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ORIGINAL ARTICLE

Insulin Resistance In Preeclampsia And Its Effect On Maternal-Fetal Outcomes

Preeklamptik Gebelerdeki İnsülin Direnci Ve Maternal-Fetal Sonuçlara Etkisi

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ABSTRACT

Aim: It is controversial whether insulin resistance and hyperinsulinemia in preeclamptic patients are due to weight gain during pregnancy or preeclampsia. This research seeks to explore the relationship between insulin resistance and factors such as weight gain, obesity, biochemical indicators, and the fetal outcomes linked to insulin resistance in pregnant women experiencing mild and severe preeclampsia, excluding those with gestational diabetes.
Methods: This research was carried out in the Perinatology Department of İzmir Tepecik Training and Research Hospital from July 2013 to January 2014, with the approval of the institution's ethics committee. Non-diabetic preeclamptic 101 pregnant women between 18 and 44 years of age in 24-40 gestational weeks were involved in the research. We recorded demographic data, biochemical parameters, weight measurements, enquiries regarding glucose metabolism, and data about fetuses. A Homeostatic Model Assessment (HOMA) value of 2.5 or above, along with an insulin sensitivity index of 6 or below, was evaluated as indicative of insulin resistance.
Results: There was no remarkable variation in both groups concerning fasting and postprandial glucose level, HOMA-IR (homeostatic model assessment insulin resistance), and insulin sensitivity index. Postprandial insulin levels were significantly elevated in the group with severe preeclampsia ($p < 0,05$). On the other hand, when we examined the effects on fetal outcomes, delivery time, birth weight, and 1 and 5 min Apgar scores were determined to be statistically significantly lower in the group suffering from severe preeclampsia.
Conclusion: In our research, it was observed that postprandial insulin levels were considerably elevated in the group with severe preeclampsia. Postprandial insulin levels can be considered to predict the impact of insulin resistance and sensitivity on disease prognosis and maternal-fetal outcomes in preeclampsia patients without gestational diabetes. Therefore, its usefulness as a parameter for predicting metabolic syndrome in later years should be investigated in large prospective randomized controlled trials.

Keywords: Hyperglycemia, insulin Sensitivity, postprandial, preeclampsia.

ÖZ

Amaç: Preeklampsi olgularında saptanan hiperinsulinemi ve insülin direncinin gebelik süresince olan kilo artışıyla mı yoksa preeklampsi patofizyolojisi ile mi ilişkili olduğu henüz tam netlik kazanmamıştır. Çalışmamızda gestasyonel diyabeti olmayan hafif ve ağır preeklampsi tanısı almış gebelerde kilo alımı, obezite, biyokimyasal parametreler ile insülin direnci arasındaki bağlantı ve fetal sonuçlarına etkisi araştırıldı.
Gereç ve yöntem: İzmir Tepecik Eğitim ve Araştırma Hastanesi Perinatoloji polikliniğinde takipli 24-40. gebelik haftaları arasındaki gestasyonel diyabet tanısı almamış preeklamptik 18-44 yaş arasındaki 101 gebe dahil edildi. Çalışma Temmuz 2013 ile Ocak 2014 arasında yürütülmüştür. Gebelerin demografik verileri, biyokimyasal parametreleri, kilo ölçümleri, glukoz metabolizmasına yönelik tetkikler ve fetüse ait veriler kaydedildi. HOMA (Homeostatic Model Assessment) değeri 2.5 ve üzerinde olması ve insülin sensitivite indeksinin 6'nın altında olması insülin direnci olarak değerlendirildi.
Bulgular: Hafif ve ağır preeklamptik olgulardan oluşan gruplar arasında açlık –tokluk glukoz, HOMA-IR (Homeostatic model assessment-insulin resistance), insülin sensitivite indeksi açısından anlamlı bir fark olmadığı fakat tokluk insülin değerlerinin ağır preeklampsi grubunda anlamlı olarak daha yüksek olduğu saptanmıştır. Doğum haftası,fetal doğum ağırlığı,1 ve 5. dk apgar skorlarına bakıldığında ise ağır preeklampsi grubunda istatistiksel olarak anlamlı daha kötü obstetrik sonuçlar elde edilmiştir.
Sonuç: Çalışmamızda tokluk insülin değerlerinin ağır preeklampsi grubunda anlamlı olarak daha yüksek olduğu saptanmıştır. Gestasyonel diyabeti olmayan preeklampsi olgularında insülin direnci ve duyarlılığının hastalığın prognozu ve maternal-fetal sonuçlar üzerindeki etkisini öngörmek için postprandiyal insülin düzeyleri dikkate alınabilir ve bu sayede ilerleyen yıllarda metabolik sendromu tahmin etmede yararlı bir parametre olarak kullanılabilirliği geniş prospektif randomize kontrollü çalışmalarla incelenmelidir.

Anahtar Kelimeler: İnsülin sensivitesi, hiperglisemi, preeklampsi, postprandiyal.

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Introduction

Insulin resistance refers to an impaired biological reaction to both exogenous and endogenous insulin. Insulin resistance is an effective phenomenon in many conditions, such as endothelial functions, carbohydrate and lipid metabolism, fluid and electrolyte balance, vascular resistance, cardiac contractility, oxidative stress, and visceral obesity. Increased insulin resistance has also been detected in preeclamptic patients. It is controversial whether insulin resistance and hyperinsulinemia in preeclamptic patients are related to weight gain during pregnancy or preeclampsia itself.

Partial insulin resistance during pregnancy can act as a stress factor affecting carbohydrate, lipid, and cardiovascular physiology, even in normal pregnancies (1). Research indicated that a fasting glucose level exceeding 100 mg/dL during pregnancy could signify a heightened risk of building up metabolic syndrome following childbirth (2).

Among individuals diagnosed with hypertensive disorders of pregnancy (HDP), preterm birth (PTB), and gestational diabetes mellitus (GDM), those who experience both HDP and PTB are at the highest risk for developing metabolic syndrome within 2 to 7 years after giving birth, regardless of risk factors present before or early in pregnancy (3).

A Brazilian retrospective cohort study examining latent risks of preeclampsia 6-15 years following childbirth, which encompassed women both with and without a prior history of preeclampsia, found a higher frequency of metabolic syndrome in the group with a history of preeclampsia (4).

Individuals diagnosed with preeclampsia encounter a heightened likelihood of developing metabolic syndrome and ischemic heart disease as they progress in age (5-9). Diagnosing metabolic syndrome during pregnancy is vital for identifying women at risk for future metabolic and cardiovascular issues.

In our study, we aim to investigate the connections among weight gain, obesity, biochemical parameters, and insulin resistance. Additionally, we assess how insulin resistance affects fetal outcomes in preeclamptic cases without gestational diabetes.

MATERIALS and METHODS

This retrospective cohort research analyzed 101 pregnant women aged 18 to 44 who were diagnosed with preeclampsia between the 24th and 40th weeks of gestation. These patients received antenatal care at the Obstetrics and Gynecology Perinatology outpatient clinic of Tepecik Training and Research Hospital. Data were gathered retrospectively from their medical records.

The research was carried out at İzmir Tepecik Training and Research Hospital in the Department of Gynecology and Obstetrics from July 2013 to January 2014, with the approval of the institution's ethics committee. This article is the result of a thesis.

Gestational age for all patients was established based on the date of their last menstrual period and further verified through ultrasound measurements conducted during the first trimester. The following data were collected: gestational age, parity, maternal age, body weight and

height, smoking history during pregnancy, weight gain throughout pregnancy, and preeclampsia criteria.

Diagnosis of preeclampsia was made in accordance with the subsequent criteria: a systolic blood pressure of 140 mmHg or higher and a diastolic blood pressure of 90 mmHg or higher, assessed a minimum of two times during a six-hour period following the 20th week of gestation. Additionally, a diagnosis required either a proteinuria level exceeding 0.3 g over 24 hours or a spot urine protein-to-creatinine ratio greater than 300 mg/mmol.

Preeclampsia with severe features is defined by any of the subsequent options: blood pressure readings of 160/110 mmHg or higher on two distinct instances; a platelet count below 100,000 per microliter; deterioration of liver function indicated via liver enzyme levels that are at least twice the normal range, or severe and persistent pain in the right upper quadrant or epigastric area; renal failure, defined as a serum creatinine level exceeding 1.1 mg/dl or an increase in the serum creatinine concentration by twofold; pulmonary edema; or the emergence of new cerebral or visual disturbances (10).

In this study, it was confirmed that participants did not have any additional illnesses, derived from an extensive medical background clinical examination, and previous laboratory tests. The research focused on pregnant women who were more than 24 weeks of gestation, were not in active labor, and did not have conditions such as premature rupture of membranes, diabetes, gestational diabetes, liver disease, cardiovascular disease, infections, chronic hypertension, gestational hypertension, or renal disease. Individuals who failed to satisfy these criteria were omitted from taking part in the study.

For the statistical analyses, cases were classified into two separate categories based on the severity of preeclampsia: mild and severe. The comparison between these groups focused on several key factors, including age, body mass index (BMI), total weight gain during pregnancy, daily cigarette consumption, hematocrit, hemoglobin, platelet count, serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic pyruvic transaminase (SGPT). Additionally, complete urinalysis and liver function tests were conducted.

Kidney function was assessed through tests measuring urea, creatinine, and uric acid levels. Other parameters analyzed included C-reactive protein (CRP), fasting glucose, glycosylated hemoglobin (HbA1c), and a lipid profile, which comprised fasting plasma lipid values such as total cholesterol, triglycerides, LDL, and HDL cholesterol. Insulin levels were measured postprandially at 120 minutes, and Doppler ultrasonography provided insights into the middle cerebral artery (MCA) and umbilical artery systole/diastole ratios.

Furthermore, the analysis examined the Homeostasis Model Assessment Insulin Resistance (HOMA-IR) index, insulin sensitivity index, gestational week at birth, birth weight, 1st and 5th-minute Apgar scores, and the duration of residence in the neonatal intensive care unit.To ensure consistency, all laboratory tests were performed on pregnant women between 24 and 28 weeks of gestation, a time frame recognized for its peak insulin resistance.

Body mass index (BMI) was determined

using the formula [weight (kg)/height (m)^2] based on patient measurements. In line with the classification established by the World Health Organization, BMI values below 25 were categorized as normal weight, values between 25 and 30 as overweight, those ranging from 30 to 40 as obese, and values above 40 as morbidly obese.

Insulin resistance was evaluated through the HOMA method. (Homeostasis Model Assessment), a method designed to evaluate the effect of fasting glucose and insulin levels on pancreatic β-cell function and insulin sensitivity. The formula used was [HOMA-IR = insulin (mU/ml) × glucose (mg/dl)/405]. Patients with a HOMA value of 2.5 or higher were identified as having insulin resistance. Additionally, the insulin sensitivity index was calculated by dividing fasting blood glucose (mg/dl) by fasting insulin level (mIU/ml), with a ratio below 6 indicating insulin resistance.

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 21 and Medcalc 9 (Acacialaan 22, B-8400 Ostend, Belgium). The normal distribution of quantitative data was evaluated using the Kolmogorov-Smirnov test, the Shapiro-Wilk test, and the coefficient of variation. To compare two independent groups, both the Independent-Samples T test and the Mann-Whitney U test were utilized. The Wilcoxon Signed Ranks Test was employed for comparing two dependent groups, whereas Pearson's Chi-Square tests were used for the comparison of categorical data. All analyses were conducted at a 95% confidence level, with a p-value of less than 0.05 considered significant.

RESULTS

The cases were assessed in two distinct groups: the first comprised cases with mild preeclampsia, while the second consisted of those with severe preeclampsia. Among the 101 patients, 51 cases (50.5%) were identified as mild preeclamptic, and 50 cases (49.5%) were classified as severe preeclamptic. The average age of the participants was 29.1 years, accompanied by a standard deviation of 6.8 years. Of these cases, 47 were nulliparous women (those who have never given birth), and 54 were multiparous women (those who have given birth more than once). Demographic information is given in Table 1.

The average BMI for both groups of pregnant women was 31.1 kg/m^2 (20.7-49.6). There was no notable difference in BMI values among individuals with mild preeclampsia (31.8 kg/m^2) and those with severe preeclampsia (30.5 kg/m^2). In the study group, 14 preeclamptic pregnant women had BMIs of 25 kg/m^2 or lower, 34 had BMIs between 25-30 kg/m^2, 48 had BMIs between 30-40 kg/m^2, and 5 had BMIs of 40 kg/m^2 or higher.

The mean weight gain among the 101 preeclamptic pregnant women during their pregnancies was 11.7±5.5 kg. No statistically remarkable difference in weight gain was found between the groups with mild and severe preeclampsia, both of which gained an average of 10.0±9.0 kg and 10.0±10.0 kg, respectively.

To review the connection among insulin resistance and weight gain, and the severity of preeclampsia, a multivariable logistic regression analysis was conducted. The findings indicated no significant correlation between insulin resistance parameters and

Table 1: Demographic data

Demographic information		Frequency (n)	Percentage %)
Diagnosis	Mild preeclampsia	51	50,5%
	Severe preeclampsia	50	49,5%
Age	<35	77	76,2%
	≥35	24	23,8%
Parity	Nulliparous	47	46,5%
	Multiparous	54	53,5%
BMI	≤25	14	13,9%
	(25-30]	34	33,7%
	(30-40]	48	47,5%
	>40	5	5,0%
Number of cigarettes smoked per day	0	88	87,1%
	1	5	5,0%
	2	3	3,0%
	3	5	5,0%

*BMI: Body Mass Index

either weight gain or BMI (p>0.05). These analyses suggested that metabolic factors such as insulin resistance, weight gain, and BMI do not play a significant role in the severity of preeclampsia.

In this study, six patients (11.8%) in the mild preeclampsia group and seven patients (14%) in the severe preeclampsia group reported a history of smoking during pregnancy. No notable difference in smoking history was detected between the two groups (p>0.05). Doppler ultrasonography results revealed no significant differences between the mild and severe preeclampsia groups. The mean MCA S/D ratios were 4.4 ± 2.9 for the mild group and 4.0 ± 2.4 for the severe group, while the UA S/D ratios were 2.9 ± 2.2 and 3.1 ± 1.3, respectively.

In terms of metabolic parameters, there were no significant differences in HbA1c values or mean fasting insulin levels between the groups. However, a statistically significant difference was marked in postprandial insulin levels (p < 0.05). The mean HOMA-IR index values were 2.1 ± 1.8 for the mild preeclampsia group and 1.8 ± 2.6 for the severe group. Additionally, the mean insulin sensitivity index values were 9.5 ± 8.3 for the mild group and 11.1 ± 12.6 for the severe group. Overall, there were no significant differences observed between the two groups in relation to the HOMA-IR index or the insulin sensitivity index (see Table 2).

When mild and severe preeclampsia patients were analyzed with regard to laboratory values, a significant difference was found in hemoglobin, hematocrit, platelet count, 24-hour urine protein, urea, uric acid, creatinine, triglyceride and total cholesterol counts (p< 0.05) (Table 3).

Upon evaluation of the groups concerning gestational age, birth weight, and APGAR scores at both 1 minute and 5 minutes, notable variations were identified (p<0.05). Within the mild preeclampsia group, 38 out of 51 newborns (74.5%) did not require intensive care. In contrast, in the severe

Table 2: Glucose metabolism, BMI and weight gain parameters of the groups

Laboratory parameters	Mild preeclampsia	Severe preeclampsia	P value
HbA1c (%)	5±0,8	5,1±0,7	0,454
Fasting insulin (mIU/ml)	9±10,2	7,3±11,9	0,366
Postprandial insulin (mIU/ml)	51,4±40,3	26,6±17,8	**0,002**
HOMA-IR index	2,1±1,8	1,8±2,6	0,289
İnsulin sensitivity index	9,5±8,3	11,1±12,6	0,377
BMI (kg/m2)	31,8±6,1	30,5±5,6	0,266
Weight gain (kg)	10,0±9,0	10,0±10,0	0,324

*HOMA-IR index: Homeostatic Model Assessment of Insulin Resistance
*BMI: Body Mass Index
*HbA1c: Glycosylated hemoglobin
*SD: Standard deviation

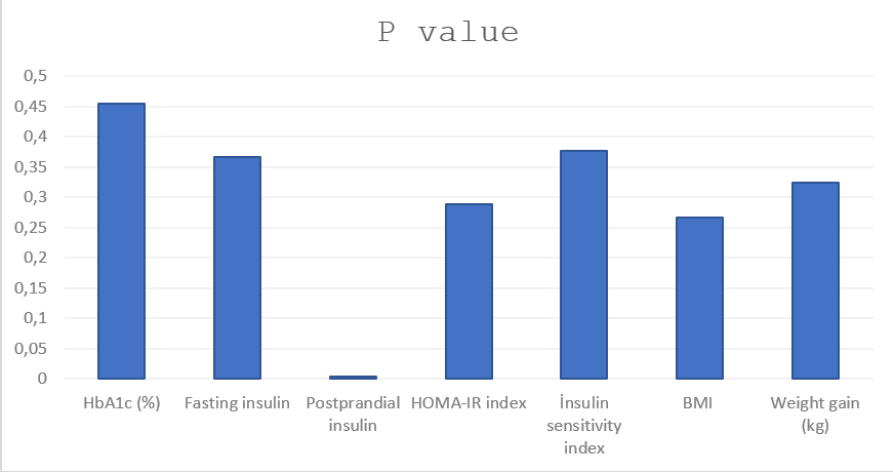

Figure 1: Graphics of glucose metabolism, BMI and weight gain parameters of the groups

preeclampsia group, 31 out of 50 newborns (62%) were admitted to the neonatal intensive care unit, reflecting a greater demand for intensive care (refer to Table 4).

DISCUSSION

Hypertension, obesity, glucose intolerance, and lipid metabolism disorders frequently co-occur. A shared characteristic of these conditions is the presence of hyperinsulinemia and Insulin resistance, which could play a big part in the development of preeclampsia. Insulin is vital for the metabolism of carbohydrates, lipids, and proteins, and it has significant effects on cardiovascular, urinary, skeletal muscle, and central nervous system functions (11,12).

A limited number of studies have investigated insulin metabolism in non-diabetic preeclamptic pregnant women and its long-term implications. Research indicates that insulin alone can stimulate the

Table 3: Laboratory parameters

Laboratory parameters	Mild preeclampsia (Mean±SD)	Severe preeclampsia (Mean±SD)	P value
Fasting glucose (mg/dl)	90,8± 19,4	85,2 ±17,6	0,133
Postprandial glucose (mg/dl)	143,5± 34,0	133,5± 40,4	0,181
Hemoglobin (g/dL)	11,36± 1,15	12,18±1,23	**0,001**
Hematocrit (%)	34,25± 3,09	35,85±3,54	**0,017**
Platelet (10^9/L)	242,06± 66,70	209,24± 53,40	**0,008**
HDL (mg/dl)	59,67±14,48	60,46±14,58	0,783
LDL (mg/dl)	158,39±81,21	169,94±80,38	0,474
Triglyceride (mg/dl)	249,14±54,95	274,92±61,79	**0,029**
Total cholesterol (mg/dl)	249,14±54,95	274,92±61,79	**0,029**
HbA1c (%)	5,07±0,88	5,19±0,78	0,454
CRP (mg/dl)	0,30±0,5	0,69±1,1	0,227
24-hour urine protein test (g/day)	0,20± 0,5	0,75±4,4	**0,002**
Blood Urea Nitrogen (mg/dl)	20,76±9,04	26,71±12,64	**0,008**
Uric Acid (mg/dl)	5,02±1,31	6,22±2,02	**0,001**
Creatinine (mg/dl)	0,60±0,16	0,67±0,17	**0,034**

*HDL: high-density lipoprotein
*LDL: low-density lipoprotein
*CRP: C-reactive protein
*SD: Standard deviation

Table 4: Fetal outcomes

Fetal outcomes	Mild preeclampsia	Severe preeclampsia Median± IQR	P
Birth week(w)	36,00±3,0	34,00±5,0	**<0,001**
Birth weight (kg)	2550±1070	1800±780	**<0,001**
Days in NICU	3±5	5±9	0,304

*NICU: Neonatal intensive care unit
* IQR: interquartile range

sympathetic nervous system (13). Typically, normal pregnancies are characterized by elevated insulin levels. However, before the onset of clinical preeclampsia, fasting insulin levels tend to be higher in preeclamptic pregnant women (14,15). Notably, this condition is not reversible in the postpartum period. Insulin resistance represents a crucial element of metabolic syndrome, which serves as a significant risk factor for cardiovascular incidents in women (16,17).

Furthermore, preeclampsia may play a part in the onset of diabetes in later stages of life, especially in cases where gestational diabetes was not diagnosed during pregnancy (18). In contrast to these previous studies, our research found no notable differences among the groups concerning HbA1c and mean fasting insulin values. Nonetheless, we observed a statistically remarkable difference in postprandial insulin levels.

Sonagra et al. conducted a study to explore insulin resistance (IR) in pregnant women with preeclampsia (n=35) compared to those without the condition (n=35). They assessed fasting plasma glucose (FPG) and fasting plasma insulin (FI) levels, as well as several IR indices, including the FPG to FI ratio (FGIR), the quantitative insulin sensitivity check index (QUICKI), and logarithmic insulin (log FI). The findings revealed that, in the preeclampsia group, mean FI and log FI were significantly elevated, while QUICKI and FGIR were notably reduced ($p<0.001$). The authors highlighted the importance of screening all pregnant women with high blood pressure for insulin resistance (19). Their conclusions are consistent with our study, indicating that monitoring for insulin resistance may be essential in cases of increased blood pressure.

Akdemir et al. approached the issue from a unique perspective by investigating the influence of preeclampsia and its intensity on insulin, HOMA-IR, and betatrophin concentrations in non-diabetic pregnant women. Their study comprised 102 non-diabetic participants, categorized into three groups: those with severe preeclampsia, those with mild preeclampsia, and a control group. The findings revealed that HOMA-IR levels were consistent across all groups. However, maternal serum insulin levels declined, while serum betatrophin levels increased as the severity of preeclampsia escalated. The authors concluded that maternal insulin, glucose, and betatrophin levels are markedly affected in cases of severe preeclampsia. (20). It is well-known that preeclampsia triggers an increased systemic inflammatory response, which can lead to damage in the vascular beds of various organs and result in maternal endothelial dysfunction (21). In our study, we noted a significant rise in postprandial insulin levels, consistent with findings from other research. However, histopathological and immunohistochemical analyses did not reveal a direct impact of preeclampsia severity on pancreatic cells. The substantial difference in insulin levels observed in both our study and the existing literature may indicate that damage to pancreatic cells is a contributing factor.

Lipatov et al. conducted a study to investigate alterations in IR, hyperinsulinemia (HI), and relevant factors associated with lipid and carbohydrate metabolism, as well as issues related to endothelial function, pro-inflammatory conditions, and prothrombotic states in pregnant women with preeclampsia. This prospective observational study examined

participants across all trimesters. The results indicated that all measured parameters in the preeclamptic group exhibited significant and abnormal increases. These changes are linked to pathological IR and HI, which represent fundamental pathways in the development of preeclampsia (PE) (22). Furthermore, our study identified significant differences in various laboratory parameters, including hemoglobin, hematocrit, platelet count, 24-hour urine protein, urea, uric acid, creatinine, triglycerides, and total cholesterol ($p < 0.05$).

Sowers et al. conducted a prospective study involving 140 African-American nulliparous pregnant women, monitoring them from 18 to 25 weeks until birth, to investigate the impact of hyperinsulinemia on the onset of preeclampsia. Insulin levels were analyzed statistically about gestational age and pre-pregnancy BMI. The study concluded, similar to our findings, that Increased blood pressure and insulin levels during the second trimester significantly contribute to the onset of preeclampsia, independent of BMI (23).

Although a high BMI is not always directly linked to metabolic syndrome, obesity is more commonly observed among individuals with this condition (24). In a comprehensive meta-analysis, O'Brien et al. (25) noted that the risk of developing preeclampsia doubles with each 5-7 kg/m^2 increase in BMI. A high BMI serves as a significant predictor of various adverse pregnancy outcomes, including preeclampsia. However, in contrast to this study, our analysis did not indicate a statistically significant difference when assessing the groups based on BMI and weight gain during pregnancy.

In a study examining the correlation between a decreased occurrence of preeclampsia in non-diabetic obese pregnant women receiving metformin and alterations in insulin resistance, researchers discovered that the median HOMA-IR levels were significantly lower in the metformin group compared to the placebo group by week 28. Furthermore, a history of chronic hypertension and weight gain during pregnancy were significant predictors of maternal preeclampsia; however, HOMA-IR did not show any significant predictive value at week 28. The authors concluded that the observed reduction in preeclampsia incidence among non-diabetic obese pregnant women receiving metformin was not attributable to changes in insulin resistance. Consistent with these findings, we also noted no significant differences in insulin resistance measurements between the severe and mild preeclampsia groups. (26).

In the study by Laughon et al., which searched the impact of uric acid concentration on IR and birth weight in normotensive pregnant women, a remarkable correlation was identified among uric acid levels and insulin resistance in mid-trimester pregnancies. Specifically, the HOMA index improved with each 1 mg/dL increase in uric acid levels among patients with a normal BMI; however, this relationship was even more pronounced in obese individuals (27). Notably, Laughon et al. did not find a connection among uric acid and IR in cases diagnosed with gestational hypertension, irrespective of whether hyperuricemia was present. In our investigation, we found a significant change in uric acid levels corresponding to the worsening of the disease in preeclamptic patients,

along with a robust association between hyperuricemia and insulin resistance.

This research has multiple constraints, such as its retrospective nature, the absence of a control group, a short follow-up duration, and a limited sample size obtained from a single clinic. While there is a concern that severe preeclampsia may contribute to premature birth and that antihypertensive treatments could affect insulin levels, we were unable to fully account for these potential influences. Furthermore, postprandial insulin was measured only at the 120-minute mark, without comparisons to measurements taken at other time points. The study also did not exclude the potential effects of medications that may induce insulin resistance, such as antihypertensives, long-term steroid therapy, and certain HIV medications.

The assessment of insulin resistance (IR) through the hyperinsulinemic-euglycemic clamp technique, recognized as the gold standard, would yield more reliable results. Despite its limitations, our study is one of the few that evaluates the impact of preeclampsia severity on glucose metabolism in non-diabetic pregnant women with preeclampsia.

CONCLUSION

This research revealed no notable differences among the groups regarding HbA1c and mean fasting insulin values; however, there was a statistically notable difference in postprandial insulin levels ($p < 0.05$).

When analyzing laboratory values in patients with mild and severe preeclampsia, significant differences were observed in hemoglobin, hematocrit, platelet count, 24-hour urine protein, urea, uric acid, creatinine, triglyceride, and total cholesterol levels ($p < 0.05$).

A review of birth weight, gestational age, and APGAR scores at 1 and 5 minutes revealed notable variations among the two groups ($p < 0.05$). In the mild preeclampsia group, 38 out of 51 newborns (66.7%) did not require intensive care, whereas in the severe preeclampsia group, 31 out of 50 newborns (70.5%) were admitted to the neonatal intensive care unit, indicating a greater need for intensive care.

Women experiencing insulin resistance may be at an increased risk for obstetric complications for instance respiratory distress syndrome, neonatal hypoglycemia, and preeclampsia. Therefore, larger-scale studies are necessary to clarify whether insulin resistance contributes to these effects in the absence of gestational diabetes mellitus (GDM).

Assessing postprandial insulin levels during pregnancy follow-up in cases of preeclampsia without GDM may aid in predicting the impact of insulin resistance and sensitivity on both maternal and fetal outcomes. Postprandial insulin levels could serve as a potential biomarker for long-term metabolic syndrome risk. Prospective randomized controlled trials will be essential in determining whether this should be included in follow-up protocols for predicting metabolic syndrome. Timely screening of preeclamptic women for insulin resistance, along with recommendations for dietary and lifestyle modifications, may help reduce complications during pregnancy and beyond.

Authors' Contribution Statement

GO: Data curation, formal analysis, investigation, methodology, conceptualization, validation, visualization, writing – original draft, writing – review and editing.

CET: Supervision

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Declaration of interest statement

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