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Original Research Article

Negative Correlation of Serum Total Bile Acid with Albuminuria in Patients with Type-2 Diabetes Mellitus: A Cross-Sectional Study

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Abstract:

Background: Diabetic nephropathy remains one of the most common microvascular complications of type-2 diabetes mellitus (T2DM) and is a major cause of chronic kidney disease worldwide. Albuminuria is an early marker of renal damage in diabetic individuals. Recent research suggests that bile acids act as metabolic signaling molecules that regulate glucose metabolism, inflammation, and insulin sensitivity. However, their association with diabetic kidney disease remains inadequately explored.

Objective: To evaluate the relationship between serum total bile acid levels and albuminuria in patients with type-2 diabetes mellitus.

Materials and Methods: This cross-sectional study was conducted at Patna Medical College, Patna, Bihar, India over a period of eight months (February 2025–October 2025). A total of 80 patients with diagnosed T2DM were enrolled. Serum total bile acid levels were measured using enzymatic assays, and urinary albumin excretion was assessed using the albumin-creatinine ratio (ACR). Patients were categorized into normoalbuminuria, microalbuminuria, and macroalbuminuria groups. Statistical analysis was performed using Pearson correlation and ANOVA tests.

Results: The mean serum bile acid level was significantly lower in patients with higher albuminuria levels ($p < 0.01$). A significant negative correlation was observed between serum total bile acid levels and urinary albumin excretion ($r = -0.42$, $p = 0.002$).

Conclusion: Serum total bile acid levels show a significant inverse relationship with albuminuria in patients with T2DM. Lower bile acid levels may be associated with worsening renal involvement in diabetic patients.

Keywords: Type-2 Diabetes Mellitus, Bile Acids, Albuminuria, Diabetic Nephropathy, Metabolic Regulation, Kidney Disease.

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Introduction

Type-2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion. It has emerged as a major global health challenge with increasing prevalence across both developed and developing countries [1]. One of the most serious complications of T2DM is diabetic nephropathy, which is the leading cause of chronic kidney disease and end-stage renal disease worldwide [2].

Albuminuria represents an early clinical indicator of diabetic kidney damage and is widely used for the screening and monitoring of diabetic nephropathy [3]. The presence of increased urinary albumin excretion reflects glomerular injury and is associated with an increased risk of cardiovascular morbidity and mortality [4].

Traditionally, bile acids were considered to be molecules primarily involved in lipid digestion and absorption. However, emerging evidence suggests that bile acids also function as important signaling molecules regulating glucose metabolism, lipid homeostasis, and inflammatory pathways [5]. These effects are largely mediated through activation of nuclear receptors such as the farnesoid X receptor (FXR) and the G-protein-coupled bile acid receptor (TGR5) [6].

Activation of these receptors has been shown to improve insulin sensitivity, reduce hepatic gluconeogenesis, and regulate energy expenditure [7]. In addition, bile acids influence renal function through modulation of metabolic and inflammatory

pathways that contribute to diabetic kidney disease [8].

Recent studies have reported alterations in bile acid metabolism in patients with diabetes and metabolic syndrome [9]. Experimental evidence indicates that bile acid signaling may exert protective effects against renal inflammation and fibrosis, two key mechanisms involved in diabetic nephropathy [10].

Furthermore, FXR activation has been shown to reduce proteinuria and improve renal function in animal models of diabetic kidney disease [11]. Clinical studies have also suggested that circulating bile acid levels may be associated with metabolic parameters such as insulin resistance, lipid metabolism, and glycemic control [12].

Despite these findings, limited clinical research has explored the relationship between serum bile acid levels and albuminuria in patients with T2DM. Understanding this relationship may provide insights into novel biomarkers or therapeutic targets for diabetic kidney disease [13].

Therefore, the present study was designed to evaluate the correlation between serum total bile acid levels and albuminuria among patients with type-2 diabetes mellitus attending a tertiary care hospital in Bihar, India.

Materials and Methods

Study Design and Setting: The present research was conducted as a hospital-based cross-sectional study to evaluate the association between serum total bile acid levels and albuminuria in patients with type-2 diabetes mellitus. The study was carried out at Patna Medical College, a tertiary care teaching hospital that provides specialized medical services to a large population in eastern India. The study was conducted over a period of eight months from February 2025 to October 2025.

Study Population: A total of 80 patients diagnosed with type-2 diabetes mellitus attending the outpatient and inpatient departments of the hospital were included in the study. Patients were recruited consecutively during the study period after obtaining informed consent. The diagnosis of type-2 diabetes mellitus was based on the diagnostic criteria recommended by the American Diabetes Association, including fasting plasma glucose ≥126 mg/dL, HbA1c ≥6.5%, or a prior confirmed diagnosis of diabetes under treatment.

Sample Size: The sample size of 80 participants was determined based on feasibility and availability of eligible patients during the study period. Previous observational studies evaluating metabolic biomarkers in diabetic nephropathy have used similar sample sizes to determine correlations between biochemical parameters and albuminuria.

Inclusion Criteria

Patients fulfilling the following criteria were included in the study:

- Adults aged 30–70 years
- Confirmed diagnosis of type-2 diabetes mellitus
- Duration of diabetes of at least one year
- Patients willing to provide informed consent for participation

Exclusion Criteria

The following patients were excluded to avoid confounding factors affecting bile acid metabolism or renal parameters:

- Patients with chronic liver disease or cholestatic disorders
- Patients with acute kidney injury or advanced chronic kidney disease (Stage IV or V)
- Pregnant or lactating women
- Patients with active infections or inflammatory diseases
- Individuals receiving medications affecting bile acid metabolism such as bile acid sequestrants
- Patients with known malignancies

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee of Patna Medical College. All participants were informed about the purpose and procedures of the study. Written informed consent was obtained from all patients before enrollment. Patient confidentiality and data privacy were maintained throughout the study.

Data Collection Procedure: A structured data collection format was used to record demographic and clinical information. The following details were obtained for each participant:

- Age
- Gender
- Duration of diabetes
- Body mass index (BMI)
- Blood pressure
- Current medications
- History of diabetic complications

Anthropometric measurements were recorded using standardized techniques. Body weight and height were measured, and BMI was calculated as weight (kg) divided by height squared (m^2).

Laboratory Investigations: After an overnight fasting period of 8–10 hours, approximately 5 mL of venous blood was collected from each participant under aseptic conditions.

The following laboratory parameters were measured:

- Fasting blood glucose
- Glycated hemoglobin (HbA1c)

- Serum creatinine
- Serum total bile acid

Blood glucose levels were estimated using the glucose oxidase-peroxidase method, while HbA1c levels were measured using high-performance liquid chromatography (HPLC). Serum creatinine was determined using an enzymatic colorimetric assay.

Measurement of Serum Total Bile Acids: Serum total bile acid levels were measured using a commercial enzymatic cycling assay kit based on the 3-α-hydroxysteroid dehydrogenase reaction. The assay quantifies total bile acids in serum samples through spectrophotometric detection. Results were expressed in micromoles per liter (μmol/L).

Assessment of Albuminuria: Urinary albumin excretion was assessed using the urinary albumin-to-creatinine ratio (ACR) obtained from a spot urine sample. Urinary albumin concentration was measured using an immunoturbidimetric method, and urinary creatinine was estimated by the Jaffe reaction method.

Patients were categorized based on ACR values into the following groups:

Category	Albumin-Creatinine Ratio (ACR)
Normoalbuminuria	<30 mg/g
Microalbuminuria	30–300 mg/g
Macroalbuminuria	>300 mg/g

This classification was used to assess the severity of renal involvement in diabetic patients.

Variables Evaluated

The primary variables evaluated in the study included:

- Serum total bile acid levels
- Urinary albumin-creatinine ratio
- Glycemic parameters (fasting glucose and HbA1c)
- Duration of diabetes

Statistical Analysis: Data were compiled and analyzed using IBM SPSS Statistics version 25.0.

Quantitative variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage.

The following statistical tests were applied:

- One-way analysis of variance (ANOVA) to compare serum bile acid levels among albuminuria groups
- Pearson correlation coefficient to assess the relationship between serum bile acid levels and albuminuria
- Chi-square test for categorical variables where applicable

A p-value <0.05 was considered statistically significant.

Results

A total of 80 patients with type-2 diabetes mellitus were included in the study. Demographic, clinical, and biochemical parameters were analyzed to determine the association between serum total bile acid levels and albuminuria.

Demographic and Clinical Characteristics: The mean age of the study population was 54.3 ± 8.2 years, with a slight predominance of male participants. The mean duration of diabetes was 7.6 ± 3.4 years, and the average HbA1c level was 8.2 ± 1.3%, indicating relatively poor glycemic control among participants.

Table 1 summarizes the baseline demographic and clinical characteristics of the study participants.

Table 1: Baseline Demographic and Clinical Characteristics of Participants (n = 80)

Parameter	Mean ± SD / n (%)
Age (years)	54.3 ± 8.2
Male	46 (57.5%)
Female	34 (42.5%)
Duration of diabetes (years)	7.6 ± 3.4
BMI (kg/m²)	26.1 ± 3.1
Fasting blood glucose (mg/dL)	154.7 ± 32.6
HbA1c (%)	8.2 ± 1.3
Serum creatinine (mg/dL)	1.18 ± 0.34
Serum total bile acid (μmol/L)	6.6 ± 2.0

As shown in Table 1, most patients were middle-aged adults with moderately elevated glycemic parameters.

Distribution of Albuminuria: Patients were categorized according to urinary albumin-creatinine

ratio (ACR) into normoalbuminuria, microalbuminuria, and macroalbuminuria groups.

The majority of patients belonged to the normoalbuminuria group (40%), followed by microalbuminuria (37.5%), while 22.5% of patients had macroalbuminuria (Figure 1).

Table 2: Distribution of Albuminuria among Study Participants

Albuminuria Category	ACR (mg/g)	Number of Patients	Percentage
Normoalbuminuria	<30	32	40%
Microalbuminuria	30–300	30	37.5%
Macroalbuminuria	>300	18	22.5%

As shown in Table 2, a considerable proportion of patients had evidence of early diabetic kidney disease in the form of microalbuminuria.

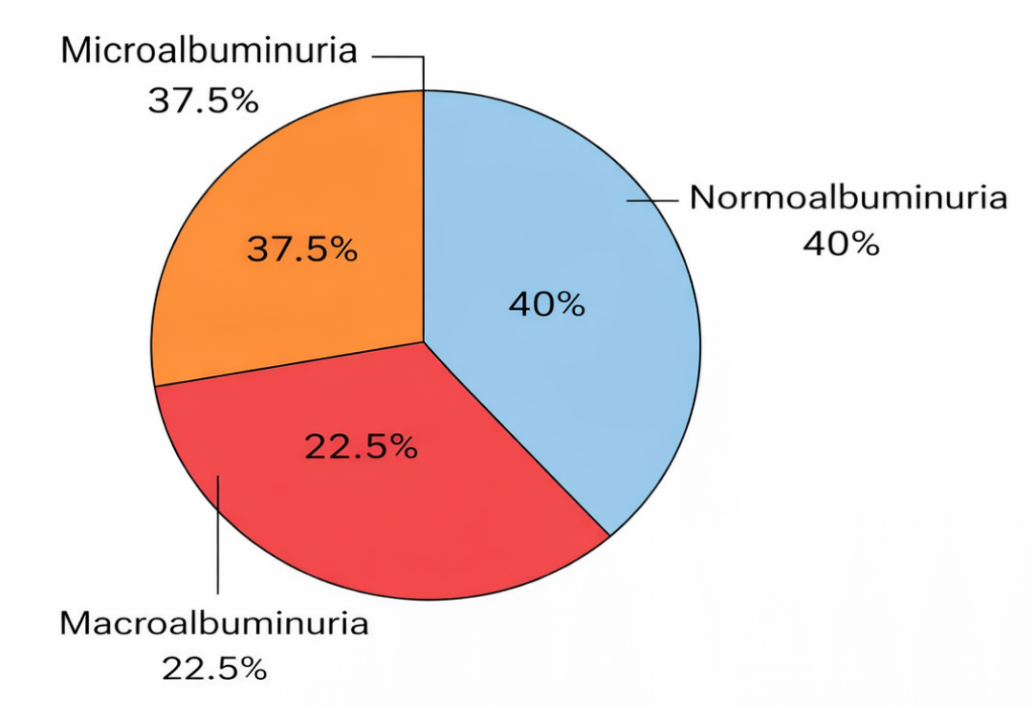

Figure 1: Distribution of Albuminuria Categories Among Study Participants

Serum Bile Acid Levels According to Albuminuria Status: Serum total bile acid levels were compared among the three albuminuria groups. The mean bile acid level was highest in the normoalbuminuria group (7.8 ± 1.9 µmol/L) and progressively decreased in the microalbuminuria and macroalbuminuria groups.

Table 3: Serum Total Bile Acid Levels in Different Albuminuria Groups

Albuminuria Category	Mean Bile Acid (µmol/L)	SD
Normoalbuminuria	7.8	1.9
Microalbuminuria	6.1	1.6
Macroalbuminuria	4.9	1.4

One-way ANOVA analysis showed a statistically significant difference among the groups.

- F value = 9.87
- p value = 0.0002

This indicates that patients with higher albuminuria had significantly lower serum bile acid levels, as presented in Table 3.

Correlation Between Serum Bile Acid and Albuminuria: Pearson correlation analysis was performed to determine the relationship between serum total bile acid levels and urinary albumin excretion.

The analysis demonstrated a moderate negative correlation.

- Correlation coefficient (r) = −0.42
- p value = 0.002

This indicates that as albuminuria increased, serum bile acid levels significantly decreased.

The correlation pattern is demonstrated in Figure 2. As shown in Figure 2, the scatter plot demonstrates a downward trend, confirming the inverse relationship between serum bile acid concentration and urinary albumin excretion.

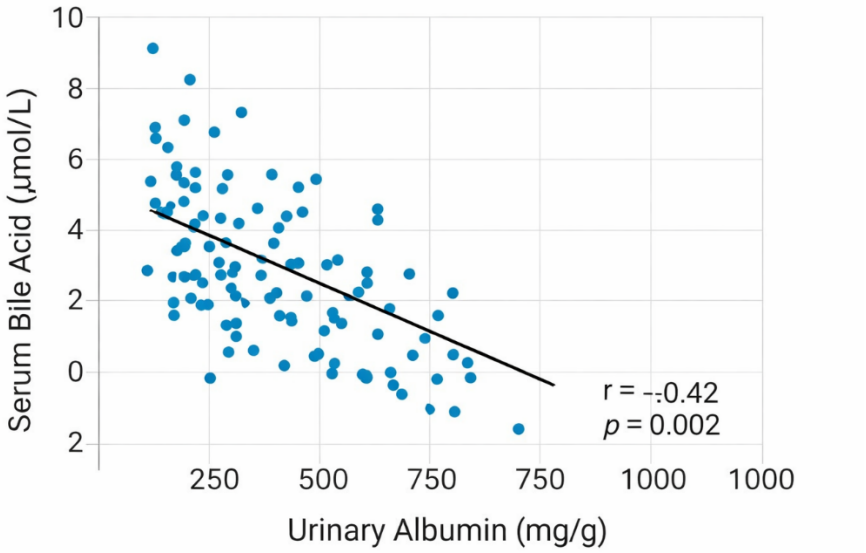

Figure 2: Scatter Plot Showing Negative Correlation Between Serum Bile Acid Levels and Albuminuria

Summary of Key Statistical Findings

- Significant difference in bile acid levels among albuminuria groups (ANOVA p = 0.0002).
- Moderate negative correlation between bile acid and albuminuria (r = −0.42).
- Higher albuminuria levels were associated with significantly lower serum bile acid concentrations.

These findings indicate a statistically significant inverse relationship between serum total bile acid levels and albuminuria in patients with type-2 diabetes mellitus.

Discussion

Diabetic nephropathy is a major complication of type-2 diabetes mellitus and remains one of the leading causes of chronic kidney disease globally (14). Early detection of renal damage is essential to prevent disease progression and improve clinical outcomes. Albuminuria serves as a well-established marker of early renal injury in diabetic patients [15].

The present study evaluated the relationship between serum total bile acid levels and albuminuria in patients with T2DM. Our findings demonstrated a significant inverse association between serum bile acid levels and urinary albumin excretion.

Patients with macroalbuminuria exhibited significantly lower serum bile acid levels compared with those having normoalbuminuria. The observed negative correlation suggests that decreased bile acid concentrations may be associated with worsening renal involvement in diabetes.

These findings are consistent with previous studies indicating that bile acids play important regulatory roles in glucose metabolism and inflammatory pathways [16]. Through activation of FXR and TGR5 receptors, bile acids influence insulin sensitivity, lipid metabolism, and energy homeostasis [17].

Experimental studies have shown that FXR activation can reduce renal inflammation, oxidative stress, and fibrosis, which are key mechanisms involved in diabetic kidney disease [18]. In addition, bile acid signaling has been reported to modulate inflammatory cytokine production and improve endothelial function [19].

Animal studies have further demonstrated that FXR agonists can decrease proteinuria and prevent progression of diabetic nephropathy [20]. These findings support the concept that bile acids may have protective effects against kidney damage in diabetic conditions.

Clinical evidence also indicates that alterations in bile acid metabolism are associated with metabolic disorders such as obesity, insulin resistance, and type-2 diabetes [21]. Reduced circulating bile acid levels may reflect impaired metabolic signaling pathways contributing to the progression of diabetic complications.

Another possible explanation for the observed association is the role of bile acids in regulating gut microbiota and metabolic inflammation [22]. Dysregulation of the gut-liver-kidney axis has been

implicated in the pathogenesis of diabetic kidney disease.

Furthermore, bile acids have been shown to improve glucose metabolism and insulin sensitivity, which may indirectly influence renal outcomes in diabetic patients [23].

The results of the present study highlight the potential role of bile acids as biomarkers for early detection of diabetic nephropathy. Monitoring serum bile acid levels may help identify patients at higher risk for renal complications.

Future longitudinal studies with larger populations are required to confirm these findings and explore the therapeutic potential of bile acid signaling pathways in diabetic kidney disease [24,25].

Limitations

This study has several limitations that should be considered when interpreting the findings. The cross-sectional design does not allow the establishment of a causal relationship between serum bile acid levels and albuminuria. The relatively small sample size may also limit the generalizability of the results to broader populations. In addition, the study was conducted at a single tertiary care center, which may introduce potential selection bias. Future multicenter studies with larger sample sizes and longitudinal follow-up are necessary to better understand the clinical significance of bile acid metabolism in diabetic nephropathy.

Conclusion

The present study demonstrated a significant negative correlation between serum total bile acid levels and albuminuria in patients with type-2 diabetes mellitus.

Lower serum bile acid levels were associated with higher levels of urinary albumin excretion, suggesting a possible link between bile acid metabolism and diabetic kidney disease.

These findings indicate that serum bile acids may serve as potential biomarkers for early detection and monitoring of diabetic nephropathy.

Further large-scale prospective studies are needed to better understand the underlying mechanisms and clinical implications.

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