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İzole Gestasyonel Proteinürinin Preeklampsiye İlerlemesi: Maternal ve Perinatal Sonuçların Retrospektif Analizi

Progression of Isolated Gestational Proteinuria to Preeclampsia: A Retrospective Analysis of Maternal and Perinatal Outcomes

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ÖZ

Giriş: Preeklampsi, gebeliklerin %3–8'inde görülen ve ciddi maternal ile fetal morbiditeye yol açan önemli bir obstetrik komplikasyondur. Ancak izole gestasyonel proteinürinin (İGP) klinik önemi ve seyri halen net değildir. Bu çalışmanın amacı, İGP'si bulunan gebelerde preeklampsi gelişme sıklığını belirlemek ve bu hastalardaki maternal ve perinatal sonuçları karşılaştırmaktır.

Yöntem: Normotansif olup İGP nedeniyle hastanemize başvuran gebeler doğuma kadar prospektif olarak takip edildi. Hastalar, gebelik sürecinde preeklampsi gelişip gelişmemesine göre iki gruba ayrıldı. Preeklampsi tanısı alan olgular ise şiddetine göre "şiddetli" ve "şiddetli olmayan" olarak sınıflandırıldı. Tüm olguların demografik özellikleri, klinik ve laboratuvar bulguları ile gebelik sonuçları değerlendirildi.

Bulgular: İGP'si bulunan 117 gebeden 41'inde (%35,0) preeklampsi gelişti. Ortalama 24 saatlik idrar proteinüri düzeyi preeklampsi grubunda daha yüksek olmasına rağmen (525 mg'a karşı 393 mg), fark istatistiksel olarak anlamlı değildi (p = 0,067). Ciddi maternal komplikasyon oranları benzer olmakla birlikte, preeklampsi gelişen olgularda erken doğum, fetal büyüme kısıtlılığı, düşük doğum ağırlığı ve yenidoğan yoğun bakım ünitesine (YYBÜ) yatış oranları anlamlı derecede yüksekti (tüm p < 0,01). Preeklampsi gelişen 41 hastanın 14'ü (%34) şiddetli kriterleri karşıladı. Şiddetli preeklampsi olgularında 24 saatlik proteinüri düzeyi en yüksek (p = 0,003), gebelik haftası ve doğum ağırlığı ise en düşüktü. Ayrıca YYBÜ'de kalış süresi anlamlı derecede uzundu.

Sonuç: Ciddi maternal komplikasyon oranları artmamakla birlikte, preeklampsiye ilerleyen olgularda neonatal sonuçlar anlamlı derecede olumsuzdur. Bu nedenle İGP, yüksek riskli bir obstetrik durum olarak değerlendirilmelidir ve gebelik süresince yakın takip gerektirir.

Anahtar Kelimeler: preeklampsi, izole proteinüri, 24 saatlik idrar-protein, izole gestasyonel proteinüri

ABSTRACT

Objective: Preeclampsia affects 3-8% of pregnancies, leading to serious maternal and fetal morbidity. The clinical significance and course of isolated gestational proteinuria (IGP) are unclear. The aim of this study was to determine the incidence of preeclampsia in pregnant women with IGP and to compare maternal and perinatal outcomes.

Method: Pregnant women with normotensive blood pressure admitted to our hospital due to IGP were followed until delivery and divided into two groups based on whether they developed preeclampsia. Patients with preeclampsia were subgrouped as severe or non-severe. Maternal characteristics, clinical and laboratory findings, and pregnancy outcomes were analyzed.

Results: Of 117 women with IGP, 41 (35.0%) developed preeclampsia. Median 24-hour proteinuria was higher in the preeclampsia group (525 mg vs. 393 mg), but the difference was minimal (p = 0.067). Although severe maternal outcomes were similar, preeclampsia cases had significantly higher rates of preterm delivery, fetal growth restriction, low birth weight, and Neonatal Intensive Care Unit (NICU) admission (all p < 0.01). Fourteen of 41 preeclamptic patients (34%) met the severe criteria. Severe preeclampsia cases had the highest 24-hour proteinuria (p = 0.003) and the lowest gestational age and birth weight. NICU length of stay was also significantly longer.

Conclusion: Although serious maternal complications are not significantly higher, neonatal outcomes are significantly worse in those who progressed to preeclampsia. Therefore, IGP should be considered a high-risk condition and requires close monitoring.

Keywords: preeclampsia, isolated proteinuria, 24 hours urine-protein, IGP

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INTRODUCTION

Preeclampsia is an important disease that occurs after the 20th week of pregnancy, is characterized by hypertension and organ dysfunction findings, and can lead to serious complications for the mother and/or fetus. It has been reported that preeclampsia develops in approximately 3-8% of pregnancies worldwide and is responsible for up to 10% of maternal deaths [1]. Traditionally; it is known that proteinuria of ≥300 mg/24 hours or ≥0.3 protein-creatinine ratio is an important criterion in the diagnosis of preeclampsia. However, updated guidelines state that proteinuria is not an absolute requirement for the diagnosis of preeclampsia and that in severe cases, diagnosis can be made without proteinuria [2]. In conclusion; although proteinuria is frequently observed, it is not a specific or necessary feature for the diagnosis of preeclampsia [1,2].

Isolated gestational proteinuria (IGP); which is a rare condition seen in approximately 0.3-1% of pregnancies, is defined as new-onset significant proteinuria in pregnancy without evidence of hypertension [3]. There are different findings in the literature regarding the clinical course of IGP. Recent evidence suggests that some pregnant women with isolated proteinuria will develop preeclampsia and therefore these patients should be carefully monitored for preeclampsia [3].

In this study, we aimed to compare the rate of preeclampsia development in pregnant women followed up with the diagnosis of isolated proteinuria and the maternal and perinatal outcomes of pregnant women who developed preeclampsia and those who did not. Thus, we aimed to contribute to the literature with data on the clinical significance and management of isolated proteinuria.

MATERIALS AND METHODS

This retrospective cohort study was conducted with institutional ethics committee approval numbered 2025-6 from the Kocaeli City Hospital Scientific Research Ethics Committee. A retrospective cohort study was conducted on pregnant women who received a diagnosis of isolated proteinuria between April 2023 and October 2024 at the Department of Gynecology and Obstetrics of Health Sciences University Kocaeli City Hospital. The medical files of these patients were meticulously reviewed to ascertain the relevant data. The definition of IGP was based on the detection of proteinuria in urine tests performed after the 20th week of pregnancy, when blood pressure was <140/90 mmHg, and urine protein levels were ≥300 mg/24 hours [1,2]. Women who were pregnant and had hypertension (blood pressure ≥140/90 mmHg) at the time of admission, as well as those with known chronic kidney disease, chronic hypertension, or a history of chronic proteinuria, were excluded from the study.

The cases include in the study were pregnant women who exhibited normal blood pressure at the initial baseline, proteinuria, and were admitted to the hospital for close monitoring. The standard prenatal care protocol was administered, include daily blood pressure monitoring, serial urine protein measurements, and laboratory evaluations as indicated (complete blood count, renal and liver function tests, coagulation profile). In instances of preeclampsia that manifested during the course of follow-up, appropriate management interventions were initiated, incl antihypertensive therapy, magnesium sulfate administration, and corticosteroid treatment for fetal lung maturation in cases of severe preeclampsia preceding 37 weeks of gestation.

The diagnosis of preeclampsia was made in accordance with the 2020 ACOG criteria, which delineate the condition as new-onset hypertension (systolic ≥140 mmHg or diastolic ≥90 mmHg) following the 20th week of gestation, in conjunction with either proteinuria (≥300 mg/24 hours) or the presence of severe characteristics (platelet count <100,000/μL, elevated liver transaminases ≥2× the upper limit of normal, persistent severe epigastric pain, serum creatinine >1.1 mg/dL or doubling of baseline, pulmonary edema, or cerebral/visual symptoms) [2]. Patients who maintained normotensive levels throughout pregnancy were designated as members of the "IGP group," while those who developed preeclampsia were classified as members of the "preeclampsia group." In the context of preeclampsia cases, patients were further classified into two subgroups: "severe" and "non-severe." This classification was determined based on the presence of any of the aforementioned severe features or blood pressure levels measuring ≥160/110 mmHg [2].

A comprehensive set of demographic data was collected, including age, gravidity, parity, body mass index. Gestational week at presentation, obstetric history, and initial presentation were also documented. In addition, the laboratory results of all cases were recorded. Laboratory data included the following parameters: hemoglobin, platelet count, blood urea nitrogen (BUN), creatinine, uric acid, liver enzymes (AST, ALT), and serum albumin levels. Furthermore, protein excretion was measured using a 24-hour urine collection method. A comprehensive evaluation of obstetric and neonatal outcomes was conducted, encompassing various metrics such as gestational age at delivery, mode of delivery, neonatal birth weight, initial and fifth minute Apgar scores, NICU admission and duration, placental abruption, HELLP syndrome, eclampsia, and maternal ICU requirement.

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) or NCSS 11 (Number Cruncher Statistical System) software. The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Data that conformed to a normal distribution were reported as the mean ± standard deviation, while data that did not conform to a normal distribution were reported as the median (minimum-maximum). Categorical variables were expressed as numerical values and percentages. In the comparison of isolated proteinuria and preeclampsia groups, an independent two-sample t-test was employed for parametric data, and the Mann-Whitney U test was utilized if the distribution was not normal. The comparison of categorical variables was conducted through the utilization of the Chi-square test or the Fisher's exact test when deemed suitable. One-way analysis of variance (ANOVA) or the Kruskal-Wallis test was used to compare the preeclampsia subgroups. In cases where a significant difference was identified, post-hoc pairwise comparisons were performed using the Tukey HSD or Mann-Whitney U test. In all tests, a p-value less than 0.05 was considered statistically significant.

RESULTS

A total of 117 pregnant women were included in the study, 76 in the isolated proteinuria (IGP) group and 41 in the preeclampsia group. Baseline demographic and clinical characteristics are summarized in Table 1. The mean age was similar between the two groups (IGP: 30.11±6.14;

preeclampsia: 30.17±5.30 years; p=0.963). Although the mean gestational age at admission was slightly higher in the isolated proteinuria group, it was not statistically significant (33.3±3.8 weeks vs 32.0±3.2 weeks; p=0.077). When obstetric histories were examined, there was no difference between the groups in terms of gravida and abortion counts (p=0.360 and p=0.207, respectively). However, parity was significantly lower in the preeclampsia group compared to the IGP group (p=0.007). Systolic and diastolic blood pressures at admission were within normal ranges for all participants and did not differ significantly between groups (systolic ~109 mmHg, diastolic ~72 mmHg; p>0.5) although; body mass index (BMI) was significantly higher in the preeclampsia group (28.63±3.52 vs 27.44±2.45; p=0.035).

Table 1. Baseline Demographic and Clinical Characteristics

	(n= 117) mean±SD median (min-max)
Age	30.13±5.84 30.00 (18-46)
Pregnancy week	32.84±3.64 33.28 (21.28-38.42)
Gravidity	2.40±1.57 2.00 (1.00-7.00)
Parity	1.02±1.17 1.00 (0.00-5.00)
Abortion	0.38±0.81 0.00 (0.00-4.00)
BMI	0.81±2.91 28.00 (21.00-42.00)
24 hour urine protein (mg)	921.37±1706.82 412.00 (300.00-13024.00)
Systolic BP (mm/Hg)	108.91±9.54 110.00 (90.00-130.00)
Diastolic BP (mm/Hg)	72.04±7.26 70.00 (50.00-80.00)

T test, BMI; body mass index, BP; blood pressure, p<0.05 was considered statistically significant.

Laboratory analyses revealed no significant differences in hemoglobin or platelet levels (Hb ~11.2 g/dL, Plt ~227×10³/µL; p>0.9). However, there was a significant difference in renal function tests in the preeclampsia group: The BUN and serum creatinine values of the preeclampsia group was significantly higher than the isolated proteinuria group (BUN: 9.34±3.56 vs 7.71±2.49 mmol/L, p=0.012; creatinine: 0.63±0.14 vs 0.57±0.12 mg/dL, p=0.015). Uric acid levels were similar (p=0.195), as were as liver enzymes and albumin levels (p>0.2 for all).(Table 2)

Twenty-four-hour urinary protein excretion was in the preeclampsia group (mean: 1428.5±2592.8 mg; median: 525 mg), in IGP group (mean: 647.8±839.0 mg; median: 393 mg). Although there was a tendency for higher amounts of proteinuria in the preeclampsia group, the difference between the two groups was only marginally statistically significant due to the wide variation (p=0.067).

According to the follow-up results, 27 of the 41 pregnant women in the preeclampsia group did not have severe criteria, while 14 pregnant women (34.1%) were defined as having severe preeclampsia. The average time from IGP diagnosis to onset of hypertension (i.e., diagnosis of preeclampsia) corresponded to approximately 35 weeks of gestation. In the isolated proteinuria group, blood pressure remained normal throughout pregnancy follow-up and preeclampsia criteria did not develop until delivery.(Table 3)

The mean gestational age for all cases was 36.0±2.8 weeks. It was significantly earlier in the preeclampsia group (34.83±2.66 weeks) compared to the IGP group (36.84±2.53 weeks; p<0.001). This difference was particularly evident in the severe preeclampsia subgroup; the mean gestational age in the severe preeclampsia cases was 34.1±2.1 weeks, approximately 2.7 weeks earlier than in the isolated proteinuria group (p<0.01).

Preterm delivery (<37 weeks) was more common in the preeclampsia group (58.5%) than in the IGP group (25.0%; p<0.001). Neonatal birth weights were also significantly lower in the preeclampsia group (2257±791 g vs 2813±789 g; p<0.001), with the lowest values seen in the severe preeclampsia group (2125±703 g). Low birth weight (<2500 g) was noted in 63.4% of the preeclampsia group versus 30.3% of the IGP group (p<0.001). Fetal growth restriction (FGR) was significantly more frequent in the preeclampsia group (19.5%) than in the IGP group (6.6%; p=0.012). Intrapartum fetal distress occurred in 24.4% of the preeclampsia group compared to 7.9% in the IGP group (p=0.004).

Apgar scores at 1 and 5 minutes were significantly lower in the preeclampsia group (1st minute: 7.19±1.38 vs 7.69±0.81, p=0.037; 5th minute: 8.36±1.13 vs 8.75±0.85, p=0.041). Umbilical artery blood gas analysis showed lower mean pH in the preeclampsia group (7.26±0.14 vs 7.33±0.09; p=0.008), suggesting a trend toward mild neonatal acidosis.

The two groups were similar in terms of maternal complications. Placental abruption occurred in 7.3% of the preeclampsia group and 2.6% of the IGP group (p=0.181). HELLP syndrome was observed in 3 patients in the preeclampsia group and 1 in the IGP group (p=0.173). HELLP (p=0,173). Maternal Intensive Care Unit (ICU) admission was more frequent in the preeclampsia group (9.8% vs 1.3%), but this did not reach statistical significance (p=0.053). Eclampsia occurred in 1 patient (2.4%) in the preeclampsia group, while no eclampsia case was observed in the isolated proteinuria group. No maternal death occurred in the entire cohort.

NICU admission was required in 43.9% of neonates born to mothers with preeclampsia compared to 15.8% in the IGP group (p=0.001). The mean length of stay in the ICU was 10.3±18.9 days in the preeclampsia group and 4.0±11.2 days in the isolated proteinuria group, and the difference was found to be statistically significant (p=0.021). In particular, the ICU duration in the non-severe preeclampsia group was prolonged to 15.1±20.3 days; this difference was significant when compared to the isolated proteinuria group (p=0.042). Although the mean ICU duration was also high in the severe preeclampsia group with a mean of 15.1±18.2 days, no statistically significant difference was detected due to the small number of cases (p>0.05).

In summary, progression from IGP to preeclampsia was associated with shorter gestational duration, lower birth weight, and increased NICU admissions. While maternal complications (e.g. abruption, HELLP) were more frequent in the preeclampsia group, these differences were not statistically significant. These findings are consistent with trends reported in the literature [3,4,5,6].

Table 2. Comparison of Demographic, Laboratory, and Neonatal Outcomes Between İsolated Proteinuria and Preeclampsia Groups

	Isolated proteinuria (n= 76) mean±SD median (min-max)	Preeclampsia (n= 41) mean±SD median (min-max)	p
Age	30.11±6.14 30.00 (18.00-46.00)	30.17±5.30 29.00 (21.00-43.00)	0.963
Pregnancy week	33.28±3.80 34.21 (21.29-38.43)	32.03±3.21 31.71 (21.85-38.00)	0.077
BMI	27.44±2.45 27.50 (24.00-37.00)	28.63±3.52 28.00 (21.00-42.00)	**0.035**
24 hour urine protein (mg)	647.80±839.03 393.00 (300.00-4757.00)	1428.48±2592.82 525.00 (308.00-13024.00)	0.067
Systolic BP (mm/Hg)	108,48±8,44 110,00 (90,00-120,00)	109.70±11.38 110.00 (90.00-130.00)	0.549
Diastolic BP (mm/Hg)	71.56±7.07 70.00 (60.00-80.00)	72.92±7.62 70.00 (50.00-80.00)	0.336
Hemoglobin (mg/dl)	11.17±1.62 11.05 (5.50-13.90)	11.18±1.51 11.20 (6.50-13.70)	0.977
PLT	225.01±53.34 229.00 (101.00-369.00)	229.87±65.39 224.00 (106.00-352.00)	0.684
BUN (mg/dl)	7.71±2.49 7.00 (3.00-15.00)	9.34±3.56 8,00 (5.00-19.00)	**0.012**
Uric acid (mg/dl)	4.42± 1.21 4.30 (2.30-9.40)	4.74± 1.33 4.30 (2.70-8.40)	0.195
Creatinine (mg/dl)	0.57±0.12 0.58 (0.26-0.81)	0.63±0.14 0.62 (0.30-0.98)	**0.015**
GFR	123.80±12.75 122.00 (94.00-171.00)	118.70±16.41 122.00 (74.00-148.00)	0.065
AST (mg/dl)	22.92± 22.23 18.00 (8.00-178.00)	33.00± 55.71 18.00 (9.00-349.00)	0.272
ALT (mg/dl)	18,78± 28,33 12.00 (3.00-187.00)	27.17± 46.94 13.00 (6.00-272.00)	0.231
Albumin (g/L)	32.65± 2.97 32.00 (25.00-39.00)	32,04± 3,43 33.00 (24.00-40.00)	0.320
Birth week	36.84± 2.53 37.14 (28.00-41.00)	34,83± 2,66 35.57 (27.42- 38.85)	**0.000**
Birth weight (gr)	2813.72± 788.69 2935.00 (710.00- 4570.00)	2257.31± 790.68 2250.00 (555.00- 3960.00)	**0.000**
APGAR 1. minute	7.69± 0.81 8.00 (4.00-9.00)	7,19± 1,38 8.00 (2.00-8.00)	**0.037**
APGAR 5. minute	8.75± 0.85 9.00 (4.00-10.00)	8.36± 1.13 9.00 (3.00-9.00)	**0.041**
Cord blood pH	7,33± 0,09 7.38 (7.00-7.44)	7.26± 0.14 7.30 (6.80-7.40)	**0.008**

Independent Samples T Test, BMI; body mass index, BP; blood pressure, PLT; platelet, BUN; blood urea nitrogen, GFR; glomerular filtration rate, AST; aspartate aminotransferase, ALT; alanine aminotransferase, $p<0.05$ was considered statistically significant.

Table 3. Comparison of Demographic, Obstetric, Laboratory Parameters and Neonatal Outcomes Between İsolated Proteinuria and Preeclampsia Subgroups

	Isolated proteinuria (n= 76) mean±SD median (min-max)	Non-severe preeclampsia (n= 27) mean±SD median (min-max)	Severe preeclampsia (n= 14) mean±SD median (min-max)	p
Age	30.11± 6.14 30.00 (18.00-46.00)	28.85± 4.84 28.00 (21.00-38.00)	32.71± 5.38 31.50 (26.00-43.00)	0.133
Pregnancy week	33.28± 3.80 34.21 (21.29- 38.43)	31.93± 3.66 31.71 (21.86-38.00)	32.22±2.21 31.92 (29.00-36.29)	0.206
Gravidity	2.44±1.40 2.00 (1.00-7.00)	2.07±1.83 1.00 (1.00-7.00)	2.78±1.88 2.50 (1.00-7.00)	0.360
Parity	1.14±1.12 1.00(0.00-5.00)	0.44±0.89 0.00(0.00-3.00)	1.50±1.50 1.00(0.00-4.00)	**0.007**
Abortion	0.31±0.75 0.00(0.00-4.00)	0.62±1.04 0.00(0.00-4.00)	0.28±0.61 0.00(0.00-2.00)	0.207
BMI	27.44±2.45 27.50(24.00-37.00)	28.74±3.78 28.00(21.00-42.00)	28.42±3.08 28.50(22.00-34.00)	0.104
24 hour urine protein (mg)	647.80±839.03 393.00(300.00-4757.00)	1008.03±1413.65 517.00(308.00-6968.00)	2239.35±3951.35 539.00(350.00-13024.00)	**0.005**
Systolic BP (mm/Hg)	108.46±8.44 110.00(90.00-120.00)	108.25±11.23 100.00(90.00-130.00)	112.50±11.56 110.00(100.00-130.00)	0.327
Diastolic BP (mm/Hg)	71.56±7.07 70.00(60.00-80.00)	71.85±8.51 70.00(50.00-80.00)	75.00±5.18 75.00(70.00-80.00)	0.266
Hemoglobin (mg/dl)	11.17±1.62 11.05(5.50-13.90)	11.21±1.26 11.10(9.30-13.60)	11.12±1.96 11.45(6.70-13.70)	0.985
PLT	225.01±53.39 229.00(101.00-369.00)	228.51±57.39 220.00(125.00-352.00)	232.50±80.99 247.00(106.00-338.00)	0.891
BUN (mg/dl)	7.71±2.49 7.00(3.00-15.00)	9.40±3.56 8.00(5.00-19.00)	9.21±3.70 7.50(5.00-19.00)	**0.018**
Creatinine (mg/dl)	0.57±0.12 0.58(0.26-0.81)	0.62±0.14 0.62(0.39-0.98)	0.64±0.14 0.63(0.30-0.86)	**0.047**
GFR	123.80±12.75 122.00(94.00-171.00)	120.77±17.05 123.00(74.00-148.00)	114.71±14.88 119.00(86.00-139.00)	0.079
Uric acid (mg/dl)	4.42±1.21 4.30(2.30-9.40)	4.83±1.50 4.30(3.20-8.40)	4.57±0.98 4.50(2.70-6.40)	0.357
AST (mg/dl)	22.92±22.23 18.00(8.00-178.00)	33.59±64.31 18.00(10.00-349.00)	31.85±35.72 18.00(9.00-131.00)	0.384
ALT (mg/dl)	18.78±28.33 12.00(3.00-187.00)	28.00±54.36 14.00(6.00-272.00)	25.57±29.39 12.50(6.00-94.00)	0.479
Albumin (g/L)	32.65±2.97 32.00(25.00-39.00)	32.44±3.37 33.00(26.00-40.00)	31.28±3.53 32.50(24.00-36.00)	0.327
Birth week	36.84±2.53 37.14(28.00-41.00)	35.21±2.86 35.85(27.43-38.86)	34.10±2.14 34.21(30.71-37.00)	**0.000**
Birth weight (gr)	2813.72±788.69 2935.00(710.00-4570.00)	2326.11±836.90 2280.00(555.00-3960.00)	2124.64±702.89 2055.00(780.00-3830.00)	**0.001**
APGAR 1. minute	7.69±0.81 8.00(4.00-9.00)	7.18±1.61 8.00(2.00-8.00)	7.21±0.80 7.00(6.00-8.00)	0.052
APGAR 5. minute	8.75±0.85 8.00(4.00-9.00)	7.18±1.61 8.00(2.00-8.00)	7.21±0.80 7.00(6.00-8.00)	0.119
Cord blood pH	7.33±0.09 7.38(7.00-7.44)	7.29±0.12 7.30(6.90-7.40)	7.21±0.18 7.30(6.80-7.40)	**0.002**
NICU duration (day)	6.05±14.56 0.00(0.00-86.00)	15.07±20.28 4.00(0.00-66.00)	15.07±18.15 8.00(0.00-58.00)	**0.021**

Oneway ANOVA Test, BMI; body mass index, BP; blood pressure, PLT; platelet, BUN; blood urea nitrogen, GFR; glomerular filtration rate, , AST; aspartate aminotransferase, ALT; alanine aminotransferase, NICU; neonatal intensive care unit, p<0.05 was considered statistically significant.

DISCUSSION

In this study, approximately one-third of pregnant women with isolated gestational proteinuria (IGP) progressed to preeclampsia, and those who did experienced significantly worse obstetric and neonatal outcomes. These findings indicate that isolated proteinuria may represent an early marker of preeclampsia. Indeed, proteinuria is one of the classical signs of preeclampsia and may precede the onset of hypertension in a subset of patients [1,2,3]. Akaishi et al. reported that 16% of women with IGP developed preeclampsia within 10 days [5], and in our cohort, the mean interval between the onset of proteinuria and subsequent preeclampsia was approximately 16 days, which is consistent with earlier reports.

A retrospective analysis by Ekiz et al. similarly demonstrated a 33.7% progression from IGP to preeclampsia and emphasized the predictive value of proteinuria levels in identifying women at risk [3]. In our study, baseline proteinuria was higher in those who later developed preeclampsia (median 525 mg vs. 393 mg). Although this difference reached only marginal statistical significance—likely reflecting the limited sample size—the significantly higher proteinuria levels observed in the severe preeclampsia subgroup underscore its potential role in risk stratification.

Obesity and impaired renal function markers also emerged as relevant predictors. The higher BMI among women who progressed to preeclampsia aligns with previous evidence indicating that obesity increases preeclampsia risk through mechanisms such as elevated placental leptin, insulin resistance, and systemic inflammation [7,8]. Additionally, elevated BUN and serum creatinine levels in the preeclampsia group—even before the onset of hypertension—may reflect early endothelial dysfunction and reduced renal perfusion, suggesting that the pathophysiological processes of preeclampsia may already be underway at the time isolated proteinuria is detected. Previous studies have reported that uric acid elevation, microalbuminuria, or biomarkers such as angiotensinogen may differentiate early in preeclampsia cases [1,9]. In our study was, uric acid levels did not differ significantly between groups, which may be attributable to the fact that most patients were evaluated in late gestation, when uric acid levels have already plateaued [1].

One of the most important findings of our study is the significantly poorer neonatal outcomes among pregnant women with IGP who progressed to preeclampsia. The mean gestational age of approximately 35 weeks in the preeclampsia group, together with a prematurity rate approaching 59%, indicates that these infants were delivered before completing pulmonary maturation and were therefore at increased risk of neonatal morbidity. As expected, rates of admission to the neonatal intensive care unit (NICU) were significantly higher in the preeclampsia group, and NICU stays were longer. Notably, all infants in the severe preeclampsia subgroup were preterm and some had very low birth weight, explaining their high intensive-care needs. The rate of fetal growth restriction (FGR) was also markedly elevated in the preeclampsia group (19.5% vs. 6.6%), consistent with the well-established association between preeclampsia and placental insufficiency [1,6].Although Apgar scores were slightly lower in the preeclampsia group, most neonates had 5-minute Apgar scores ≥7, indicating that the need for emergency resuscitation was rare in both groups.

This aligns with findings by Shinar et al., who similarly observed lower Apgar scores in cases progressing from IGP to preeclampsia but no major differences in maternal outcomes [4]. Consistent with the literature, we identified small differences in Apgar scores without significant maternal complications.

Regarding maternal outcomes, placental abruption and HELLP syndrome were more common in the preeclampsia group, but these differences did not reach statistical significance. This may reflect limited sample size for these relatively rare complications or may suggest that preeclampsia developing from isolated proteinuria often follows a milder clinical course. Severe preeclampsia occurred in 14 cases (34%), whereas the remaining women did not exhibit blood pressure values exceeding 160/110 mmHg or evidence of severe organ dysfunction. This indicates that preeclampsia arising from isolated proteinuria is frequently classified as non-severe. As expected, the subgroup that progressed to severe disease had the earliest deliveries and the lowest birth weights. These findings highlight the importance not only of predicting the development of preeclampsia in women with isolated proteinuria, but also of identifying those at risk for severe disease.

CONCLUSION

The presence of IGP should not be regarded as a benign or incidental finding in pregnancy. Our study demonstrated that approximately one-third of women with IGP progressed to preeclampsia, and that this transformation negatively affects neonatal outcomes. Therefore, pregnant women with IGP should be considered to be at high risk for preeclampsia; they should be closely monitored and early intervention should be made when necessary. Although it is seen that progression from isolated proteinuria to preeclampsia can mostly occur in the late stages of pregnancy and in milder forms, it is still associated with significantly increased rates of prematurity and neonatal morbidity [3,6].

In clinical practice, blood pressure monitoring and proteinuria monitoring should be planned for cases with isolated proteinuria, and they should also be counseled on the warning signs of preeclampsia, such as; persistent headache, visual disturbances, and epigastric pain [2,4]. If possible, preeclampsia-specific biomarkers such as; PlGF and sFlt-1 can be used in these patients and may assist in identifying patients at higher risk [1,9]. For such cases, timely planning of delivery and referral to a tertiary center may improve outcomes.

In conclusion, pregnancies with isolated gestational proteinuria should be evaluated in high risk pregnancies category and managed with a multidisciplinary approach to improve maternal and perinatal outcomes. Further multicenter, prospective studies are necessary to identify reliable predictors of progression and establish standardized management protocols for this understudied clinical entity.

Ethics Committee Approval: This study was conducted in accordance with the principles of the Declaration of Helsinki. The current study collected data from the gynecology and obstetrics department of Kocaeli City Hospital. A retrospective study was conducted by obtaining data from the Hospital Management System (KEYDATA). It was approved by the Kocaeli City Hospital Ethics Committee with the approval number 2025-6.

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