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Original Research Article

Acute Phase Reactants (Serum CRP, Serum Ferritin) in Patients with Type II Diabetes Mellitus and Its Correlation with Albuminuria

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Abstract

Background: Chronic inflammation is an important mechanism facilitating the onset of Type II Diabetes Mellitus (T2DM) and its complications. Serum C-reactive protein (CRP) and ferritin are acute-phase reactants that may reflect systemic inflammation. Albuminuria is a commonly accepted early marker of diabetic nephropathy. Understanding the relation of inflammatory markers with albuminuria may aid in identifying patients at greatest risk.

Aim: To assess serum CRP and ferritin levels in T2DM patients and analyze their correlation with albuminuria.

Methods: This hospital-based cross-sectional study comprised 125 patients with T2DM aged over 35 years from a tertiary care hospital in India. Serum CRP and ferritin levels and spot urine albumin-to-creatinine ratio (ACR) were measured. Based on albumin-to-creatinine ratio levels, "patients were divided into three groups: normoalbuminuria (<30 mg/g), microalbuminuria (30-300 mg/g), and macroalbuminuria (>300 mg/g)". Pearson's correlation and ANOVA were used to evaluate the correlations among CRP, ferritin, and ACR.

Results: Among the 125 patients, 45.6% had microalbuminuria, and 30.4% had macroalbuminuria. Mean serum CRP and ferritin were 27.09 ± 51.39 mg/L and 276.21 ± 179.81 ng/mL, respectively. "Serum ferritin showed a statistically significant positive correlation with urine ACR ($r = 0.250$, $p = 0.005$), whereas CRP did not show a significant association with ACR ($r = -0.079$, $p = 0.383$). HbA1c also correlated positively with albuminuria ($r = 0.271$, $p = 0.002$)".

Conclusion: Serum ferritin and HbA1c levels share a parallel relationship, with albuminuria occurring in type II diabetes mellitus (T2DM). This may suggest that bad glycemic control, subclinical inflammation, and early kidney damage all intertwine in their run. It has been shown that ferritin may be a better biomarker than CRP when it comes to assessing the risk of diabetic nephropathy.

Keywords: Type 2 Diabetes Mellitus, CRP, Ferritin, Albuminuria, Inflammation, and Diabetic Nephropathy.

Introduction

Type II Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, progressive β-cell dysfunction, and sustained hyperglycemia. It has blown into a global epidemic, with the number of affected individuals increasing sharply in developing countries.

According to the World Health Organization (WHO), more than 422 million people had diabetes worldwide in 2016, a number that could increase further in the coming decades, while countries such as India were estimated to have around 69.2 million cases in 2015, which is expected to climb to 87 million by 2030 [1,2]. T2DM is associated with microvascular and macrovascular complications, including retinopathy, neuropathy, cardiovascular disease, and mainly diabetic nephropathy-a chief cause of ESRD worldwide [3,4]. Albuminuria is one of the earliest clinical markers of diabetic nephropathy-notably increased permeability of the glomerulus and closely tied to cardiovascular morbidity and mortality [5].

The emerging idea is that inflammatory mechanisms underpin the initiation and progression of diabetic complications, especially nephropathy [6]. Some of the inflammatory mechanisms involve AGEs, oxidative stress, the polyol pathway, and protein kinase C (PKC) activation leading to endothelial dysfunction and thus glomerular damage [7,8]. C-reactive protein (CRP), a hepatic acute-phase protein induced by interleukin-6, is a

sensitive biomarker of systemic inflammation. Elevated CRP levels are associated with insulin resistance, endothelial dysfunction, and increased risk of cardiovascular and renal complications in T2DM [9,10]. Ferritin, another acute phase reactant and intracellular iron-storage protein, also rises in inflammatory conditions. Elevated serum ferritin has been linked to oxidative stress, insulin resistance, and metabolic syndrome in diabetic populations [11,12].

Both CRP and ferritin have been investigated as potential markers of diabetic nephropathy. Their association with urine albumin-to-creatinine ratio (ACR), a surrogate marker of renal dysfunction, could help in early identification and risk stratification of patients prone to diabetic kidney disease [13,14].

Given the paucity of studies correlating these inflammatory markers specifically with albuminuria in Indian T2DM populations, this study aims to explore the relationship between serum CRP, serum ferritin, and albuminuria, and evaluate their potential utility as predictive biomarkers for diabetic nephropathy.

Material & Methods

"This hospital-based cross-sectional study was conducted in the Department of General Medicine at Santosh Medical College & Hospital, Ghaziabad, Uttar Pradesh, India".

A total of 125 patients diagnosed with T2DM, aged above 35 years, were recruited for the study. The age cutoff was selected to minimize the overlap with Type I diabetes and other atypical forms. Patients were enrolled from both outpatient and inpatient departments over the study period. Ethical clearance was obtained "from the Institutional Ethics Committee prior to study initiation, and written informed consent was obtained from each participant after explaining the objectives and procedures of the study".

Patients with known malignancies, active infections, chronic kidney disease (CKD), cardiovascular disease, cerebrovascular accidents, or immunological disorders were excluded from the study. Additionally, individuals who were pregnant, smokers, "or had uncontrolled hypertension (systolic blood pressure >160 mmHg or diastolic blood pressure >90 mmHg)" were also excluded to reduce confounding factors.

Detailed clinical histories were recorded, "including age, gender, and duration of diabetes. Anthropometric measurements such as height, weight, and body mass index (BMI) were documented". Blood pressure was measured in a resting state using a standard sphygmomanometer and mean arterial pressure (MAP) was calculated.

Venous blood was collected; the patients had fasted since the last night, and the samples were analyzed for other biochemical parameters. FBS was estimated glucose oxidase-peroxidase method, while HbA1c estimation was done through turbidimetric immunoassay. Serum creatinine was measured by Jaffe's kinetic method. Serum CRP was determined by turbidimetric immunoassay, serum ferritin by electrochemiluminescence immunoassay (ECLIA). A spot urine sample was collected and later used for measuring albumin-to-creatinine ratio (ACR) by immunoturbidimetric method.

Based on the urine ACR values, patients were stratified in three groups: "normoalbuminuria, <30 mg/g; microalbuminuria, 30–300 mg/g; and macroalbuminuria, >300 mg/g. Routine laboratory investigations were performed, including complete blood counts", liver function tests, ECG, chest radiographs, and abdominal ultrasonography, to rule out other systemic illnesses.

Statistical Analysis: "Data entry and statistical analysis were done using the SPSS 21.0 for Windows. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as percentages. Comparisons between groups were performed using independent t-tests and one-way ANOVA for continuous variables", whereas chi-square was used for categorial data. The relationship between serum CRP, serum ferritin, and urine ACR was analysed by Pearson correlation coefficient. A p-value of less than 0.05 was accepted as significant level for all analyses.

Observation and Results

In the study, "a total of 125 patients with Type II Diabetes Mellitus were included. The average age of the participants was 52.80 ± 11.52 years". Most of the individuals were in the age range of 41-60 years (56%). There was a female preponderance among the study population as 77 (61.6%) females participated as against 48 (38.4%) males.

The mean serum CRP and serum ferritin levels in the entire cohort were 27.09 ± 51.39 mg/L and 276.21 ± 179.81 ng/mL, respectively. The mean urine albumin-to-creatinine ratio (ACR) was 416.29 ± 631.91 mg/g, with 45.6% of patients having microalbuminuria and 30.4% having macroalbuminuria. Only 24.0% had normoalbuminuria, indicating significant renal involvement in the diabetic population studied (figure 1).

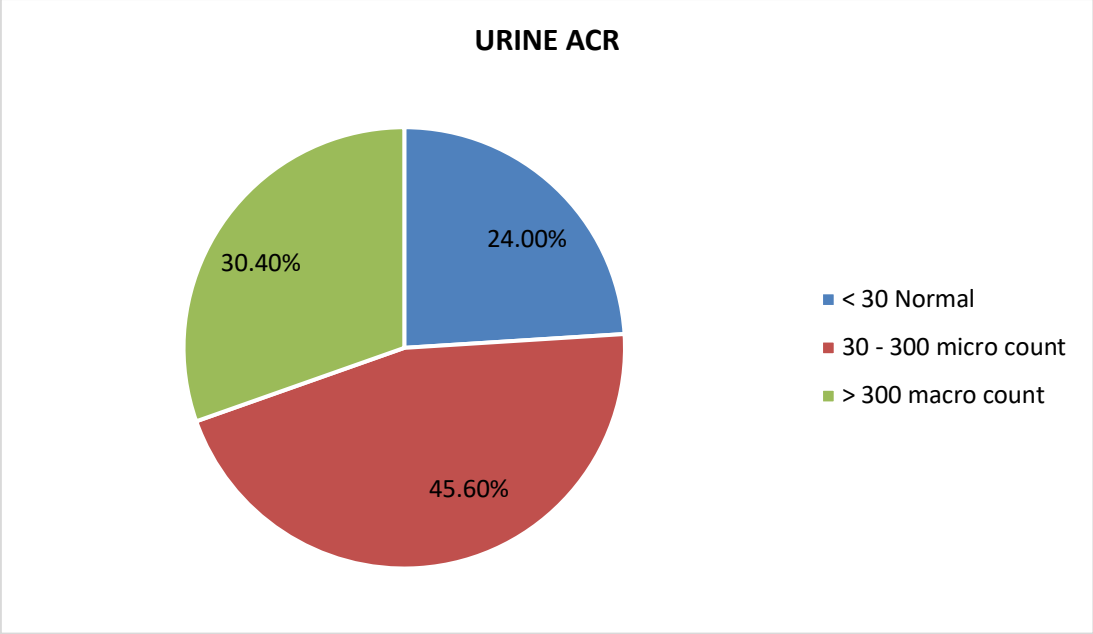

Figure 1: Distribution of patients based on urine albumin-to-creatinine ratio (ACR) categories

There was no significant difference in age, gender, or duration of diabetes across ACR groups. However, glycemic control—as measured by HbA1c—was significantly worse in patients with higher levels of albuminuria (p = 0.001). This supports the role of long-term hyperglycemia in the progression of diabetic nephropathy. When comparing inflammatory and renal parameters, serum ferritin levels were significantly higher in patients with macroalbuminuria compared to those with normoalbuminuria (p = 0.033). CRP levels, although elevated in more than half of the cohort, did not differ significantly across ACR categories (p = 0.852). Similarly, serum creatinine and estimated glomerular filtration rate (eGFR) did not show statistically significant differences (table 2).

Table 1: Comparison of clinical and biochemical parameters across albuminuria

Parameter	Normoalbuminuria (<30 mg/g)	Microalbuminuria (30-300 mg/g)	Macroalbuminuria (>300 mg/g)	p-value
Duration of Diabetes (years)	3.60 = 2.50	3.86 = 3.27	3.32 = 2.90	0.685
BMI (kg/m2)	27.01 = 5.73	25.87 ± 4.54 #	24.70 # = 3.91	0.133
FBS (mg/dL)	143.03 + 44.78	135.44 + 29.94	140.63 = 34.76	0.595
HbAlc (%)	6.97 + # 1.14	7.52 + 1.24	8.19 + 1.46	0.001
CRP (mg/L)	22.74 = 60.60	29.34 = 53.12	27.15 = 40.97	0.852
Serum Ferritin (ng/mL)	221.53 + 166.69	266.96 + 160.53	333.27 + 204.14	0.033
Serum Creatinine (mg/dL)	1.05 = 0.49	1.22 + 0.68	1.23 ± 0.59	0.397
eGFR (mL/min/1.73 m2)	79.63 ± 31.31	70.44 ± 28.44	71.45 = 32.62	0.385

"Pearson's correlation analysis revealed a significant positive correlation between serum ferritin and urine ACR (r = 0.250, p = 0.005), while CRP did not correlate significantly (r = –0.079, p = 0.383). HbA1c levels showed a significant positive correlation with ACR (r = 0.271, p = 0.002)", indicating poor glycemic control was associated with worsening albuminuria (table 3).

Table 2: Correlation of key variables with urine ACR

Variable	Pearson Correlation (r)	p-value
Serum Ferritin	**0.250**	**0.005**
Serum CRP	–0.079	0.383
HbA1c	**0.271**	**0.002**
Serum Creatinine	0.081	0.368
GFR	–0.060	0.504
Duration of Diabetes	–0.019	0.833

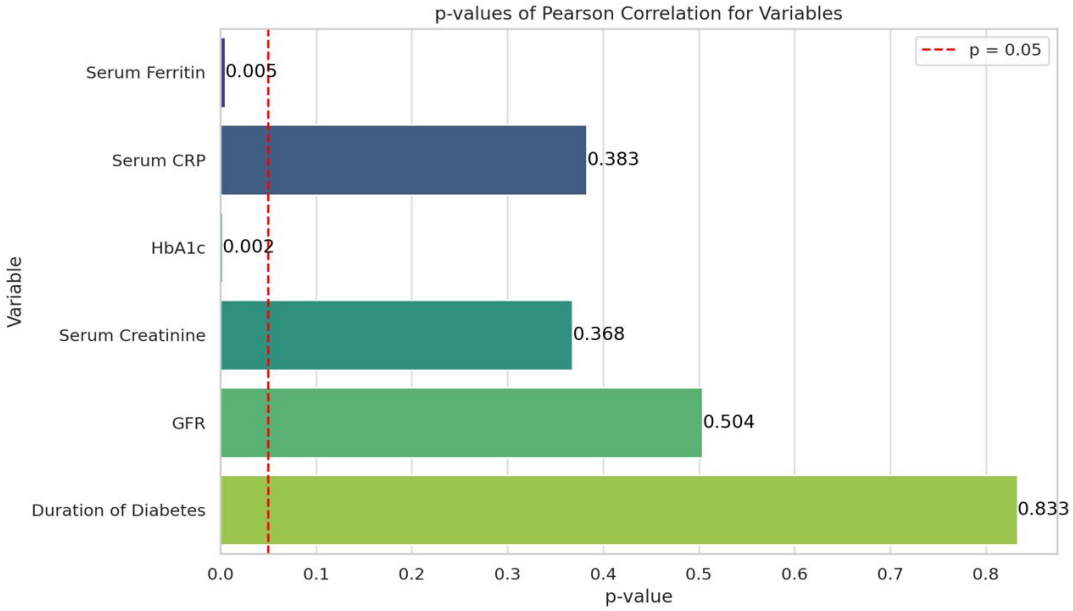

Figure 2:

Here is a bar graph displaying the p-values for each variable's correlation, with a red dashed line indicating the significance threshold ($p = 0.05$):

- Variables to the left of the red line are statistically significant.
- In this case, Serum Ferritin and HbA1c show significant correlations with $p < 0.05$

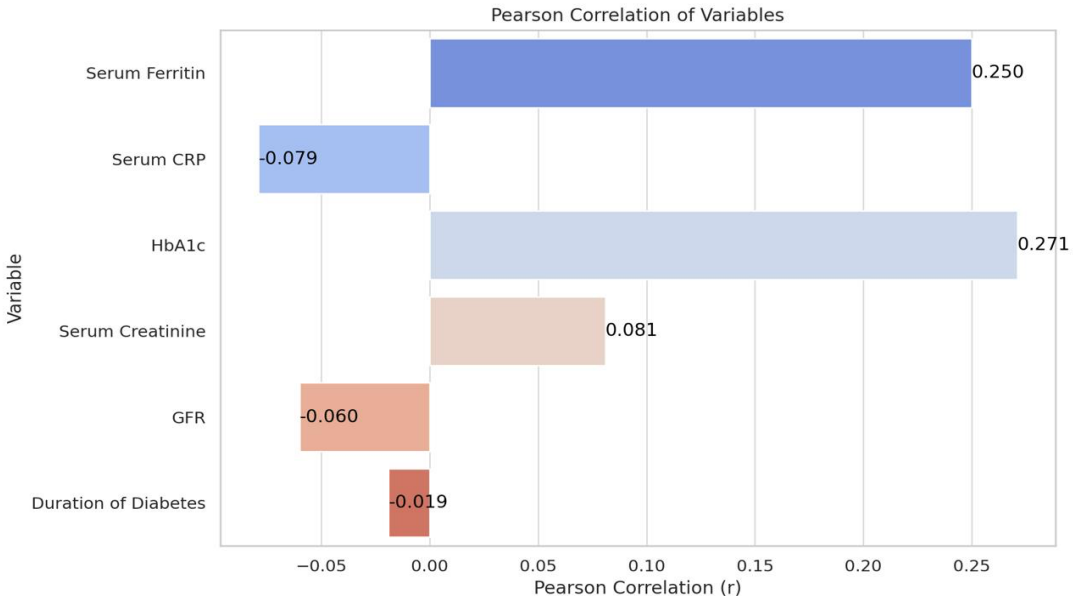

Figure 3:

Here is a bar graph visualizing the Pearson correlation coefficients (r) for each variable. Positive and negative correlations are color-coded to help distinguish direction and strength.

These findings suggests that elevated serum ferritin levels are significantly associated with albuminuria and may serve as an early indicator of diabetic nephropathy. CRP, although elevated in more than half of the patients, did not show a statistically significant association with ACR in this cohort. Glycemic control, as reflected by HbA1c, was also strongly correlated with worsening albuminuria.

Discussion

This study converses the association of acute phase reactants-serum CRP and serum ferritin-with albuminuria in Type II Diabetes Mellitus (T2DM) cases.

The finding of this study goes to emphasize the complicated interplay between chronic

inflammation, glycemic control, and early renal dysfunction in diabetes. The study population had a mean age of 52.80 ± 11.52 years, in agreement with Sanjib Dey et al. and Tyagi et al., who stated similar age distributions in diabetic patients [13,18]. Most participants in the current study were women (61.6%); however, gender did not alter the albuminuria distribution significantly, which concurred with Chowta et al. and Mahajan et al. [14,17].

Almost half of the subjects (45.6%) showed early microalbuminuria while 30.4% had more advanced macroalbuminuria, representing early and advanced stages of diabetic nephropathy. These findings strengthen those of Tyagi et al. and Tejeswini et al., who also encountered high levels of albuminuria in ambulatory T2DM populations [18,21].

With the increase in albuminuria, HbA1c also increased and this increase was statistically very significant ($p = 0.001$), implying that poor glycemic control tends to have its effect on the kidneys. This stands in agreement with Umaamaheshwari et al. and Rangappa et al., who found that higher HbA1c is a predictor for microvascular complications, including nephropathy [19,20].

Serum ferritin, an acute phase reactant and iron-storage protein, showed a statistically "significant positive correlation with albuminuria ($r = 0.250$, $p = 0.005$). This suggests its role as a marker of chronic low-grade inflammation and possibly early kidney injury". Similar associations were reported by Mohamed et al., Hsu et al., and Tejeswini et al., who found higher ferritin levels in patients with micro- and macroalbuminuria [12,21,22]. These results highlight the potential of ferritin as a biomarker not only for inflammation but also for predicting diabetic nephropathy.

Interestingly, serum CRP did not show a significant correlation with urine ACR in our cohort ($r = –0.079$, $p = 0.383$). While elevated CRP levels were observed in over half of the participants (56.8%), the lack of a significant association with albuminuria suggests that CRP may reflect generalized systemic inflammation rather than being specific to renal injury. This contrasts with some studies such as Mohajedi et al. and Tyagi et al., who found significant associations between CRP and albuminuria [15,18]. These discrepancies may be due to population differences, CRP assay sensitivities, or varying levels of background inflammation.

Furthermore, renal function markers such as serum creatinine and eGFR did not significantly differ across albuminuria categories. This supports the notion that albuminuria may be an earlier marker of diabetic kidney disease, preceding measurable declines in filtration function. Thus, reliance solely on serum creatinine or eGFR may delay diagnosis of early nephropathy.

Inflammatory changes in diabetic nephropathy are well-recognized. Cytokines like IL-6 and TNF-α induce hepatic synthesis of CRP, while ferritin levels rise due to increased oxidative stress and iron dysregulation. The significant association between serum ferritin and ACR suggests that subclinical inflammation and oxidative mechanisms play a pivotal role in renal microvascular injury [6,10].

Our findings further reinforce the use of HbA1c and serum ferritin as important indicators in risk stratification for diabetic nephropathy. While CRP remains a valuable inflammatory marker, it may have less specificity in early kidney damage detection among diabetic patients.

Conclusion & Recommendations

This study highlights a significant association between elevated serum ferritin and albuminuria in patients with Type II Diabetes Mellitus, suggesting that ferritin may serve as an early inflammatory biomarker of diabetic nephropathy. Although CRP levels were raised in a majority of patients, they did not significantly correlate with urinary albumin excretion, indicating that CRP may not be a reliable standalone marker for renal involvement in diabetes.

Routine screening of diabetic patients using ACR, serum ferritin, and HbA1c may facilitate early identification of individuals at risk for diabetic kidney disease and allow for timely interventions. Further longitudinal studies are warranted to validate ferritin's predictive value and explore its utility in guiding therapeutic strategies.

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