine index and urinary creatinine excretion in TB patients. Proteins and creatinine are highly soluble in water, so they will undergo similar changes in dilution or concentration of urine according to the hydration status of the body. Creatinine excretion varies among individuals according to age, sex, and body size, but it still shows good accuracy and correlation with urinary creatinine. This is probably because the index is independent of errors in urine collection. Thus, the uniformly high correlation coefficients are sufficiently strong evidence for the creatinine protein index for the assessment of persistent proteinuria. The main limitation of the protein creatinine index is a wide daily variation in the urinary protein excretion rate associated with changes in posture, physical activity, protein intake, and hemodynamic factors. Further research studies are recommended. Every TB patient needs further evaluation of their micronutrients status to find out the correlation with *Mycobacterium TB*, and very little studies are done on the follow-up of TB patients.

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