

Evaluation of the relationship between proteinuria levels and perinatal and neonatal outcomes

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ABSTRACT

Objective: To evaluate the relationship between proteinuria levels and maternal and neonatal outcomes.

Material and Methods: This study retrospectively evaluated a total of 2,266 pregnant women who received follow-up care and delivered at our hospital between January 2018 and 2024. Of these, 76 patients who exhibited proteinuria during pregnancy were included in the analysis. We assessed demographic, laboratory, and obstetric data for all participants, including age, smoking status, gravida, blood urea nitrogen (BUN) levels, platelet count, 24-hour proteinuria values, gestational hypertension (GHT), fetal growth restriction (FGR), preeclampsia, preterm birth (PTB), Apgar scores, and birth weight.

Results: The severe group had significantly higher rates of gestational hypertension (GHT), preeclampsia, preterm birth (PTB), and fetal growth restriction (FGR) compared with the other groups ($p < 0.001$ for all). Apgar scores at 1 and 5 minutes were lower, and birth weight was significantly reduced in the severe group ($p < 0.001$). The rate of NICU admissions was also higher in the severe group ($p < 0.001$).

Conclusion: This study shows that severe proteinuria is associated with hypertensive diseases, fetal growth restriction, preterm birth, and neonatal complications. Close monitoring of pregnant women with proteinuria and early intervention may play an important role in reducing possible complications. Evaluation of proteinuria levels together with maternal and fetal risk factors may optimize clinical management to improve pregnancy outcomes.

Keywords: Maternal, perinatal, preeclampsia, proteinuria.

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INTRODUCTION

Urine analysis, one of the most common screening tests performed during pregnancy, is considered a critical tool for the detection of proteinuria. Although proteinuria has historically been considered a marker of preeclampsia, it can also be a nonspecific indicator of renal disease. Various mechanisms may contribute to the development of proteinuria during pregnancy, including increased plasma protein concentration, increased glomerular permeability, decreased tubular protein reabsorption, and renal hemodynamic changes.^[1–3] In normal renal function, glomerular filtration rate and protein filtration dynamics are affected by factors such as molecular weight, shape, and electrical charge. Guidelines published by the American College of Obstetricians and Gynecologists (ACOG) in 2013 suggested that proteinuria should not be considered a necessary criterion for the diagnosis of preeclampsia. However, proteinuria remains an important risk marker when evaluated together with hypertensive disorders.^[4] Preeclampsia is associated with serious maternal and perinatal complications and includes pathophysiologic processes that lead to systemic inflammation, endothelial dysfunction, and multiorgan damage, along with new-onset gestational hypertension.^[5,6] Significant physiological changes that occur during pregnancy affect renal hemodynamic changes, endocrine regulation, and tubular function. Pregnancy-related hyperfiltration and increased renal blood flow alter renal function, while increased renal venous pressure and changes in glomerular permeability, along with the effects of uteroplacental circulation, contribute to proteinuria.^[7,8] It has been observed that the risks of preeclampsia, fetal growth restriction, premature birth, and loss of maternal renal function are increased in pregnant women with chronic kidney disease. Proteinuria is an important indicator of glomerular damage and, when present in high amounts and persistently, can cause serious complications such as glomerular sclerosis, tubulointerstitial damage, and end-stage renal failure.^[9] Proteinuria is classified into different degrees during pregnancy, and these degrees differ in terms of clinical significance. Physiologic, i.e., transient proteinuria, can be observed during pregnancy due to increased renal blood flow and glomerular filtration rate. This situation typically ranges from 150 to 300 mg per day and is not considered clinically significant or associated with any pathological processes.^[10] Determination of proteinuria levels may be important in predicting pregnancy outcomes, regardless of the presence of concomitant preeclampsia. However, some studies suggest that the severity of proteinuria is not directly associated with preeclampsia complications, and scientific debates continue on this issue.^[11] In this context, it is important to analyze the associations of different proteinuria levels with maternal and fetal morbidity. This study aimed to evaluate the relationship between proteinuria levels and maternal and neonatal outcomes.

MATERIAL AND METHODS

The present study had a retrospective observational design following the principles of the Helsinki Declaration. Informed consent documents were received from all patients. The study received approval from our hospital's Ethics Committee (Date: 26/03/25, Number: 2025/430). A total of 2266 pregnant women who underwent pregnancy follow-

up in the Gynecology and Obstetrics Clinic of our hospital and gave birth in our clinic between January 2018 and January 2024 were retrospectively evaluated. Among these patients, 77 patients with proteinuria during pregnancy were included in the study. The inclusion criteria were proteinuria detected during pregnancy in laboratory examination results and urine protein levels >0.3 g/24 hours on different days. Patients with multiple pregnancies, primary hypertension, nephropathy and diabetes, patients with incomplete follow-up and birth record data, and patients with missing laboratory data were excluded from the study. Demographic and laboratory data of all patients, such as age, smoking, gravida, parity, body mass index (BMI), blood urea nitrogen (BUN), serum creatinine, serum uric acid, aspartate transaminase (AST), alanine transaminase (ALT), platelet count, and 24-hour proteinuria value, were evaluated retrospectively. All patients' data on gestational hypertension (GHT), fetal growth restriction (FGR), gestational diabetes mellitus (GDM), preeclampsia, preterm birth (PTB), preterm pre-labor rupture of membranes (PPROM), 1st and 5th minute Apgar scores, neonatal intensive care unit (NICU) history, and birth weight were evaluated retrospectively. The American Diabetes Association criteria were used to diagnose GDM.^[12] GHT was diagnosed in accordance with the most recent bulletin of the ACOG.^[13] The Delphi criteria were used to diagnose FGR.^[14] Preterm birth (PTB) is defined as a birth (live-born or stillborn) ≥20+0 weeks of gestation that occurs at <37+0 weeks of gestation.^[15] PPROM is defined as the rupture of fetal membranes before 37 weeks of gestation.^[16] Patients were evaluated in three groups according to their proteinuria levels: mild proteinuria (300 mg <24-hour proteinuria <1000 mg), moderate proteinuria (1000 <24-hour proteinuria <3500 mg), and severe proteinuria (24-hour proteinuria >3500 mg).^[13,17]

Statistical Analysis

Statistical analysis was performed using the SPSS version 26.0 software package (IBM Inc., Chicago, IL, USA). The normality of the distribution was evaluated with the Kolmogorov–Smirnov and Shapiro–Wilk tests based on whether the data demonstrated normal distribution. Standard deviation (SD) was used to evaluate normally distributed data. Categorical variables were presented using frequency and percentage (%). Chi-square tests were used in the analysis of categorical data. Continuous variables were compared among groups using analysis of variance (ANOVA) and Student's t-test. A logistic regression analysis of proteinuria severity for adverse pregnancy outcomes was performed. The results were evaluated at 95% confidence intervals (CI). P-values of <0.05 were regarded as statistically significant.

RESULTS

The mean BMI of the severe group was significantly higher compared with the other groups ($p=0.046$). BUN and creatinine levels were significantly lower in the mild group compared with the other groups ($p=0.036$ and $p=0.027$, respectively). AST and ALT levels were significantly higher in the severe group compared with the other groups ($p=0.021$ and $p=0.018$, respectively) (Table 1).

GHT and preeclampsia rates were significantly higher in the severe group compared with the other groups ($p < 0.001$ and $p < 0.001$, respectively). PTB and FGR rates were significantly higher in the

Table 1: Comparison of demographic and laboratory data between groups

	Mild (n=42) Mean±SD	Moderate (n=22) Mean±SD	Severe (n=13) Mean±SD	p
Age (years)	31.9±4.7	32±4.8	32.0±4.6	0.540
BMI (kg/m ²)	26.2±2.2	26.3±2.5	27.3±3.1	0.046
Smoking, n (%)	3 (7.1%)	2 (9%)	1 (7.6%)	0.120
Gravidity	2.07±1.08	1.99±1.14	1.98±1.12	0.390
Parity	0.91±0.66	0.90±0.75	0.89±0.73	0.760
BUN (mmol/L)	4.28±1.46	5.52±3.66	7.58±4.12	0.036
Creatinine (mmol/L)	52.66±12.18	67.73±38.62	79.26±41.12	0.027
Uric acid (mmol/L)	356.4±99.4	399.8±99.9	471.1±122.2	0.032
AST (U/L)	32.26±26.66	34.72±29.16	52.22±33.18	0.021
ALT (U/L)	20.72±11.82	21.22±12.36	35.18±28.68	0.018
Platelet (n/mL)	230.7±61.33	222.6±58.22	201.2±88.16	0.042

SD: Standard deviation; BMI: Body mass index; BUN: Blood urea nitrogen; AST: Aspartate transaminase; ALT: Alanine transaminase.

Table 2: Comparison of perinatal outcomes between groups

	Mild (n=42) n (%)	Moderate (n=22) n (%)	Severe (n=13) n (%)	p
GHT	7 (16.6)	5 (22.7)	4 (30.7)	<0.001
GDM	4 (9.5)	2 (9)	1 (7.6)	0.140
Preeclampsia	5 (11.9)	5 (22.7)	8 (61.5)	<0.001
PTB	8 (19)	8 (36)	7 (53.8)	<0.001
PPROM	5 (11.9)	3 (13.6)	2 (15.3)	0.160
FGR	4 (9.5)	5 (22.7)	6 (46.1)	<0.001

GHT: Gestational hypertension; GDM: Gestational diabetes mellitus; PTB: Preterm birth; PPRM: Preterm pre-labor rupture of membranes; FGR: Fetal growth restriction.

severe group compared with the other groups ($p < 0.001$ and $p < 0.001$, respectively) (Table 2).

Apgar 1st and 5th min scores were significantly lower in the severe group compared with the other groups ($p < 0.001$ and $p < 0.001$, respectively). Birth weight was significantly lower in the severe group compared with the other groups ($p < 0.001$). The NICU rate was significantly higher in the severe group compared with the other groups ($p < 0.001$) (Table 3).

DISCUSSION

Although there are numerous studies on proteinuria in the literature, studies examining the effects of proteinuria levels on perinatal and neonatal outcomes are limited. Our study revealed that the rates of GHT, preeclampsia, FGR, PTB, and NICU admission were higher

Table 3: Comparison of neonatal outcomes between groups

	Mild (n=42) Mean±SD	Moderate (n=22) Mean±SD	Severe (n=13) Mean±SD	p
Apgar (1 st min)	7.5±0.8	7.2±0.6	6.7±0.7	<0.001
Apgar (5 th min)	8.1±0.6	7.3±0.9	6.8±1.1	<0.001
Birth weight (gr)	2970±540	2420±610	1980±590	<0.001
NICU, n (%)	7 (16.6)	8 (36)	9 (69.2)	<0.001

SD: Standard deviation; NICU: Neonatal intensive care unit.

in pregnant women with severe proteinuria compared with those with mild and moderate proteinuria. These results support previous studies showing that proteinuria is an important marker of maternal and fetal morbidity.

One of the most important findings of our study is that the rates of GHT and preeclampsia are higher in patients with severe proteinuria. This is related to endothelial dysfunction and renal hemodynamic changes associated with proteinuria. Similarly, the study by Dong et al.^[18] found that the rate of preeclampsia was increased in pregnant women with severe proteinuria. Morikawa et al.^[19] suggested that severe proteinuria was associated with systemic inflammation and oxidative stress and might worsen hypertensive conditions in pregnancy.

In addition, the significantly higher FGR and PTB rates in the severe proteinuria group indicate that proteinuria has adverse effects on fetal development. The study by Jiao et al.^[20] also showed that the rate of delivery before the 37th week of gestation was increased in pregnant women with severe proteinuria. It is well known that placental insufficiency, an important feature of preeclampsia, contributes to FGR and preterm birth. The study by Hu et al.^[21] also supports the

increased FGR rates in cases of severe proteinuria. These findings indicate that severe proteinuria may be an important clinical marker for impaired placental function.

In our study, newborns born to mothers with severe proteinuria had lower 1st and 5th minute Apgar scores and lower birth weights compared with the mild proteinuria group. The study by Wang et al.^[22] also showed that severe proteinuria was an independent risk factor for low Apgar scores. Özkara et al.^[23] supported this conclusion by showing that the rate of NICU admission increased as the severity of proteinuria increased. The higher NICU admission rates in the severe proteinuria group emphasize the long-term effects of intrauterine growth retardation and prematurity on newborn health.

In terms of biochemical markers, BMI, AST, and ALT levels were significantly higher in the severe proteinuria group. This suggests that metabolic and hepatic dysfunctions may also play a role in maternal and neonatal complications. Similarly, the study by Alves Ferreira et al.^[24] showed that AST and ALT levels were higher in patients with severe proteinuria. In addition, Fishel Bartal et al.^[25] found that the rate of proteinuria increased as the BMI value increased, similar to our study. At the same time, the increase in liver enzymes in patients with severe proteinuria is an indicator of hepatic involvement seen in severe preeclampsia and HELLP syndrome.

One of the important advantages of our study is that it has a large sample size covering a wide range of patients. This increases the reliability of the results obtained. In addition, criteria that comply with international standards were used in the diagnosis of obstetric complications such as preeclampsia, GHT, fetal growth retardation, and premature birth, thus supporting the scientific validity of the study.

However, the retrospective nature of the study may lead to the possibility that some clinical variables were recorded incompletely. In addition, because it was conducted in a single center, the generalizability of the results to different patient groups may be limited. The study only examined neonatal outcomes in the early postnatal period, and there are no data on long-term infant health.

Considering all these advantages and disadvantages, our study makes significant contributions to the existing literature. However, larger, multicenter, and long-term prospective studies are needed to evaluate the relationship between proteinuria and pregnancy outcomes in more detail.

CONCLUSION

This study highlights the important association between proteinuria severity and adverse maternal and neonatal outcomes. Severe proteinuria is associated with hypertensive disease, FGR, preterm birth, neonatal complications, low birth weight, and higher rates of NICU admission. These findings suggest that close monitoring of pregnant women with proteinuria and early intervention may play an important role in reducing potential complications. Given the ongoing debate about the predictive value of proteinuria for preeclampsia and adverse perinatal outcomes, further research is needed to develop risk stratification strategies and optimize the management of affected pregnancies. Proteinuria levels should be assessed in conjunction with other maternal and fetal risk factors, and careful monitoring should be provided to improve pregnancy outcomes.

Statement

Ethics Committee Approval: The Buca Seyfi Demirsoy Training and Research Hospital Ethics Committee granted approval for this study (date: 26.03.2025, number: 2025/430).

Informed Consent: Informed consent documents were received from all patients.

Conflict of Interest: The authors have no conflict of interest to declare.

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