ORIGINAL ARTICLE

**DOI:** 10.4274/hamidiyemedj.galenos.2023.64325

Hamidiye Med J 2023;4(2):110-116

# The Effect of the Level of Serum C-reactive Protein on Proteinuria and Lipid Values, Echocardiography Findings, and Clinical Course in Adult Patients with Nephrotic Syndrome

## Erişkin Nefrotik Sendromlu Hastalarda C-reaktif Protein Seviyesinin Proteinüri, Lipid Değerleri, Ekokardiografi Bulguları ve Klinik Gidiş Değişkenleri Üzerine Etkisi

İdris Yıldırım[1], Zeki Kemeç[2], Mehmet Emin Yılmaz[3]

[1]*University of Health Sciences Türkiye, Hamidiye Faculty of Medicine; İstanbul Sultan 2. Abdülhamid Han Training and Research Hospital, Clinic of Gastroenterology, İstanbul, Türkiye*

[2]*Batman Training and Research Hospital, Clinic of Nephrology, Batman, Türkiye*

[3]*Dicle University Faculty of Medicine, Department of Nephrology, Diyarbakır, Türkiye*

ABSTRACT

**Background:** This study investigates the effect of the level of serum C-reactive protein (CRP) on proteinuria and lipid values, echocardiography (ECHO) findings, and clinical course in adult patients with nephrotic syndrome (NS).

**Materials and Methods:** All medical records of 1440 patients hospitalized with the NS diagnosis in the Nephrology Clinic of Dicle University between 2000 and 2010 and whose treatment was started after being followed up, were scanned within the scope of this study and files of 104 patients, who were considered to have sufficient data were reviewed retrospectively. Study variables include demographic data, physical examination findings at admission, blood count parameters, biochemical parameters, proteinuria level, ECHO findings, and length of hospital stay. According to their serum CRP level, patients were divided into two groups to evaluate the relevant variables: Patients with a CRP level above 5 mg/L were defined as group I, and patients with a CRP level equal to or above 5 mg/L were accepted as group II. The normal range of CRP in the laboratory of our hospital was 0-5 mg/L.

**Results:** The following results were obtained as a result of the comparison of the groups according to their serum CRP levels: 124-hour urine (volume) (p=0.003), serum calcium (p=0.001), albumin (p=0.001), total protein (p=0.035), high-density lipoprotein (p=0.038) and hemoglobin (p=0.032) levels at hospitalization were lower significantly in group I compared to group II. 2- Length of hospital stay (p=0.030), creatinine (p=0.009), lactate dehydrogenase (p=0.006), platelet (p=0.005) and spot urinary protein (p=0.038) level in group I was significantly higher than group 2.

**Conclusion:** In adult NS patients, an increase in proteinuria, deterioration in kidney functions, a decrease in daily urine volume, a prolonged hospitalization period, and a decrease in serum albumin levels has an association with high serum CRP levels. In this study, no significant correlation was found between CRP value and cardiac parameters left atrium dilatation, ratio of current velocities E and A, left ventricular posterior wall thickness at end diastole, ejection fraction measured in echocardiography.

**Keywords:** C-reactive protein, nephrotic syndrome, proteinuria, lipid values, echocardiographic findings

ÖZ

**Amaç:** Bu çalışmada, serum C-reaktif protein (CRP) seviyesinin erişkin nefrotik sendrom (NS) tespit edilen olgularda proteinüri ve lipid değerleri, ekokardiyografi (EKO) bulguları ile klinik gidişat değişkenlerine etkilerinin araştırılması amaçlanmıştır.

**Gereç ve Yöntemler:** Çalışma kapsamında, 2000-2010 yıllarında Dicle Üniversitesi Tıp Fakültesi Nefroloji Kliniği'nde NS tanısıyla yatırılmış, tedavi süreci başlamış bütün olgulara ait dosyalar (1440 hasta) taranmış, toplam 104 hastaya ait dosyalar retrospektif bir şekilde incelenmiştir. Çalışma değişkenleri, hasta demografik verileri, kliniğe yatıştaki fizik muayene bulguları, hemogram ve biyokimyasal parametreler, proteinüri düzeyi, EKO bulguları ve hastanede yatış süresi idi. Hastalar, ilgili değişkenlerin değerlendirilmesi

**Address for Correspondence:** İdris Yıldırım, University of Health Sciences Türkiye, Hamidiye Faculty of Medicine; İstanbul Sultan 2. Abdülhamid Han Training and Research Hospital, Clinic of Gastroenterology, İstanbul, Türkiye

Phone: +90 505 710 81 22 E-mail: idrisyildirim2000@yahoo.com **ORCID ID:** orcid.org/0000-0001-7887-2886

**Received:** 18.11.2022 **Accepted:** 28.03.2023

ÖZ

amacıyla serum CRP düzeyine göre iki gruba ayrıldı: CRP seviyesi 5 mg/L üzerinde olan hastalar grup I, CRP seviyesi 5 mg/L'ye eşit ve üzerinde olan hastalar grup II olarak belirlendi. Hastanemiz laboratuvarında normal CRP aralığı 0-5 mg/L idi.

**Bulgular:** Grupların serum CRP seviyelerine göre karşılaştırılması aşağıdaki sonuçları ortaya çıkardı: 1- Grup I'de kliniğe yatışta kontrol edilen 24 saatlik idrar (hacmi) (p=0,003), serum kalsiyum (p=0,001), albümin (p=0,001), total protein (p=0,035), yüksek dansiteli lipoprotein (HDL) (p=0,038) ve hemoglobin (p=0,032) seviyeleri, grup II'ye göre anlamlı derecede düşüktü. 2- Grup 1'de, yatış süresi (p=0,030), kreatinin (p=0,009), laktat dehidrogenaz (p=0,006), trombosit (p=0,005) ve spot idrar protein (p=0,038) seviyeleri grup 2'ye kıyasla anlamlı derecede yüksekti.

**Sonuç:** Erişkin NS'li hastalarda proteinüri düzeyinde artış, böbrek işlevlerinde bozulma, günlük idrar miktarında düşme, hastane yatış süresinde uzama ve serum albümin düzeyinde düşme, yüksek serum CRP seviyesi ile ilişkilidir. Araştırmamızda CRP değeri ile EKO ile ölçümlenen kardiyak parametrelerin sol atrium dilatasyonu, E ve A akım hızları oranı, dilatasyonda sol ventrikül arka duvar kalınlığı, ejeksiyon fraksiyonu arasındaki ilişkinin anlamlı olmadığı görülmüştür.

**Anahtar Kelimeler:** C-reaktif protein, nefrotik sendrom, proteinüri, lipid değerleri, ekokardiyografi bulguları

## Introduction

Nephrotic syndrome (NS) is one of the clinical syndromes that lead to various complications, such as edema and hyperlipidemia. The definition of this syndrome includes massive proteinuria of more than 40 mg/m$^2$ per hour, which leads to hypoalbuminemia of less than 30 g/L, caused by increased permeability of the basal membrane damaged in the kidney glomeruli, primarily due to infectious or thromboembolic factors. It can occur primarily due to a kidney-specific disease, or may develop as a result of glomerular permeability abnormality due to diabetes, congenital infections, neoplasia, systemic lupus erythematosus, or a particular use of a drug. There is a trigger factor such as an upper respiratory tract infection in nearly 50% of the cases, an allergic reaction in one-third, and less frequently, an insect bite, treatment with psychiatric drugs, and vaccination. The first causes include focal glomerulosclerosis, minimal change nephropathy, hereditary nephropathies, and membranous nephropathy. Diabetes mellitus (DM) is the second cause. Immune causes include antibody vasculitis, systemic lupus erythematosus, Goodpasture's syndrome, Berger's disease, membranoproliferative or extramembranous glomerulonephritis, acute infectious glomerulonephritis, toxicity (non-steroidal anti-inflammatory drugs), alloantibodies due to enzyme replacement therapy, and thrombotic microangiopathy. Infectious causes include hepatitis B and C virus, hepatitis, HIV, immunodeficiency, toxoplasmosis, cytomegalovirus, and parvovirus B1. In addition, preeclampsia, paraproteinemia, and amyloidosis can be counted among the causes. The most common cause of NS in children is minimal changes in glomerulonephritis; in white adults, it is membranous nephropathy. However, in African populations, the main cause is focal segmental glomerulosclerosis. Clinical data shows that the NS could be frequently recurrent, steroid-sensitive, steroid-resistant, and steroid-dependent. The creation of phospholipase antibodies, the deposition of the immune complex, or the formation of alloantibodies are among the causes of NS syndrome (1,2,3,4,5,6).

C-reactive protein (CRP) is a major acute phase reactant that is seen to rise acutely and rapidly in case of infection and tissue damage in the human body which is among the non-specific laboratory findings. It triggers hepatic production in cases of various tissue damage, infection and inflammation. The American Heart Association recommends determining serum hs-CRP levels in all patients at risk for cardiovascular disease. Normal levels of CRP are mostly 2 mg/L or less. Standard methods make it possible to measure CRP in the range of 3-8 mg/L. It is possible to detect CRP levels below this limit with current "high sensitivity" (hs-CRP) methods. Today, hs-CRP measurements are used in risk determination. The diagnostic value of CRP, which is one of the non-specific indicators for inflammation, is quite high in many clinical situations. In line with today's accepted values; a CRP value below 1 mg/L is low risk, 1-3 mg/L is moderate risk, and above 3 mg/L is high risk. In many studies, CRP is used as an activity indicator and clinical course predictor for different diseases (7,8,9,10).

## Material and Methods

A total of 1440 patient files hospitalized with the NS diagnosis and followed up and treated in the Nephrology Service of Dicle University between 2000 and 2010 were retrospectively analyzed. One hundred-four patients, with sufficient data, were included in the study. Informed consent was obtained from all patients. This research, which is a thesis study, was carried out following the Local Ethics Committee of Batman University approval dated 04.02.2021 and numbered 3671 and the Declaration of Helsinki.

**Inclusion Criteria:**

- Those with NS with a histopathological diagnosis based on primary or secondary causes.
- Diabetic patients with proteinuria in the nephrotic range.
- Patients with adequate parameters for the study.

**Exclusion Criteria:**

- Patients without histopathological diagnosis.
- Patients with malignancy.
- Patients with signs of acute coronary syndrome or heart failure.
- Patients with cerebrovascular disease.
- Patients with active connective tissue disease.
- Patients with a chronic inflammatory disease with acute exacerbation.
- Patients with signs of infection.

Study parameters include; histopathological diagnoses, demographic data, amount of fluid taken in and out from clinical admission until discharge, arterial blood pressure, blood count parameters [hemoglobin, white blood cell (WBC), platelet, hematocrit], biochemical parameters [glucose, urea, uric acid, sodium (Na), calcium (Ca), creatinine (Kr), chlorine (Cl), magnesium (Mg), potassium (K), aspartate transaminase (AST), phosphorus (P), alanine transaminase, lactate dehydrogenase (LDH), high-density lipoprotein (HDL), cholesterol, triglyceride (TG), albumin, low-density lipoprotein (LDL), CRP, total protein], fibrinogen, immunoglobulin panel [immunoglobulin M (IgM), immunoglobulin A (IgA), immunoglobulin G (IgG)], complement proteins (C3, C4), erythrocyte sedimentation rate (ESR), 24-hour urine protein, urine analysis (urine leukocytes, protein, erythrocytes and urine density), echocardiogram findings [ejection fraction (EF), left atrium thickness (LAD), interventricular septum thickness (EA), left ventricular posterior wall thickness (SVPDK)] and length of hospital stay. All study parameters are shown in Table 1.

We divided the patients into two groups: CRP level >5 mg/L in group 1 and CRP level ⩽5 mg/L in group 2. Data collected from both groups were compared and analyzed. In addition, the serum CRP and other study variables of the patients at admission to hospital and discharge were compared within each group, and the relationship between them was analyzed.

**Ethical statement:** The Non-Interventional Clinical Research Ethics Committee of Batman University approved the permission for this study with a letter dated 04/02/2021 and numbered 3671, and the study was carried out following the Helsinki Declaration criteria.

### Statistical Analysis

Study data were analyzed in computer virtual environment with SPSS for Windows 20.0 software program. For comparisons between groups, chi-square and Student's t-tests were used for independent variables, and Wilcoxon signed-rank test (Wilcoxon signed-rank test) was used for dependent variables. Pearson correlation analysis was used to compare dependent variables and serum CRP levels. Data were expressed as mean ± standard deviation. Data were analyzed with a 95% confidence interval. The p-value <0.05 was considered statistically significant.

## Results

The study participation includes a total of 104 patients. Of the study participants, 53% (55) were female, and 47% (49) were male. While the mean serum CRP level in group I was 31.70±21.75 mg/L, it was 2.21±1.58 mg/L in group II.

**Table 1. Comparison of the clinical admission and discharge variables of the groups**

| | Group 1 (n=49) | | | Grup 2 (n=55) | | |
|---|---|---|---|---|---|---|
| **Variables** | **Clinical admission** | **Clinical discharge** | **p** | **Clinical admission** | **Clinical discharge** | **p** |
| CRP (mg/L) | 31.70±21.75 | 20.62±16.23 | <0.001 | 2.21±1.58 | 1.73±1.51 | 0.002 |
| SBP (mm/Hg) | 126.09±18.11 | 113.53±17.82 | <0.001 | 125.00±23.12 | 116.26±16.70 | <0.001 |
| DBP (mm/Hg) | 75.36±10.20 | 71.58±10.51 | 0.018 | 76.11±12.55 | 70.95±10.07 | 0.001 |
| Urea (mg/dL) | 84.63±60.75 | 66.12±36.68 | 0.031 | 63.44±58.60 | 53.79±43.77 | 0.122 |
| Kr (mg/dL) | 2.56±2.49 | 2.04±1.57 | 0.118 | 1.55±1.40 | 1.43±1.45 | 0.169 |
| Albumin (g/dL) | 1.86±1.05 | 1.82±0.97 | 0.445 | 2.60±1.02 | 2.55±0.89 | 0.476 |
| LDL (mg/dL) | 195.29±119.01 | 157.21±94.07 | <0.001 | 155.06±88.80 | 140.96±71.77 | 0.009 |
| Cholesterol (mg/dL) | 289.85±138.48 | 243.21±106.65 | <0.001 | 249.60±94.31 | 230.82±76.75 | 0.002 |
| TG (mg/dL) | 238.53±126.16 | 192.02±91.41 | <0.001 | 219.01±117.33 | 205.41±104.20 | 0.039 |
| 24-hour protein (mg/day) | 6031.70±3367.30 | 4778.12±3936.80 | 0.001 | 4811.61±4079.16 | 3402.55±3380.13 | <0.001 |

CRP: C-reactive protein, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, Cr: Creatinine, LDL: Low-density lipoprotein, TG: Triglyceride

The difference between the groups was statistically significant (p<0.001). The age range of the patients was determined as 18-80 years. The patients' mean age with normal serum CRP level (group 2) and high CRP level (group 1) were 35.92±16.25 years and 46.68±20.34 years, respectively. It was observed that those with higher serum CRP levels were older, and the difference was statistically significant (p=0.004). Renal histopathological reports of 104 patients who were diagnosed between 2000-2010 and whose data matched the research criteria were also obtained. Distribution of cases according to the NS subtype is shown in the table (Table 2).

**Table 2. Distribution of patients by nephrotic syndrome subtypes**

| Primary NS | | Secondary NS | |
|---|---|---|---|
| | n | | n |
| FSGS | 19 | DM | 17 |
| MN | 14 | Amiloidosis | 18 |
| MPGN | 16 | SLE | 13 |
| MDH | 3 | | |
| IgAN | 3 | | |
| RPGN | 1 | | |

n: Number of patients, FSGS: Focal segmental glomerulosclerosis, MN: membranous glomerulonephritis, MPGN: Membranoproliferative glomerulonephritis, MDH: Minimal change disease, IgAN: IgA nephropathy, RPGN: Rapidly progressive glomerulonephritis, DM: Diabetes mellitus, SLE: systemic lupus erythematosus

Daily amount of proteinuria (p=0.003), albumin (p=0.001), Ca (p=0.001), total protein (p=0.035), HGB (p=0.032) and HDL (p=0.038) serum level at hospitalization were statistically significantly lower in group 1 than in group 2 (Table 3).

Again, Length of hospital stay (p=0.030), age (p=0.004), creatinine (p=0.009), platelets (p=0.005), LDH (p=0.006), ESR (p<0.001), spot urine protein (p=0.038), C4 (p<0.001) and 24-hour proteinuria (p<0.001) levels in group I were statistically significantly higher than group II. However, although serum LDL (p=0.051) levels were high, there was no significant difference between the groups (Table 2).

Serum CRP (p<0.001), diastolic blood pressure (DBP) (p=0.018), systolic blood pressure (SBP) (p<0.001), cholesterol (p<0.001), urea (p=0.031), TG (p<0.001), LDL (p<0.001) and proteinuria (p=0.001) levels measured at hospital admission in group 1 were found to be significantly higher than the values measured at discharge (Table 3).

When the values at hospital admission were compared with values at discharge in group 2, statistically significant elevation in variables such as CRP (p=0.002), DBP (p=0.001), SBP (p<0.001), TG (p=0.039), cholesterol (p=0.002), LDL (p=0.009), daily proteinuria was found (Table 3).

In the evaluation of correlation analysis of serum CRP level with other study variables, a positive correlation was

**Table 3. Comparison of group parameters**

| Variables | Group 1 (n=49) | Group 2 (n=55) | p |
|---|---|---|---|
| **Clinical hospitalization urine amount (volume) (mL)** | 1162.19±693.52 | 1586.50±695.73 | 0.003 |
| Ca (mg/dL) | 8.13±0.65 | 8.59±0.70 | 0.001 |
| Albumin (g/dL) | 1.86±1.05 | 2.60±1.02 | 0.001 |
| Total protein (g/dL) | 5.19±1.04 | 5.68±1.19 | 0.035 |
| HDL (mg/dL) | 43.87±14.35 | 51.60±20.50 | 0.038 |
| HGB (g/dL) | 11.64±2.62 | 12.66±2.14 | 0.032 |
| CRP (mg/L) | 31.70±21.75 | 2.21±1.58 | <0.001 |
| Lenght of hospitalization (days) | 11.21±10.06 | 7.50±7.10 | 0.030 |
| Age (years) | 46.68±20.34 | 35.92±16.25 | 0.004 |
| Creatinine (mg/dL) | 2.56±2.49 | 1.55±1.40 | 0.009 |
| LDH (U/L) | 314.02±152.88 | 248.36±87.93 | 0.006 |
| Platelets ($x10^9$/L) | 347.29±143.58 | 285.42±76.30 | 0.005 |
| ESR (mm/h) | 70.51±30.29 | 38.53±27.28 | <0.001 |
| C4 (mg/dL) | 31.68±11.80 | 23.88±9.43 | <0.001 |
| Urine protein (mg/day) | 438.41±137.85 | 363.88±197.55 | 0.038 |
| LDL (mg/dL) | 195.29±119.01 | 155.06±88.80 | 0.051 |
| 24-hour protein (mg/day) | 6953.65±2791.69 | 3948.12±2550.09 | <0.001 |

n: Number of patients, CRP: C-reactive protein, Cr: Creatinine, LDH: Lactate dehydrogenase, ESR: Erythrocyte sedimentation rate, C4: complement 4, LDL: Low-density lipoprotein, Ca: Calcium, HDL: High-density lipoprotein, HGB: Hemoglobin

found between CRP elevation and creatinine (p=0.003), urea (p=0.015), LDH (p=0.015), ESR (p=0.004), WBC (p=0.004), C4 (p=0.023), urinary erythrocyte (p=0.041), urinary leukocytes (p=0.032), daily proteinuria (p=0.044) levels. However, a negative correlation was found between CRP elevation and 24-hour urine (p=0.043). The relationship between echocardiography findings (EF, LAD, SVPDK, EA) and serum CRP level in patients with NS is not statistically significant (p>0.05).

## Discussion

As an acute phase reactant, CRP increases secondary to infection and tissue damage. The values, which reach the peak levels within 1-2 days, decrease to the normal level with the restoration of the tissue structure and function (11). CRP is used to determine the response to treatment, to evaluate the course of the infection, and to detect the inflammatory response in chronic rheumatological diseases such as vasculitis and rheumatoid arthritis (12). High serum CRP level was associated with macro and microalbuminuria independent of hypertension, DM and other potential factors (p<0.001) (13). Our study found a positive correlation between spot urine protein and serum CRP levels (p=0.038). Similar to our study, it has been determined in another study that the increase in serum CRP level is associated with the incidence and prevalence of proteinuria (p=0.042) (14). In other studies, the rate of nephropathy was higher and the development time of nephropathy was shorter in diabetic patients with high hsCRP levels than those with normal hsCRP levels (15). High CRP levels in type 2 diabetic patients have been associated with an increased prevalence of albuminuria (16). Hs-CRP was found to be independently associated with diabetic nephropathy (17). The diabetic nephropathy patients' hs-CRP concentrations were significantly higher than the control group, which includes DM patients without nephropathy and healthy people. Moreover, hs-CRP concentration in the macro albuminuria group was significantly higher compared to the microalbuminuria group and the non-albuminuria group (18). Diabetic patients with complications had significantly higher hs CRP and microalbuminuria than uncomplicated diabetic patients and the control group (19). the results showed that patients with decreased hs-CRP have a lower risk of decline in kidney development and function of proteinuria (20). It has been understood in our study that the amount of 24-hour urine protein was significantly higher in the high CRP value group than the low CRP value group (<0.001). A positive correlation was found between CRP and proteinuria (p=0.044), urea (p=0.015), creatinine (p=0.003) levels in cases with nephrotic proteinuria. Low-grade inflammatory markers (hsCRP, IL-6) have been associated with diabetic nephropathy in type 1 diabetic patients (21). One study showed that both MBL and hsCRP concentrations are associated with progression of kidney disease in type 1 diabetes (22). The hs-CRP cumulative exposure has been associated with following CKD increased risk and is helpful in risk estimation (23). In a different study, CRP, serum amyloid A and IL-6, which are acute phase indicators, were associated with diabetic nephropathy and glomerular basement membrane thickness (p<0.005) (24). However, in a study of Tencer et al. (25), no statistically significant relationship was found between the increase in proteinuria and the CRP level in 166 cases with glomerulonephritis (MPGN, MN, IgAN) (p>0.005). hs-CRP, s-albumin, and WBC are inflammatory markers and studies have been conducted showing them to be associated with the progression of IgAGN (26). Previous studies show the significant role of inflammation in increasing the risk of cardiovascular diseases. Regarding hs-CRP, some studies show that this inflammatory index can predict long-term cardiovascular risk, enriches traditional risk assessment with prognostic information, and predict cardiovascular risk not reflected by traditional risk factors (27). In one study, high plasma hs-CRP and IL-6 levels were found to be associated with LVH and systolic dysfunction in patients with CKD (28). Independent of cardiovascular risk factors, high hs-CRP level was associated with microalbuminuria. Additionally, high hs-CRP levels were associated with an increased risk of developing microalbuminuria in people with CVD risk factors (29). The relationship between CRP and echocardiography indicators (LAD, EA, SVPDK, EF) was not statistically significant (p>0.05). In the study, it was observed that the systolic (p<0.001) and diastolic (p=0.018) blood pressure values measured before discharge in high CRP levels patients were significantly lower than the values measured during their hospitalization. It is thought that the fact that the patients are in the active phase of NS and the use of diuretic, anti-proteinuric and reno-protective drugs in addition to immunosuppressive drugs during the hospitalization period may also be effective. Ueland et al. (30) observed that the hs-CRP level is significantly increased in patients with familial hypercholesterolemia. It was observed that hs-CRP level remained high in these cases, despite the anti-hyperlipidemic treatment (pravastatin 20-40 mg/g) (30). On the other hand, it was observed in this study that cholesterol (p=0.081), TG (p=0.423), LDL (p=0.051) levels were higher in patients with high CRP levels compared to patients with normal CRP levels. However, this relationship was not found to be statistically significant. In our study, it was determined that the cholesterol, TG, LDL levels measured during the discharge process of the patients in group I were significantly lower than the values measured

during the hospitalization period (p<0.001). It is thought that this may be associated with the significant decrease in the level of CRP and proteinuria due to anti-hyperlipidemic and immunosuppressive treatment given during hospitalization. It was also determined that a positive correlation is between CRP level and the length of stay in the hospital rather than a statistically significant relationship (r=0.134, p=0.178).

## Conclusion

The present study found that an increase in proteinuria, deterioration in kidney functions, decrease in daily urine volume, prolonged hospitalization and decrease in serum albumin levels in adult NS patients are associated with high serum CRP level and CRP level can be used as a fine parameter for the follow-up of patients. In our study, it was determined that the relationship between the level of CRP and cardiac parameters measured by Echocardiography (LAD, EA, SVPDK, EF) was not statistically significant.

### Ethics

**Ethics Committee Approval:** The Non-Interventional Clinical Research Ethics Committee of Batman University approved the permission for this study with a letter dated 04/02/2021 and numbered 3671, and the study was carried out following the Helsinki Declaration criteria.

**Informed Consent:** Informed consent was obtained from all patients.

**Peer-review:** Internally and externally peer-reviewed.

### Authorship Contributions

Concept: İ.Y., M.E.Y., Design: İ.Y., Z.K., M.E.Y., Data Collection or Processing: İ.Y., Analysis or Interpretation: İ.Y., Literature Search: İ.Y., Z.K., Writing: İ.Y., Z.K., M.E.Y.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

## References

1. Tapia C, Bashir K. Nephrotic Syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. [Crossref]
2. Hill AJ, Stone DE, Elliott JP, Gerkin RD, Ingersoll M, Cook CR. Management of Nephrotic Syndrome in the Pregnant Patient. J Reprod Med. 2016;61:557-561. [Crossref]
3. Raina R, Krishnappa V. An update on LDL apheresis for nephrotic syndrome. Pediatr Nephrol. 2019;34:1655-1669. [Crossref]
4. Dumas De La Roque C, Prezelin-Reydit M, Vermorel A, Lepreux S, Deminière C, Combe C, et al. Idiopathic Nephrotic Syndrome: Characteristics and Identification of Prognostic Factors. J Clin Med. 2018;7:265. [Crossref]
5. Dumas De La Roque C, Combe C, Rigothier C. Actualité sur les mécanismes physiopathologiques des syndromes néphrotiques idiopathiques : lésions glomérulaires minimes et hyalinose segmentaire et focale [Up to date of pathophysiology mechanism of idiopathic nephrotic syndromes: Minimal change disease and focal and segmental glomerulosclerosis]. Nephrol Ther. 2018;14:501-506. [Crossref]
6. Kodner C. Nephrotic syndrome in adults: diagnosis and management. Am Fam Physician. 2009;80:1129-1134. [Crossref]
7. Matsuo S, Tsumori M, Yamamoto Y, Takahashi H. [Clinical and laboratory correspondence to outpatients with the extreme value of C-reactive protein]. Rinsho Byori. 1992;40:1307-1311. [Crossref]
8. Kofler S, Nickel T, Weis M. Role of cytokines in cardiovascular diseases: a focus on endothelial responses to inflammation. Clin Sci (Lond). 2005;108:205-213. [Crossref]
9. Kılıçturgay K: Enflamasyonun akut faz cevabıyla izlenmesi. immunoloji, 3rd ed. Nobel kitapevleri: İstanbul; 2003;226. [Crossref]
10. Acartürk E. C-Reaktif Protein ve Koroner Arter Hastaliği [C-reactive protein and coronary artery disease]. Anadolu Kardiyol Derg. 2004;4:203-204. [Crossref]
11. Kushner I, Ballow SP. Laboratory evaluation of inflammation (erythrocyte sedimentation rate and the acute phase reactans). İn: Kelley W, Harris E, Ruddy S, editors. Textbook of Rheumatology. 5th ed. Philadelphia: W.B. Saunders Company; 1997;699-705. [Crossref]
12. Marnell L, Mold C, Du Clos TW. C-reactive protein: ligands, receptors and role in inflammation. Clin Immunol. 2005;117:104-111. [Crossref]
13. Sabanayagam C, Lee J, Shankar A, Lim SC, Wong TY, Tai ES. C-reactive protein and microalbuminuria in a multi-ethnic Asian population. Nephrol Dial Transplant. 2010;25:1167-1172. [Crossref]
14. Iseki K, Iseki C, Kinjo K. C-reactive protein is a predictor for developing proteinuria in a screened cohort. Nephron Clin Pract. 2011;117:c51-c56. [Crossref]
15. Sinha SK, Nicholas SB, Sung JH, Correa A, Rajavashisth TB, Norris KC, et al. hs-CRP Is Associated With Incident Diabetic Nephropathy: Findings From the Jackson Heart Study. Diabetes Care. 2019;42:2083-2089. [Crossref]
16. Abrahamian H, Endler G, Exner M, Mauler H, Raith M, Endler L, et al. Association of low-grade inflammation with nephropathy in type 2 diabetic patients: role of elevated CRP-levels and 2 different gene-polymorphisms of proinflammatory cytokines. Exp Clin Endocrinol Diabetes. 2007;115:38-41. [Crossref]
17. Varma V, Varma M, Varma A, Kumar R, Bharosay A, Vyas S. Serum Total Sialic Acid and Highly Sensitive C-reactive Protein: Prognostic Markers for the Diabetic Nephropathy. J Lab Physicians. 2016;8:25-29. [Crossref]
18. Liu Q, Jiang CY, Chen BX, Zhao W, Meng D. The association between high-sensitivity C-reactive protein concentration and diabetic nephropathy: a meta-analysis. Eur Rev Med Pharmacol Sci. 2015;19:4558-4568. [Crossref]
19. El Boukhrissi F, Benbella I, Ouleghzal H, Safi S, Bamou Y, Balouch L. Evaluation of ultrasensitive CRP and microalbuminuria as cardiovascular risk markers in type 2 diabetic moroccan patients. Tunis Med. 2017;95:982-987. [Crossref]
20. Liu L, Gao B, Wang J, Yang C, Wu S, Wu Y, et al. Reduction in Serum High-Sensitivity C-Reactive Protein Favors Kidney Outcomes in Patients with Impaired Fasting Glucose or Diabetes. J Diabetes Res. 2020;2020:2720905. [Crossref]
21. Saraheimo M, Teppo AM, Forsblom C, Fagerudd J, Groop PH. Diabetic nephropathy is associated with low-grade inflammation in Type 1 diabetic patients. Diabetologia. 2003;46:1402-1407. [Crossref]
22. Hansen TK, Forsblom C, Saraheimo M, Thorn L, Wadén J, Høyem P, et al. Association between mannose-binding lectin, high-sensitivity C-reactive protein and the progression of diabetic nephropathy in type 1 diabetes. Diabetologia. 2010;53:1517-1524. [Crossref]
23. Gao J, Wang A, Li X, Li J, Zhao H, Zhang J, et al. The Cumulative Exposure to High-Sensitivity C-Reactive Protein Predicts the Risk of Chronic Kidney Diseases. Kidney Blood Press Res. 2020;45:84-94. [Crossref]

24. Dalla Vestra M, Mussap M, Gallina P, Bruseghin M, Cernigoi AM, Saller A, et al. Acute-phase markers of inflammation and glomerular structure in patients with type 2 diabetes. J Am Soc Nephrol. 2005;16:S78-S82. [Crossref]
25. Tencer J, Thysell H, Westman K, Rippe B. Elevated plasma levels of acute phase proteins in mesangioproliferative glomerulonephritis, membranous nephropathy and IgA nephropathy. Scand J Urol Nephrol. 1995;29:5-9. [Crossref]
26. Kaartinen K, Syrjänen J, Pörsti I, Hurme M, Harmoinen A, Pasternack A, et al. Inflammatory markers and the progression of IgA glomerulonephritis. Nephrol Dial Transplant. 2008;23:1285-1290. [Crossref]
27. Ridker PM. High-sensitivity C-reactive protein, inflammation, and cardiovascular risk: from concept to clinical practice to clinical benefit. Am Heart J. 2004;148:S19-S26. [Crossref]
28. Gupta J, Dominic EA, Fink JC, Ojo AO, Barrows IR, Reilly MP, et al. Association between Inflammation and Cardiac Geometry in Chronic Kidney Disease: Findings from the CRIC Study. PLoS One. 2015;10:e0124772. [Crossref]
29. Yang SK, Liu J, Yi B, Mao J, Zhang XM, Liu Y, et al. Elevated High Sensitivity C-Reactive Protein Increases the Risk of Microalbuminuria in Subjects With Cardiovascular Disease Risk Factors. Ther Apher Dial. 2017;21:387-394. [Crossref]
30. Ueland T, Vissers MN, Wiegman A, Rodenburg J, Hutten B, Gullestad L, et al. Increased inflammatory markers in children with familial hypercholesterolaemia. Eur J Clin Invest. 2006;36:147-152. [Crossref]