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RESEARCH ARTICLE

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Association of Selenoprotein P Levels with Proteinuria Severity in Newly Diagnosed Type 2 Diabetes Mellitus

Selenoprotein P Düzeylerinin Yeni Tanı Konmuş Tip 2 Diabetes Mellitus Hastalarında Proteinüri Şiddeti ile İlişkisi

Cahit Ucar[1], Mustafa Turgut Yildizgoren[2], Mevlut Hakan Goktepe[3], Adem Ay[4], Gurkan Yarbas[1], Bilal Ilanbey[4]

[1]Necmettin Erbakan University, Faculty of Medicine, Department of Internal Medicine, Konya, Türkiye
[2]Necmettin Erbakan University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Konya, Turkey
[3]Necmettin Erbakan University, Faculty of Medicine, Department of Family Medicine, Konya, Türkiye
[4]Kırşehir Ahi Evran University, Faculty of Medicine, Department of Medical Biochemistry, Kırşehir, Türkiye

ABSTRACT

Objective: Diabetic nephropathy is one of the leading causes of chronic kidney disease and progression to end-stage renal failure. Identifying new biomarkers that correlate with nephropathy severity may improve risk stratification and clinical decision-making processes. The aim of this study was to evaluate the relationship between serum selenoprotein levels, renal function parameters, and proteinuria severity in newly diagnosed diabetes mellitus patients.

Materials and Methods: Ninety patients with diabetes mellitus were divided into three groups according to their proteinuria status: those without proteinuria (n=30), those with microalbuminuria (30–300 mg/g, n=30), and those with macroalbuminuria (>300 mg/g, n=30). Demographic characteristics, glycemic indicators, renal function tests, and serum selenoprotein P concentrations were evaluated.

Results: Selenoprotein P levels showed a gradual increase across groups (1,61 [1,23–2,10], 3,28 [2,79–4,07], and 7,13 [5,51–8,34], respectively; p < 0,001). Proteinuria severity showed a strong positive correlation with selenoprotein P (r=0.794, p<0.001), creatinine (r=0.532, p<0.001), and HbA1c (r=0.406, p<0.001), and negatively correlated with GFR (r=−0.681, p<0.001).

Conclusion: Increased selenoprotein P concentrations are closely associated with worsening proteinuria and renal dysfunction and support its potential as an early biomarker of diabetic nephropathy.

Keywords: Diabetic nephropathy, Selenoprotein P, Proteinuria severity

ÖZET

Amaç: Diyabetik nefropati, kronik böbrek hastalığının ve son dönem böbrek yetmezliğine gidişin önde gelen nedenlerinden biridir. Nefropati şiddeti ile paralellik gösteren yeni biyobelirteçlerin tanımlanması, risk sınıflandırması ve klinik karar verme süreçlerini geliştirebilir. Bu çalışmanın amacı yeni tanı almış diyabetes mellitus hastalarında serum selenoprotein P düzeylerinin, böbrek fonksiyon parametreleri ve proteinüri şiddeti ile ilişkisini değerlendirmektir.

Gereç ve Yöntemler: Doksan diyabetes mellitus hastası proteinüri durumlarına göre üç gruba ayrıldı: proteinürisi olmayanlar (n=30), mikroalbüminürisi olanlar (30–300 mg/g, n=30) ve makroalbüminürisi olanlar (>300 mg/g, n=30). Demografik özellikler, glisemik göstergeler, böbrek fonksiyon testleri ve serum selenoprotein P konsantrasyonları değerlendirildi.

Bulgular: Selenoprotein P düzeyleri gruplar arasında kademeli olarak artış gösterdi (sırasıyla 1,61 [1,23-2,10], 3,28 [2,79-4,07] and, 7,13 [5,51-8,34], p <0,001). Proteinüri şiddeti; selenoprotein P (r=0,794, p<0,001), kreatinin (r=0,532, p<0,001) ve HbA1c (r=0,406, p<0,001) ile güçlü pozitif korelasyon, GFR (r=−0,681, p<0,001) ile ise negatif korelasyon sergiledi.

Sonuç: Artmış selenoprotein P konsantrasyonları, kötüleşen proteinüri ve böbrek fonksiyon bozukluğu ile yakından ilişkilidir ve diyabetik nefropatinin erken biyobelirteci olma potansiyelini desteklemektedir.

Anahtar Kelimeler: Diyabetik nefropati, Selenoprotein P, Proteinüri şiddeti

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Corresponding Author: Cahit Ucar, Necmettin Erbakan University, Faculty of Medicine, Department of Internal Medicine, Konya, Türkiye
e-mail: cahitdr@hotmail.com

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INTRODUCTION

Diabetes mellitus (DM) is a major global health problem with increasing prevalence in both developed and developing countries (1). Characterized by chronic hyperglycemia, DM is closely associated with the development of vascular complications. These complications include microvascular manifestations (retinopathy, neuropathy, and nephropathy) and macrovascular disorders, which significantly increase cardiovascular morbidity and mortality. Among these, diabetic nephropathy (DN) stands out as the primary cause of chronic kidney disease (CKD) and the most important predictor of end-stage renal disease (ESRD) worldwide, placing a serious burden on both patients and healthcare systems (2).

Early detection and effective monitoring of DN are critical for improving renal and cardiovascular outcomes. Proteinuria, especially albuminuria, is among the classic early markers of diabetic kidney damage. Microalbuminuria indicates the onset of nephropathy, while macroalbuminuria is a strong indicator of advanced kidney damage and adverse cardiovascular events. However, the predictive power of albuminuria is limited and does not fully reflect the underlying pathophysiological mechanisms of DN. Therefore, research continues into new and more sensitive biomarkers that can more accurately reflect disease activity and progression (3–5).

Selenoproteins are a unique family of proteins containing selenocysteine in their structure and perform essential functions in antioxidant defense, immune response regulation, and cellular redox balance (6, 7). Enzymes such as glutathione peroxidases and thioredoxin reductases play a critical role in protecting kidney tissue against oxidative stress, one of the main mechanisms of diabetic renal damage (8). Impaired selenoprotein expression may increase oxidative damage, endothelial dysfunction and progressive nephron loss (9). Selenoprotein P, in particular, has been associated with renal function loss and diabetic complications in recent years (10, 11). However, data on the direct relationship between circulating selenoprotein levels and proteinuria severity in DN are limited, and further studies in this area are needed.

The aim of this study was to investigate whether selenoprotein levels are associated with proteinuria severity in newly diagnosed with type 2 diabetes mellitus (DM). As a secondary objective, the relationship between selenoprotein levels and glycemic control (HbA1c) and renal function indicators (GFR, creatinine, urea) was planned to be evaluated. Thus, their potential as candidate biomarkers in diabetic nephropathy was attempted to be elucidated.

MATERIALS AND METHODS

Study Population

This cross-sectional study included 90 patients with newly diagnosed type 2 diabetes who were diagnosed between September 2024 and December 2025. Individuals with acute infections, chronic inflammatory diseases, advanced chronic kidney disease (stages 4–5), or other systemic diseases that could affect kidney function were excluded from the study.

Patients were divided into three groups based on their proteinuria status:

Group 1: Those without proteinuria (n=30)

Group 2: Microalbuminuria (30–300 mg/g, n=30)

Group 3: Macroalbuminuria (>300 mg/g, n=30)

Demographic and clinical data were recorded (age, gender, body mass index [BMI]), and biochemical parameters were evaluated (fasting glucose, HbA1c, urea, creatinine, estimated glomerular filtration rate [GFR], and selenoprotein levels). Selenoprotein measurement was performed by ELISA according to the manufacturer's instructions.

Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Necmettin Erbakan University Faculty of Medicine (Approval No: 2025/6052, Date: October 10, 2025).

Statistical Analysis

Statistical analyses were performed using SPSS 22.0 software (IBM Corp., Armonk, NY, USA). Continuous data were presented as mean ± standard deviation. Normal distribution was assessed using the Shapiro–Wilk test. The Kruskal–Wallis test was used for group differences; the Bonferroni-corrected Mann–Whitney U test was applied for pairwise comparisons. Categorical data were evaluated using the chi-square test. The relationships between proteinuria severity and biochemical parameters were examined using Spearman correlation analysis. $p<0.05$ was considered statistically significant.

RESULTS

Ninety newly diagnosed type 2 DM patients were included in the study. Thirty (33.3%) had no proteinuria, 30 (33.3%) had microalbuminuria, and 30 (33.3%) had macroalbuminuria. The mean age was similar across groups (p=0.804). No significant differences were found between groups in terms of gender distribution (male/female, p=0.670) and BMI (p=0.981). Group comparisons of clinical and laboratory data are summarized in Table 1. Serum creatinine levels were significantly higher in the macroalbuminuria group compared to both the microalbuminuria and proteinuria-free groups (p<0.001). HbA1c values were significantly higher in the macroalbuminuria group (9.74±2.61%) compared to microalbuminuria (7.80±0.86%) and non-proteinuric (7.64±0.87%) patients (p<0.001). Estimated GFR gradually decreased as proteinuria severity increased (101.47±12.99, 90.96±15.03, and 70.93±10.87 mL/min/1.73 m^2; p<0.001).

Selenoprotein levels showed a gradual and statistically significant increase across the three groups (1.88±1.17, 3.44±1.08, and 6.56±2.12; p<0.001). The highest levels were detected in the macroalbuminuria group (Figure 1).

Table 2 summarizes the correlation analyses. A strong positive correlation was found between proteinuria severity and selenoprotein (r=0.794, p<0.001), creatinine (r=0.532, p<0.001), and HbA1c (r=0.406, p<0.001). In contrast, a strong negative correlation was found with GFR (r=-0.681, p<0.001). No significant relationship was found between proteinuria severity and age, BMI, fasting glucose, or urea levels (p>0.05 for all comparisons). Additionally, the inverse correlation between

Table 1. Comparison of Clinical and Laboratory Parameters Between Groups

Parameters	No proteinuria (n=30)	Microalbuminuria (n=30)	Macroalbuminuria (n=30)	p-value
Age (years)	58.0 (54.5–65.0)	58.5 (52.3–63.8)	58.0 (54.3–65.0)	0.804
BMI (kg/m²)	28.2 (26.2–30.4)	28.4 (26.2–30.0)	28.3 (26.4–30.2)	0.981
Urea (mg/dL)	25.1 (21.0–32.5)	24.0 (20.1–31.4)	24.0 (20.5–30.2)	0.676
Creatinine (mg/dL)	0.83 (0.70–0.93)[a]	0.83 (0.69–0.91)[a]	1.17 (1.02–1.33)[b]	<0.001
Glucose (mg/dL)	159.8 (130.9–194.7)	158.9 (132.3–188.2)	179.9 (145.8–191.1)	0.445
HbA1c (%)	7.5 (6.9–8.2)[a]	7.7 (7.1–8.5)[a]	8.6 (8.1–11.2)[b]	<0.001
GFR (mL/min/1.73m²)	100.6 (94.1–105.8)[c]	93.4 (77.4–105.5)[b]	70.1 (65.1–77.7)[a]	<0.001
Selenoprotein P	1.61 (1.23–2.10)[a]	3.28 (2.79–4.07)[b]	7.13 (5.51–8.34)[c]	<0.001

Bold p values indicate statistical significance ($p < 0.05$).
Data are presented as median (25^{th}-75^{th} percentiles/interquartile range). Overall group comparisons were performed using the Kruskal–Wallis test. Post-hoc pairwise comparisons were conducted with Bonferroni-adjusted Mann–Whitney U tests. Different superscript letters ([a], [b], [c]) indicate statistically significant differences between groups ($p < 0.05$); identical letters denote no significant difference.
For creatinine and HbA1c: b>a. For GFR: c> b>a. For selenoprotein: c> b>a.

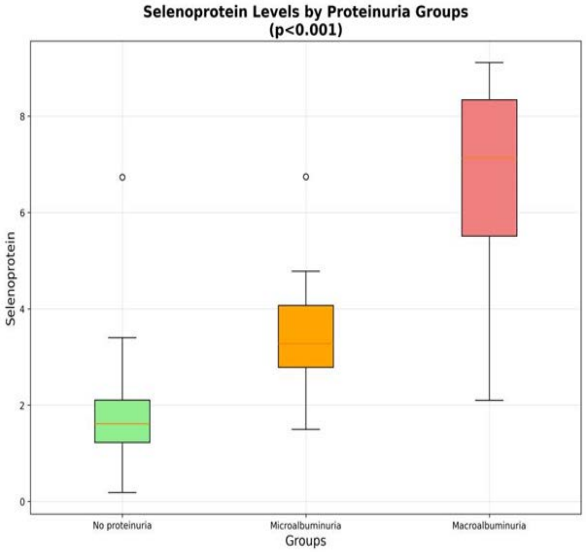

Figure 1. Serum selenoprotein concentrations across proteinuria groups in newly diagnosed type 2 diabetic patients. Box plots illustrate median values, interquartile ranges, and outliers. A progressive and significant increase in selenoprotein levels was observed from patients without proteinuria to those with microalbuminuria and macroalbuminuria (p<0.001).

Table 2. Correlation Analysis Between Proteinuria Severity and Parameters

Parameters	Correlation (r)	p-value
Age	0.019	0.861
BMI	0.020	0.849
Urea	-0.085	0.421
Creatinine	0.532	<0.001
Glucose	0.101	0.340
HbA1c	0.406	<0.001
GFR	-0.681	<0.001
Selenoprotein	0.794	<0.001

Bold p values indicate statistical significance ($p < 0.05$)

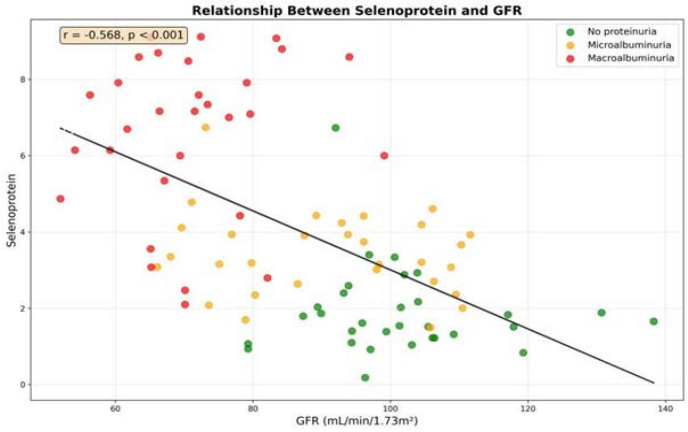

Figure 2. Scatter plot showing the relationship between serum selenoprotein P levels and estimated glomerular filtration rate (GFR). Each point represents an individual patient stratified by proteinuria status (green: no proteinuria, yellow: microalbuminuria, red: macroalbuminuria). Selenoprotein levels demonstrated a strong inverse correlation with GFR (r = –0.681, p < 0.001).

selenoprotein and GFR was demonstrated by a scatter plot; increased selenoprotein levels were consistently associated with decreased renal function (Figure 2).

DISCUSSION

The present study demonstrates that higher proteinuria levels in newly diagnosed DM are significantly associated with impaired renal function, suboptimal glycemic control, and altered selenoprotein concentrations. Patients with macroalbuminuria exhibited significantly higher creatinine and HbA1c levels and lower GFR values compared to patients with microalbuminuria and those without proteinuria. Furthermore, serum selenoprotein levels showed a progressive and significant increase with increasing severity of proteinuria.

Correlation analysis confirmed strong positive relationships between proteinuria severity and selenoprotein, creatinine, and HbA1c, while GFR showed a strong negative relationship. Among all parameters evaluated, selenoprotein showed the closest correlation with kidney impairment, highlighting its potential role in monitoring disease progression.

Diabetic nephropathy is one of the leading causes of chronic kidney disease and end-stage renal failure on a global scale. Traditional clinical markers such as albuminuria, serum creatinine, and estimated glomerular filtration rate (eGFR) remain the most commonly used tools for diagnosis and staging (12). The current findings are consistent with previous studies showing that more advanced proteinuria is associated with reduced kidney function and poor glycemic control. These results support the role of HbA1c as a critical factor in nephropathy progression and confirm the clinical utility of GFR and creatinine as traditional markers of kidney damage (13, 14).

A novel finding of this study is the strong association between selenoprotein levels and proteinuria severity. Selenoproteins play a role in redox regulation and defense against oxidative stress; these mechanisms are closely linked to both diabetes mellitus and kidney damage (10). High selenoprotein levels may reflect an adaptive response to increased oxidative load in diabetic nephropathy. On the other hand, altered selenoprotein homeostasis may contribute to kidney damage through disruption of antioxidant pathways. This dual interpretation highlights the need for mechanistic studies to clarify whether the observed elevation is protective or pathogenic (7).

Clinically, the elevation of selenoprotein levels in stages of proteinuria and their strong correlation with renal function parameters suggest that this protein may be a promising biomarker for diabetic nephropathy. Detecting its increase early could provide clinicians with an additional tool to identify patients at higher risk of progressive renal failure, thereby guiding closer monitoring and more targeted interventions (15).

Study Limitations

This study is subject to several limitations that need to be taken into account. First, the cross-sectional design does not allow for causal inference, thereby constraining the interpretation of observed associations. Second, the modest sample size limits statistical power and reduces the generalizability of the findings. Third, selenoprotein P concentrations were measured at a single time point, without serial assessments to capture longitudinal variation. Lastly, dietary selenium intake, a potential determinant of serum levels, was not assessed. Future investigations should employ prospective designs with larger and more diverse populations to validate these findings and to elucidate underlying mechanisms more comprehensively.

CONCLUSION

In conclusion, elevated serum selenoprotein P concentrations are closely linked to worsening proteinuria and renal dysfunction in diabetic patients, supporting their potential role as an early biomarker of nephropathy. Larger prospective cohorts are needed to confirm these findings.

DECLARATIONS

Conflict of Interest: *The authors declare that there is no conflict of interest related to this study.*

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Address correspondence to: *Cahit Ucar, Necmettin Erbakan University, Faculty of Medicine, Department of Internal Medicine, Konya, Türkiye*
e-mail: *cahitdr@hotmail.com*

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