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Evaluation of dyslipidemia in preeclamptic pregnant women and determination of the predictive value of the hemato-lipid profile: A prospective, cross-sectional, case-control study

Preeklamptik gebelerde dislipideminin değerlendirilmesi ve hemato-lipid profilin prediktif değerinin belirlenmesi: Prospektif, kesitsel, olgu-kontrol çalışması

Rauf Melekoğlu[1], Şeyma Yaşar[2], Nesibe Zeyveli Çelik[1], Halis Özdemir[3]

[1]*İnönü University Faculty of Medicine, Department of Obstetrics and Gynecology, Malatya, Turkey*

[2]*İnönü University Faculty of Medicine, Department of Biostatistics and Medical Informatics, Malatya, Turkey*

[3]*Malatya Training and Research Hospital, Clinic of Obstetrics and Gynecology, Division of Perinatology, Malatya, Turkey*

Abstract

Objective: In this study, we examined the serum hematologic and lipid parameters of pregnant women with preeclampsia and an age- and gestational-age matched normotensive control group. We also compared the ratios of hemato-lipid parameters defined as systemic inflammatory markers and determined the predictive value of these values in preeclampsia.

Materials and Methods: All patients diagnosed with late-onset preeclampsia or severe preeclampsia between 34 and 40 weeks of gestation at Inonu University Faculty of Medicine between March 2019 and October 2020 were included.

Results: A total of 253 pregnant women were included in the study period. When the study groups were compared in terms of hematological and blood lipid profile; while serum lymphocyte, triglyceride, and total cholesterol levels were significantly higher in the preeclampsia group than in the control group ($p<0.001$, $p<0.001$, $p=0.013$, respectively); high-density lipoprotein (HDL)-cholesterol levels were found to be significantly lower ($p=0.017$). The cut-off value for the monocyte/HDL ratio in predicting severe preeclampsia was 16.65 with 59.0% sensitivity and 85.4% specificity [the area under the receiver operating characteristic 0.756, 95% confidence interval (CI) 0.681-0.821, $p<0.001$]. Multivariate analysis showed that the monocyte/HDL ratio was independently associated with both preeclampsia and severe preeclampsia [odds ratio (OR): 1.094; 95% CI 1.009-1.185 and OR: 1.731; 95% CI 1.218-2.459, respectively].

Conclusion: This study demonstrated that serum triglyceride and total cholesterol levels were significantly higher and serum HDL-cholesterol levels were significantly lower in pregnant women with late-onset preeclampsia compared to normotensive pregnant women. Additionally, this study revealed that the measurement of monocyte/HDL ratio in the pregnant population could be a useful clinical tool for predicting preeclampsia.

Keywords: Dyslipidemia, pregnancy, HDL cholesterol, monocytes, preeclampsia

PRECIS: We evaluated the hemato-lipid profile of pregnant women with preeclampsia, and determined the predictive value of the ratios of hematological and lipid parameters in preeclampsia.

Address for Correspondence/Yazışma Adresi: Assoc. Prof. Rauf Melekoğlu,
İnönü University Faculty of Medicine, Department of Obstetrics and Gynecology, Malatya, Turkey
Phone: +90 506 616 60 23 **E-mail:** rmelekoglu@gmail.com **ORCID ID:** orcid.org/0000-0001-7113-6691

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Öz

Amaç: Bu çalışmada preeklamptik gebeler ile preeklampsi ile komplike olmayan gebelerin serumlarında hematolojik ve lipid parametreleri değerlendirildi. Ayrıca sistemik enflamatuvar marker olarak da tanımlanan hemato-lipid parametrelerin oranları karşılaştırılıp bu oranların preeklampsideki prediktif değeri belirlendi.

Gereç ve Yöntemler: Çalışmaya İnönü Üniversitesi Tıp Fakültesi Hastanesi'nde 01.03.2019-01.10.2020 tarihleri arasında gebeliğin 34-40. haftasında geç başlangıçlı preeklampsi ve şiddetli preeklampsi tanısı alan ve çalışma kriterlerine uygun tüm hastalar alınmış olup katılımcıların serum örneklerinde rutin laboratuvar testlerinin yanında lipid profili analizi yapılıp, gebelerin perinatal ve neonatal sonuçları kaydedildi.

Bulgular: Çalışma periyodu içinde toplam 253 gebe çalışmaya dahil edildi. Çalışma grupları hematolojik ve kan lipid profili açısından karşılaştırıldığında; preeklampsi grubunda kontrol grubuna göre serum lenfosit, trigliserid ve total kolesterol seviyeleri anlamlı olarak yüksek iken (sırasıyla p<0,0001, p<0,001, p=0,013); yüksek yoğunluklu lipoprotein (HDL)-kolesterol düzeyleri anlamlı olarak düşük saptandı (p=0,017). Hematolojik ve lipid parametrelerinin oranları değerlendirildiğinde kontrol grubu ile karşılaştırıldığında monosit/HDL oranı ve monosit/lenfosit oranlarının hem preklampsi hem de şiddetli preeklampsi grubunda anlamlı olarak yüksek olduğu saptandı (sırasıyla p=0,007, p<0,0001 ve p=0,021, p<0,0001). Şiddetli preeklampsi prediksiyonunda monosit/HDL oranı için cut-off değeri %59,0 sensitivite, %85,4 spesifite ile 16,65 [alıcı çalışma karakteristiğinin altındaki alan 0,756, %95 güven aralığı (GA) 0,681-0,821, p<0,0001] saptandı. Multivariate analiz monosit/HDL oranının bağımsız olarak hem preeklampsi hem de şiddetli preeklampsi ilişkili olduğunu gösterdi [sırasıyla risk oranı (OR): 1,094; %95 GA 1,009-1,185 ve OR: 1,731; %95 GA 1,218-2,459].

Sonuç: Bu çalışma geç başlangıçlı preeklampsi saptanan gebelerde normotansif gebelere göre serum trigliserid ve total kolesterol düzeylerinin anlamlı oranda yüksek, serum HDL-kolesterol düzeylerinin ise anlamlı oranda düşük olduğunu göstermekle birlikte gebe popülasyonunda monosit/HDL oranı ölçümünün preeklampsi gelişiminin prediksiyonu açısından yararlı olabileceğini ortaya koymuştur.

Anahtar Kelimeler: Dislipidemi, gebelik, HDL kolesterol, monosit, preeklampsi

Introduction

Preeclampsia is a complex systemic disease specific to human pregnancies that increase maternal and fetal morbidity and mortality in developed and developing countries. It complicates 5-10% of all pregnancies and is diagnosed by the detection of proteinuria and/or end-organ dysfunction with hypertension [blood pressure (BP) ≥140/90 mmHg] beginning after 20 weeks of gestation in a previously normotensive woman[1]. The pathophysiology of preeclampsia includes both maternal and fetal/placental factors. Many biomarkers have been studied to predict the development of pre-eclampsia[2,3]. Implantation of the embryo and development of the placenta that includes the trophoblast invasion are essential points for a healthy pregnancy[4]. Because of abnormal spiral artery invasion and impaired trophoblast function, the inflammatory process begins and causes alterations in angiogenic factors that proceed to placenta-mediated diseases, including preeclampsia in pregnancy. Also, it has been shown that inappropriate trophoblastic invasion and placentation, which affect the pathophysiology of preeclampsia, cause a systemic inflammatory response by releasing reactive oxygen species and cytokines from the placenta into the maternal circulation due to placental ischemia/hypoxia[5].

Circulating monocytes express tissue factors in inflammatory or pro-thrombotic conditions and change them to the procoagulant phenotype. It has been shown that high-density lipoprotein (HDL) can inhibit the expression of tissue factors in monocytes by preventing p38 activation and inhibiting phosphoinositide 3-kinase[6]. Additionally, it has been suggested that HDL neutralizes the pro-inflammatory and pro-oxidant effects of monocytes by inhibiting the migration of macrophages and increasing the oxidation of low-density lipoprotein (LDL) by promoting the outflow of accumulated cholesterol from cells in the vascular wall. Furthermore, HDL has also been shown to protect endothelial cells from inflammation and oxidative stress by controlling the activation of monocytes and the proliferation of monocyte precursor cells[7]. Many studies have shown that high monocyte count and low HDL cholesterol levels may be associated with inflammation and oxidative stress, and it has been reported that monocyte/HDL cholesterol ratio can be used as a new prognostic marker in many cardiovascular diseases, especially in atherosclerosis and metabolic syndrome[8,9]. However, there is no study in the literature evaluating the monocyte/HDL-cholesterol ratio, which is defined as a systemic inflammatory marker in many studies in preeclamptic patients.

Since the inflammatory response has been suggested to be an important process in preeclampsia, many researchers have investigated the change in leukocyte count to find the relationship between leukocyte counts and preeclampsia. They have found that leukocyte counts increase, especially in patients with preeclampsia and severe preeclampsia[10,11]. Moreover, the neutrophil count is higher in preeclamptic pregnant women than healthy ones. Researchers have found that severe inflammation in preeclampsia often accompanies neutrophil activation and develops simultaneously with clinical symptoms in these patients[12]. Some investigators have suggested that in the preeclamptic group, neutrophils and lymphocytes release various inflammatory cytokines to activate inflammatory cells and immune response, leading to endothelial dysfunction. Therefore, neutrophil and lymphocyte levels can be used as predictive markers of preeclampsia[13]. However, many hematological parameters such as neutrophil count and lymphocyte count in adults are affected by geographic location, nutritional characteristics, racial characteristics, and many other factors. To date, several studies have been conducted on predictive markers of preeclampsia, but unfortunately, only a few have been found to be significant.

In this study, we aimed to evaluate the hematological and lipid parameters in the serum of pregnant women with late-onset preeclampsia and those normotensive control groups, to compare the rates of these parameters defined as systemic inflammatory markers, and to evaluate the predictive value of these rates in preeclampsia.

Materials and Methods

Ethical Committee approval was obtained from the Inonu University School of Medicine Clinical Research Ethics Committee for the study, and the researchers committed to comply with the World Medical Association Declaration of Helsinki (including improvements added in 2013) for the conduct of medical research on human subjects throughout the study (approval number: 2019/56). All participants gave their written informed consent prior to their inclusion in the study. In this prospective, cross-sectional, case control study, lipid profile analysis was conducted in addition to routine laboratory tests in serum samples of all patients diagnosed with late-onset preeclampsia and severe preeclampsia at 34-40 weeks of pregnancy between 01.03.2019 and 01.10.2020 in the Inonu University Faculty of Medicine Department of Obstetrics and Gynecology. The perinatal and neonatal outcomes of the participants were recorded. The study's control group consisted of age and gestational age-matched normotensive pregnant women who applied to our clinic in the same period.

All pregnant women who met the following criteria were enrolled in this study: (i) Singleton viable pregnant women between 18 and 45 years old; (ii) 34^{+0}- 40^{+0} weeks of gestation (gestational age confirmed by first-trimester ultrasonography); (iii) Body mass index between 19.5-40.0 kg/m^2; (iv) Normal fetal anatomy.

The exclusion criteria were as follows: (i) Multiple pregnancy; (ii) Major fetal anomalies (fatal anomalies or require prenatal and postnatal surgery); (iii) Chromosomal anomalies, genetic syndromes, and macroscopic placental anomalies; (iv) Fetal death; (v) Patients with eclampsia, ablatio placentae, disseminated intravascular coagulation; (vi) Presence of maternal systemic disease that may affect the serum lipid profile (previously known dyslipidemia, diabetes mellitus, chronic liver disease, renal failure, hypo- hyperthyroidism, cardiovascular diseases, autoimmune diseases, cancer, active bacterial or viral infections, smoking or alcohol use); (vii) Drug use (corticosteroids, non-steroidal anti-inflammatory drugs, antilipidemic and immuno-suppressive drugs).

Procedure

All patients diagnosed with late-onset preeclampsia or severe preeclampsia at 34-40 weeks of pregnancy in the Gynecology and Obstetrics Clinic of Inonu University School of Medicine and who delivered in our center between 01.03.2019 and 01.10.2020 were included in the study. Preeclampsia was diagnosed in a pregnant woman with a systolic BP of 140 mmHg and/or diastolic BP of 90 mmHg in two BP taken four hours apart beginning after the 20th week of pregnancy in addition to the presence of proteinuria and/or end-organ dysfunction findings. Proteinuria was diagnosed when the quantity of protein in 24-hour urine exceeded 300 mg, or when it was considered unacceptable to wait for the results of protein analysis in 24-hour urine, the existence of protein in urine protein analysis with a dipstick was +2, and/or a protein/creatinine ratio of 0.3 in spot urine was used for detecting proteinuria. Signs of end-organ damage dysfunction was defined as the presence of thrombocytopenia (<100X10^3 mcL), liver dysfunction (doubling of blood transaminase levels from average concentration), presence of kidney failure (serum creatinine above 1.1 mg/dL, or doubling of creatinine levels in the absence of other renal diseases), the presence of pulmonary edema, the presence of either cerebral or visual symptoms. Severe preeclampsia was diagnosed when the systolic BP was 160 mmHg and above and/or the diastolic BP was 110 mmHg and above on two measurements at least 4 hours apart in a pregnant woman who met the criteria for preeclampsia or when end-organ dysfunction was noted. In the presence of non-severe preeclampsia, patients were followed up with weekly maternal and fetal monitoring unless there was an indication for delivery before the 37th week of pregnancy. As long as there was no deterioration in fetal or maternal status during the follow-up examinations, delivery was planned at 37 weeks of pregnancy. In the presence of severe preeclampsia at the 34th gestational week and above, delivery was scheduled as soon as the maternal condition was stabilized. Patients diagnosed with severe preeclampsia were hospitalized, and emergency hypertension treatment, eclampsia prophylaxis (loading and maintenance magnesium sulfate therapy), and antenatal corticosteroids (12 mg betamethasone intramuscularly in two doses, 24 h apart) were administered according to standard protocols. When vaginal delivery is not contraindicated, labor induction was performed according to standard protocols. Venous blood samples were collected after 12 h of fasting in the prenatal period. Total cholesterol (TC), triglyceride, and HDL cholesterol values were analyzed with the original reagent by Abbott Architect C8000 system (Abbott Diagnostics, USA), and HDL cholesterol was analyzed by direct enzymatic method without precipitation. LDL cholesterol was calculated using the Friedewald formula (TC= LDL-cholesterol+ HDL-cholesterol + Triglyceride/5).

Age (year), gravida, parity, body mass index (kg/m^2), systolic BP (mmHg), diastolic BP (mmHg), leukocytes (mm^3), neutrophils (mm^3), lymphocytes (mm^3), monocytes (mm^3), hemoglobin (g/dL) of all patients in the study and control groups, platelet (mm^3), blood urea nitrogen, creatinine (mg/dL), aspartate aminotransaminase (u/L), alanine aminotransferase (u/L), lactate dehydrogenase (u/L), uric acid, 24-hour urine protein (mg), triglyceride (mg/dL), TC (mg/dL), LDL cholesterol (mg/dL), HDL cholesterol (mg/dL), monocyte/HDL ratio, neutrophil/HDL ratio, neutrophil/lymphocyte, monocyte/lymphocyte,

platelet/lymphocyte, LDL/HDL, gestational week at the time of serum sample collection, gestational week at birth, type of delivery, birth weight, APGAR 1 minute, APGAR 5 minute, cord blood pH, cord blood base deficit, neonatal intensive care unit requirement parameters were recorded.

Power Analysis: The sample size calculation presented in the study was based on the fact that the effect that creates an increase in the monocyte/HDL ratio of 1.3 (2.4 standard deviations) in pregnant women complicated with pre-eclampsia was considered statistically significant. It was revealed that at least 61 volunteers in each group were required to detect this difference at 80% power and 5% (two-sided) significance level.

Statistical Analysis

Data were summarized with the median [minimum-maximum (min-max)]. The normality of data distribution was determined by the Kolmogorov-Smirnov test. Mann-Whitney U, Pearson chi-square test, Yates Corrected chi-square test, and Fisher's Exact chi-square test were used where appropriate for statistical analysis. Receiver operating characteristics (ROC) analysis was performed to determine the most appropriate cut-off points of the relevant variables for predicting preeclampsia and severe preeclampsia. DTROC web-based application developed by Inonu University Faculty of Medicine, Department of Biostatistics and Medical Informatics was used in ROC analysis [Yasar S, Arslan AK, Yologlu S, Colak C. DTROC: Diagnostic tests and ROC Analysis Software (Web-based software), accessed on 2019-10-20 from http://biostatapps.inonu.edu.tr/DTROC/]. For other analyses, IBM Statistical Package for the Social Sciences Statistics 22.0 program was used. Logistic regression analysis was performed for odds ratio estimations. A value of $p<0.05$ was considered statistically significant.

Results

A total of 253 pregnant women were included in the study period. While 61 of these patients were diagnosed with severe preeclampsia, preeclampsia (non-severe) was diagnosed in 96 patients. The control group consisted of age and gestational age-matched 96 normotensive pregnant women administered to our clinic in the same period. When the study groups were compared in terms of hematological and lipid profile; serum lymphocyte, triglyceride, and TC levels were significantly higher ($p<0.001$, $p<0.001$, $p=0.013$, respectively), and HDL-cholesterol levels were found to be considerably lower ($p=0.017$) in the preeclampsia group compared with the control group. There was no significant difference between the two groups regarding leukocytes, neutrophils, monocytes, and LDL-cholesterol ($p=0.589$, $p=0.074$, $p=0.222$, and $p=0.171$, respectively). When pregnant women complicated with severe preeclampsia were compared with the control group, serum leukocytes, neutrophils, monocytes, triglycerides, total cholesterol, LDL-cholesterol were found to be significantly higher ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$ and $p=0.022$, respectively) while serum HDL-cholesterol levels were found to be similar ($p=0.564$). When the ratios of hematological and lipid parameters were evaluated, it was found that monocyte/HDL ratio and monocyte/lymphocyte ratios were found to be significantly higher in both preeclampsia and severe preeclampsia groups compared to the control group ($p=0.007$, $p<0.001$, and $p=0.021$, $p<0.001$, respectively). A comparison of monocyte/HDL cholesterol and monocyte/lymphocyte ratios of the study groups compared to the control group is shown in Figure 1. The clinical characteristics and laboratory data of the study and control groups are summarized in Table 1.

ROC analysis was performed to determine the sensitivity, specificity and recommended cut-off values of monocyte/HDL, neutrophil/HDL, neutrophil/lymphocyte, monocyte/lymphocyte, thrombocyte/lymphocyte, and LDL/HDL ratios in terms of predicting the development of preeclampsia and severe preeclampsia. In the prediction of preeclampsia, cut-off value for Monocyte/HDL ratio was 19.34 [area under the receiver operating characteristics (AUROC) 0.613, 95% confidence interval (CI) 0.541-0.683, $p=0.006$] with 78.1% sensitivity and 93.33% specificity; cut-off value for neutrophil/lymphocyte ratio was 4.37 (AUROC 0.612 95% CI 0.532-0.612, $p=0.006$) with 88.5% sensitivity and 37.5% specificity; and cut-off value for monocyte/lymphocyte ratio was detected as 0.314 (AUROC 0.596, 95% CI 0.523-0.666, $p=0.021$) with 57.30% sensitivity, 68.80% specificity. In the prediction of severe preeclampsia, cut-off value for Monocyte/HDL ratio was 16.65 (AUROC 0.756, 95% CI 0.681-0.821, $p<0.001$) with 59.0% sensitivity and 85.4% specificity, cut-off value for neutrophil/HDL ratio was 137.5 (AUROC 0.612 95% CI 0.531-0.688, $p=0.016$) with 59.0% sensitivity and 62.5% specificity, and cut-off value for monocyte/lymphocyte ratio was 0.452 (AUROC 0.710, 95% CI 0.633-0.780, $p<0.001$) with 60.7% sensitivity and 79.2% specificity. The sensitivity, specificity and recommended cut-off values determined after ROC analysis of hematological and lipid parameters to predict the development of preeclampsia and severe preeclampsia are summarized in Table 2 and Table 3. ROC curves are shown in Figure 2.

When the correlations between the parameters in the preeclampsia group were examined; a significant negative correlation was detected between monocyte/HDL ratio and TC ($r=-0.324$; $p=0.001$), LDL-cholesterol ($r=-0.376$; $p<0.001$) and HDL-cholesterol ($r=-0.580$; $p<0.001$). Also, a significant positive correlation was found between the monocyte/HDL ratio and the leukocyte count ($r=0.229$; $p=0.025$) and the monocyte/lymphocyte ratio ($r=0.581$; $p<0.001$). When the correlations between the parameters in the severe preeclampsia group were analyzed; there was a significant negative correlation between monocyte/HDL ratio and TC ($r=-0.395$; $p=0.002$), LDL-cholesterol ($r=-0.316$; $p=0.016$) and HDL-cholesterol ($r=-0.632$; $p<0.001$) and a significant positive correlation was found between body mass index and monocyte/HDL ratio ($r=0.284$; $p=0.027$). The correlations between parameters in the control group, preeclampsia, and severe preeclampsia groups are summarized in Table 4.

Multivariate analysis showed that the monocyte/HDL ratio was independently associated with both preeclampsia and severe preeclampsia [odds ratio (OR): 1.094; 95% CI, 1.009-1.185 and OR: 1.731; 95% CI, 1.218-2.459, respectively] (Table 5 and Table 6).

Discussion

This study demonstrated that serum triglyceride and TC levels were significantly higher, and serum HDL-cholesterol levels were significantly lower in pregnant women with late-onset preeclampsia compared to normotensive pregnant women. Furthermore, the findings imply that the monocyte/HDL and monocyte/lymphocyte ratios are higher in pregnant women with preeclampsia, particularly in severe preeclampsia. These ratios might be valuable laboratory markers for predicting pre-eclampsia and assessing disease severity.

Several studies examining lipid levels during pregnancy and preeclampsia have been reported conflicting results[14]. Preeclampsia is characterized by maternal endothelial dysfunction. Numerous endothelial dysfunctional markers have been identified in preeclamptic women, including an imbalance of anticoagulant and procoagulant factors and increased levels of fibronectin, endothelial cell adhesion molecules, and other coagulation cascade factors[15]. High lipid levels in the bloodstream cause their accumulation within endothelial cells. This accumulation reduces prostacyclin release, resulting in oxidative stress via endothelial dysfunction, a critical mechanism in the preeclampsia pathophysiology[16]. This study found significant elevations in serum triglyceride and TC levels and a substantial reduction in serum HDL-cholesterol levels in patients with late-onset preeclampsia. Consistently, a meta-analysis of studies examining the association between maternal hyperlipidemia and preeclampsia was recently suggested that women with pre-eclampsia had significantly higher triglyceride, total cholesterol, and non-HDL cholesterol levels and lower HDL-cholesterol level than normotensive women[17]. Significantly elevated total cholesterol, triglyceride, and LDL-cholesterol levels in pregnant women with preeclampsia suggested that these lipid measurements obtained in pregnancy follow-up may help identify women at increased risk of developing preeclampsia.

Preeclampsia is a hypertensive disorder associated with severe maternal and neonatal morbidity and mortality. Therefore, pregnant women at high risk of developing preeclampsia or severe preeclampsia should be identified as soon as possible to avoid adverse pregnancy outcomes. However, efforts for

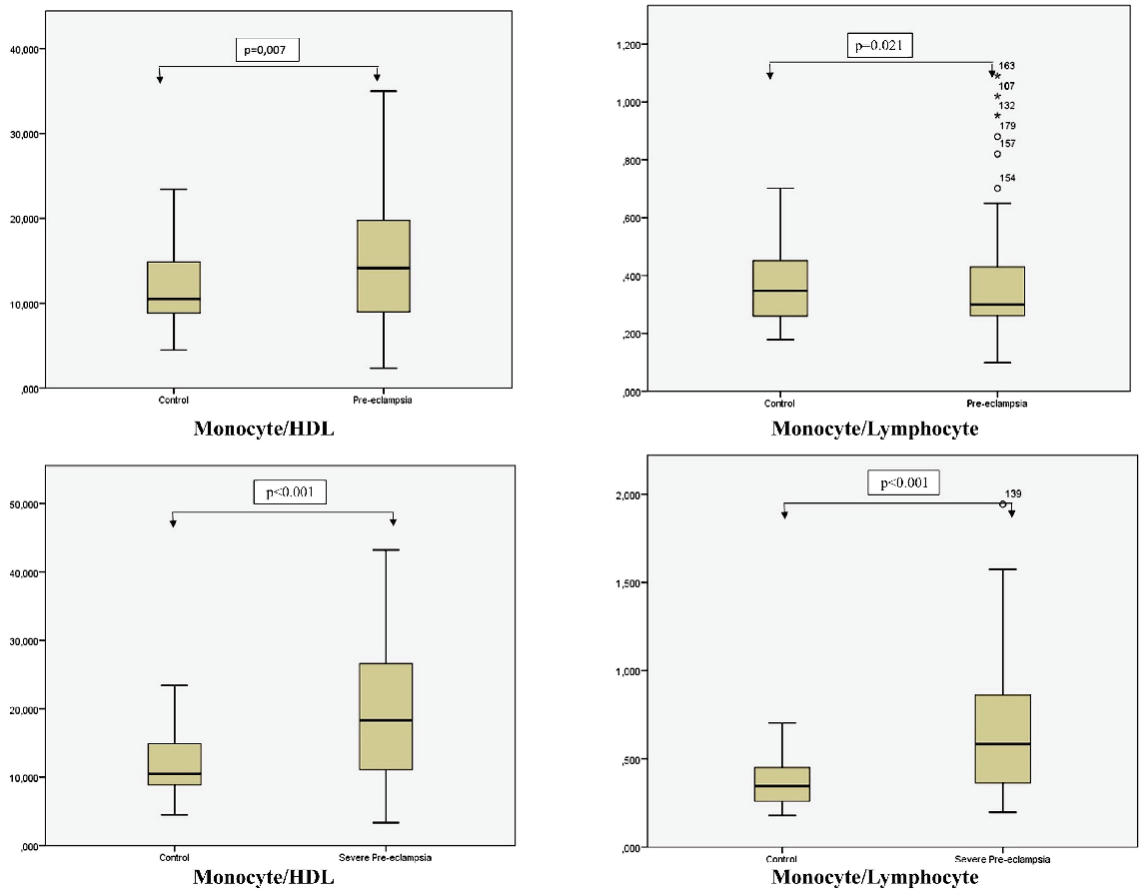

Figure 1. Comparison of monocyte/HDL cholesterol and monocyte/lymphocyte ratios of the study groups compared to the control group

HDL: High-density lipoprotein

Table 1. Clinical characteristics and laboratory data of the study and control groups

Characteristics	Control (n=96)	Preeclampsia (n=96)	Severe preeclampsia (n=61)	p-value[a]	p-value[b]	p-value[c]
Age (years)*	31 (20-42)	32 (18-44)	32 (20-44)	0.179	0.342	0.687
BMI (kg/m^2)*	29.65 (19.38-37.10)	32.8 (20.94-45.70)	29.14 (20.2-47.26)	**0.004**	**0.045**	**<0.001**
Systolic blood pressure (mmHg)*	110 (94-130)	140 (130-155)	170 (150-240)	**<0.001**	**<0.001**	**<0.001**
Diastolic blood pressure (mmHg)*	70 (60-93)	90 (80-102)	110 (90-133)	**<0.001**	**<0.001**	**<0.001**
Hemoglobin (g/L)*	12 (7.5-14.4)	11.5 (6.2-15)	11.7 (9.2-15.5)	0.704	0.414	0.697
Hematocrit (%)*	35 (25.7-40.9)	35.85 (22.4-44.4)	36.3 (26.4-44)	**0.005**	0.134	0.258
Platelet (10^3/mL)*	214 (97-307)	244 (71-431)	232 (84-475)	**0.012**	0.776	0.068
WBC (x10^3/µL)*	10.38 (5.60-14.09)	10.18 (6.14-18.9)	12.40 (6.72-23.70)	0.589	**<0.01**	**<0.001**
Neutrophil (x10^3/µL)*	7.53 (3.73-11.87)	6.29 (4.02-14.53)	8.75 (4.52-22.16)	**0.04**	**0.001**	**<0.001**
Lymphocyte (x10^3/µL)*	1.87 (1.21-2.85)	2.18 (1.11-4.62)	1.88 (0.71-4.56)	**<0.001**	0.860	0.022
Monocytes (x10^3/µL)*	0.67 (0.36-1.19)	0.66 (0.15-1.53)	1.16 (0.24-1.98)	0.222	**<0.001**	**<0.001**
BUN (mg/dL)*	6.05 (2.93-13.60)	8.37 (4.26-14.77)	10.6 (6.05-24.39)	**<0.001**	**<0.001**	**<0.001**
Creatinine (mg/dL)*	0.56 (0.40-0.74)	0.62 (0.51-0.86)	0.64 (0.43-1.07)	**<0.001**	**<0.001**	**0.181**
AST (U/L)*	16 (8-36)	18 (11-35)	20 (12-120)	**0.033**	**<0.001**	**0.003**
ALT (U/L)*	15 (6-53)	12 (6-27)	14 (6-172)	**0.018**	0.461	**0.006**
LDH (U/L)*	200 (152-309)	228 (135-411)	301 (172-701)	**0.002**	**<0.001**	**<0.001**
Uric acid (mg/dL)*	3.94 (2.76-5.9)	5.09 (2.24-6.9)	4.9 (2.57-8.03)	**<0.001**	**<0.001**	0.239
INR*	1 (0.88-1.27)	0.93 (0.83-1.17)	0.88 (0.76-1.15)	**<0.001**	**<0.001**	**<0.001**
APTT (sec)*	25.7 (16.9-68.6)	23.95 (14.8-51.1)	23.4 (18.5-36.7)	0.321	0.288	0.453
Fibrinogen (mg/dL)*	410.6 (306.9-633.7)	474.9 (298.9-759.0)	439.2 (134.8-726.6)	**<0.001**	0.166	**0.024**
CRP (mg/dL)*	0.46 (0.30-2.28)	0.68 (0.30-5.38)	1.4 (0.30-7.61)	0.258	**<0.001**	**<0.001**
Glucose (mg/dL)*	87 (65-161)	86 (58-197)	81 (53-197)	0.072	0.295	0.571
Triglyceride (mg/dL)*	208 (101-295)	242 (109-495)	255 (104-499)	**<0.001**	**<0.001**	0.419
Total cholesterol (mg/dL)*	186 (132-279)	194 (128-378)	245 (115-427)	**0.013**	**<0.001**	**0.005**
LDL-cholesterol (mg/dL)*	114.3 (61.3-163.4)	98.6 (21.5-210)	128.7 (42.5-272.7)	0.171	**0.022**	**0.005**
HDL-cholesterol (mg/dL)*	57.5 (34.4-107.0)	53.6 (31.8-79.5)	57.6 (36.5-126.3)	**0.017**	0.564	**0.008**
Neutrophil/Lymphocyte*	3.74 (2.06-8.72)	3.40 (1.10-5.90)	4.28 (1.89-20.14)	**0.007**	0.107	**<0.001**
Monocyte/Lymphocyte*	0.34 (0.17-0.70)	0.39 (0.09-1.09)	0.58 (0.19-1.94)	**0.021**	**<0.001**	**<0.001**
Platelet/Lymphocyte*	120.53 (41.28-200)	127.01 (29.06-208.48)	106.35 (38.99-388.7)	0.940	0.122	0.381
Monocyte/HDL*	10.51 (4.49-23.43)	14.15 (2.34-34.98)	18.30 (3.36-43.22)	**0.007**	**<0.001**	**0.003**
Neutrophil/HDL*	120.82 (47.04-256.37)	122.57 (58.24-303.98)	140.61 (44.42-449.08)	0.371	**0.018**	0.098
LDL/HDL*	1.82 (0.61-3.21)	1.98 (0.46-3.29)	2.04 (0.89-4.49)	0.846	0.149	0.275
Gravidity*	3.0 (1.0-7.0)	3.0 (1.0-6.0)	3.0 (1.0-7.0)	0.146	0.962	0.322
Parity*	1.0 (0.0-5.0)	1.0 (0.0-5.0)	0.0 (0.0-5.0)	0.388	0.084	0.292
Gestational age at birth (weeks)*	37 (34-39)	34 (39-37)	39 (37-34)	**0.006**	**<0.001**	**<0.001**
Birthweight (g)*	2925 (2230-3550)	2230 (3550-2740)	3550 (2740-1680)	**<0.001**	**<0.001**	**<0.001**

Table 1. Continued

Characteristics		Control (n=96)	Preeclampsia (n=96)	Severe preeclampsia (n=61)	p-value[a]	p-value[b]	p-value[c]
1st minute Apgar score*		8 (5-9)	5 (9-8)	9 (8-6)	**0.023**	**<0.001**	**<0.001**
5th minute Apgar score*		9 (6-10)	6 (10-9)	10 (9-7)	**0.040**	**<0.001**	**<0.001**
Umbilical cord pH*		7.37 (7.27-7.44)	7.27 (7.44-7.33)	7.44 (7.33-7.04)	**<0.001**	**<0.001**	**0.003**
Umbilical cord base excess*		-4.9 (-9.6-1.7)	-9.6 (-1.7-4.8)	-1.7 (-4.8-12.1)	**0.021**	0.106	0.863
Preeclampsia in obstetric history**		0 (0)	4 (4.1)	12 (19.6)	0.061	**<0.001**	**<0.001**
FGR in obstetric history**		4 (4.2)	20 (20.8)	24 (39.3)	**0.001**	**<0.001**	**0.020**
Mode of delivery**	Vaginal	22 (22.9)	16 (16.6)	5 (8.2)	0.365	**0.030**	0.201
	Cesarean section	74 (77.1)	80 (83.3)	56 (91.8)			
Gender**	Female	52 (54.2)	49 (51.0)	33 (54.1)	0.773	0.993	0.709
	Male	44 (45.8)	47 (49.0)	28 (45.9)			
NICU requirement**		11 (11.5)	27 (28.1)	42 (68.8)	**0.007**	**<0.001**	**<0.001**

*Median (min-Max) **n (%), BMI: Body mass index, WBC: White blood count, BUN: Blood urea nitrogen, AST: Aspartate Aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, INR: International normalized ratio, APTT: Activated partial thromboplastin time, CRP: C-reactive protein test, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, FGR: Fetal growth restriction, NICU: Neonatal intensive care unit.
[a]Shows statistical significance between preeclampsia and control groups.
[b]Shows statistical significance between severe preeclampsia and control groups.
[c]Shows statistical significance between preeclampsia and severe preeclampsia groups.
Significant p values are shown in bold

Table 2. ROC analysis showing the predictive value of inflammatory markers for preeclampsia

Variables	Cut-off	Sensitivity	Specificity	LR+	LR-	PPV	NPV	AUC (95% CI)	p-value
Neutrophil/ Lymphocyte	4.378	88.5 (80.4-94.1)	37.5 (27.8-48.0)	1.42	0.31	58.61	76.53	0.612 (0.532-0.612)	**0.006**
Monocyte/ Lymphocyte	0.314	57.3 (46.8-67.3)	68.8 (58.5-77.8)	1.83	0.62	64.75	61.71	0.596 (0.523-0.666)	**0.021**
Platelet/Lymphocyte	136.204	40.6 (30.7-51.1)	74.0 (64.0-82.4)	1.56	0.80	60.96	55.47	0.503 (0.430-0.576)	0.941
Monocyte/HDL	19.346	78.1 (69.4-88.2)	96.9 (91.1-99.4)	9.0	0.74	90.06	57.41	0.613 (0.541-0.683)	**0.006**
Neutrophil/HDL	86.376	91.7 (84.2-96.3)	24.0 (15.8-33.7)	1.21	0.35	54.7	74.2	0.537 (0.464-0.609)	0.375
LDL/HDL	2.663	16.7 (9.8-25.6)	95.8 (89.7-98.9)	4.00	0.87	80.0	53.5	0.508 (0.435-0.581)	0.848

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, LR: Likelihood ratio, PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the curve, ROC: Receiver operating characteristic, CI: Confidence interval. Significant p values are shown in bold

predicting pre-eclampsia remain elusive up to now. Given that inflammation is thought to be a critical step in preeclampsia development, several studies have been conducted to reveal alterations in hematological inflammatory markers in preeclampsia[18,19]. Systemic inflammatory indices formed from peripheral blood cells have recently gained much importance due to both simplicity of measurement and availability. These combined parameters are derived from basic measures such as the neutrophil-lymphocyte ratio and monocyte-lymphocyte ratio. They have been extensively used to make a diagnosis or predict the severity of septicemia, spondyloarthritis, and hepatocellular cancer[20-22]. Monocyte-lymphocyte ratio and neutrophil-lymphocyte ratio are hematological inflammatory indices determined by activators of inflammation (neutrophils/monocytes) and regulators of inflammation (lymphocytes) that are assumed to be effective predictors of systemic inflammation and immune balance. Although abnormal white blood cell counts have been documented in preeclampsia, their relevance in clinical evaluation, differential diagnosis, and prognostic assessment remains unknown. Recently, Kang et al.[23] carried out a meta-analysis including 3.982 patients who evaluated the predictive role of neutrophil-to-lymphocyte ratio in preeclampsia. They suggested that the neutrophil-to-lymphocyte ratio is a potential predictive biomarker because of its

considerable elevation in preeclamptic pregnancies, particularly in pregnant women with severe preeclampsia. Besides, Wang et al.[24] investigated the contribution of systemic hematological inflammation indices (including neutrophil-lymphocyte ratio and monocyte-lymphocyte ratio) to the pathogenesis of preeclampsia. In pregnant women with preeclampsia, they found higher monocyte-lymphocyte and monocyte-lymphocyte ratios. These results are in accordance with our findings. Therefore, the predictive value of the monocyte-lymphocyte ratio in preeclampsia and severe preeclampsia may arise due to its indicator properties for systemic inflammatory/immune response.

Preeclampsia is a multisystem condition with unknown pathogenetic mechanisms. Given that the only treatment option is delivery, early detection and prevention are critical for avoiding adverse perinatal outcomes. As a result, interest in the role of novel biomarkers that could aid in identifying high-risk pregnant women and give light on the disorder's etiology is developing. Our study data indicate that the monocyte/HDL ratio is higher in preeclamptic pregnant

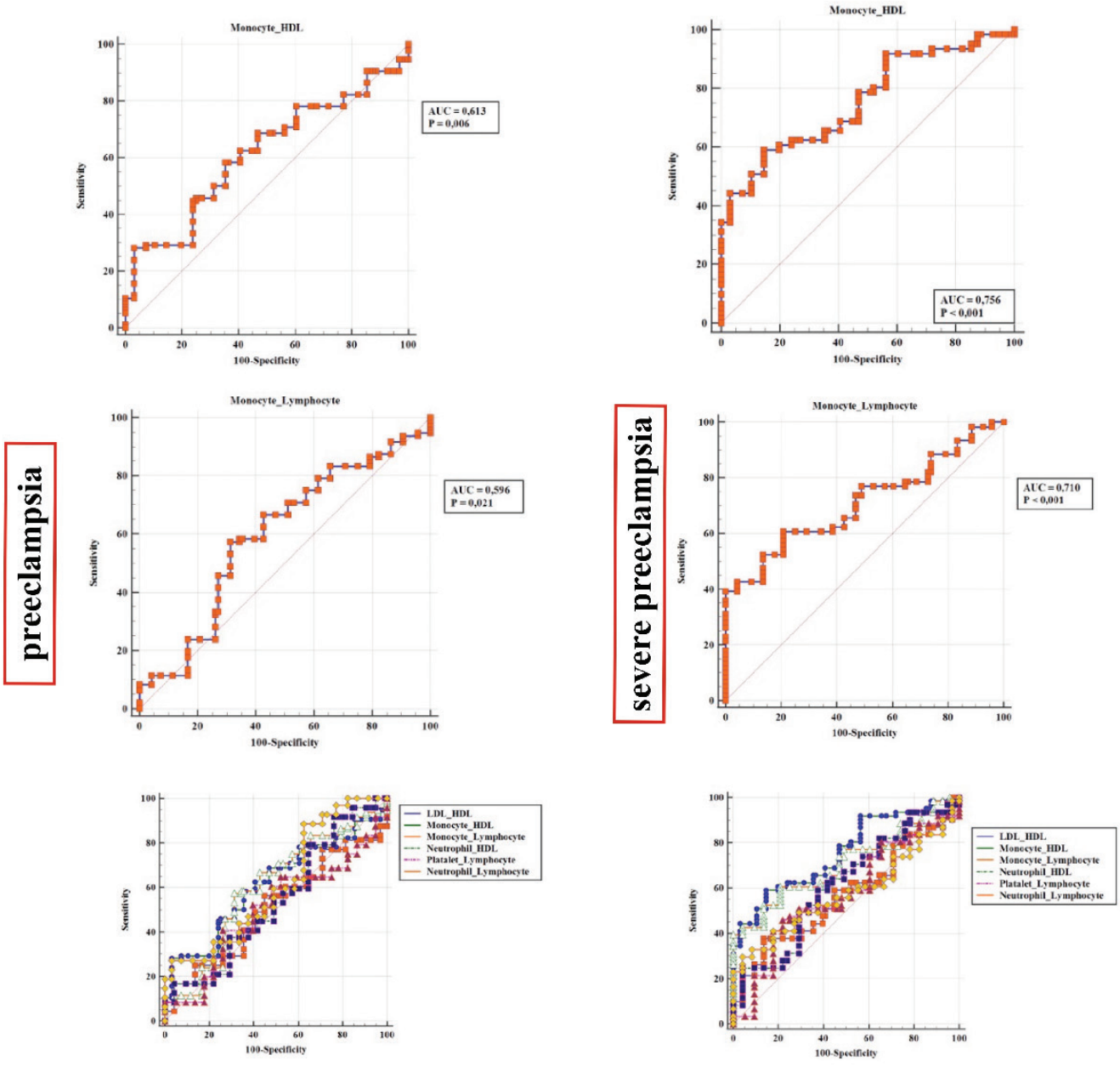

Figure 2. Receiver operating characteristic analysis showing the utility of monocyte/HDL and monocyte/lymphocyte ratios in patients with preeclampsia and severe preeclampsia

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, AUC: Area under the curve

Table 3. ROC analysis showing the predictive value of inflammatory markers for severe preeclampsia

Variables	Cut-off	Sensitivity	Specificity	LR+	LR-	PPV	NPV	AUC (95% CI)	p-value
Neutrophil/ Lymphocyte	7.628	29.5 (18.5-42.6)	95.8 (89.7-98.9)	7.08	0.74	87.6	57.6	0.576 (0.495-0.655)	0.136
Monocyte/ Lymphocyte	0.452	60.7 (47.3-72.9)	79.2 (69.7-86.8)	2.91	0.50	74.4	66.8	0.710 (0.633-0.780)	**<0.001**
Platelet/Lymphocyte	94.889	45.9 (33.1-59.2)	78.1 (68.5-85.9)	2.10	0.69	67.7	59.1	0.573 (0.492-0.652)	0.131
Monocyte/HDL	16.652	59.0 (45.7-71.4)	85.4 (76.7-91.8)	4.05	0.48	80.2	67.6	0.756 (0.681-0.821)	**<0.001**
Neutrophil/HDL	137.575	59.0 (45.7-71.4)	62.5 (52.0-72.2)	1.57	0.66	61.1	60.4	0.612 (0.531-0.688)	**0.016**
LDL/HDL	2.353	37.7 (25.6-51.0)	86.5 (78.0-92.6)	2.78	0.72	73.6	58.1	0.568 (0.487-0.647)	0.166

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, LR: Likelihood ratio, PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the curve, CI: Confidence interval, ROC: Receiver operating characteristic

women, and it is a useful biochemical marker for clinical prognosis and disease severity assessment in patients with preeclampsia. Also, the results of this study revealed that the monocyte/HDL ratio is independently associated with both preeclampsia and severe preeclampsia. To the best of our knowledge, this is the first report evaluating maternal serum monocyte/HDL ratio in pregnant women with preeclampsia and severe preeclampsia. Monocytes account for approximately 3-8% of all circulating leukocytes and, along with other granular and agranular cell lines such as basophils, eosinophils, lymphocytes, and neutrophils, are critical elements of innate immunity[25]. Monocytes play an essential role in the onset and regression of inflammation in tissues; this is accomplished primarily through phagocytosis, the release of pro-inflammatory mediators, the presence of reactive oxygen species, and activation of the acquired immune system. By contrast, HDL cholesterol counteracts monocytes' pro-inflammatory and pro-oxidant effects by inhibiting the oxidation of LDL molecules and macrophage migration, as well as promoting cholesterol efflux from these cells[26]. Along with the well-established anti-inflammatory and antioxidant properties of HDL-cholesterol, it has been recently claimed that these molecules act as a suppressive factor in regulating monocyte activation, proliferation, and differentiation of monocyte progenitor cells. The monocyte count to HDL-cholesterol ratio has been reported to be a novel predictor and prognostic indicator of mortality and morbidity in various chronic inflammatory diseases, including cardiovascular disease, chronic kidney disease, abdominal aortic aneurysm, intracerebral hemorrhage, hypertension, and metabolic syndrome[27]. In accordance, recently, Dincgez Cakmak et al.[28] found higher serum monocyte/HDL ratio levels in women with polycystic ovary syndrome (PCOS) that underlie chronic low-grade inflammation in the molecular mechanisms of this syndrome. They showed that monocyte/HDL ratio was an independent predictor of metabolic syndrome in patients with PCOS. Previous studies showed a significant association between monocyte/HDL ratio and inflammation and oxidative stress. Our findings are parallel to the previous studies' observations that confirm our results.

Study Limitations

The current study has a few limitations, such as a cross-sectional study design and the single-center population. However, the number of participants in the study was sufficient to assess the predictive value of inflammatory markers. The major limitation of the study was that only pregnant women with late-onset preeclampsia were included in the study, and cases that presented before 34 weeks of gestation were not included. Additionally, we could only analyze hemato-lipid parameters from the third trimester. Serial maternal serum measurements, including measurements in the first and second trimesters, were not performed during pregnancy. The study's main strength was the first assessment of monocyte/HDL ratio in pregnant women complicated with preeclampsia and severe preeclampsia. The prospective cohort design was additional strength.

Conclusion

This study found that serum triglyceride and TC levels were significantly higher in pregnant women with late-onset preeclampsia, while serum HDL-cholesterol levels were significantly lower. Furthermore, when hematological and lipid parameters were compared, it was shown that preeclamptic and severe preeclamptic pregnant women had considerably greater monocyte/HDL and monocyte/lymphocyte ratios, whereas the monocyte/HDL ratio was independently related to preeclampsia and severe preeclampsia. The results of this study also revealed that the measurement of monocyte/HDL ratio in the pregnant population could be a useful clinical tool for predicting the development of preeclampsia, and further studies must reveal the role of dyslipidemia in elucidating the pathophysiology of complications associated with preeclampsia.

Table 4. Correlations between hemato-lipid profile and inflammatory markers in the control and study groups

Correlations															
Groups			BMI	Hemoglobin	PLT	WBC	Total cholesterol	LDL-cholesterol	HDL-cholesterol	Neutrophil/ Lymphocyte	Monocyte/ Lymphocyte	Platelet/ Lymphocyte	Monocyte/ HDL	Neutrophil/ HDL	LDL/ HDL
Control	Age	Spear rho	-0.030	-0.066	-0.076	0.011	0.042	-0.046	0.010	-0.004	-0.120	-0.004	-0.119	-0.050	-0.078
		p-value	0.770	0.523	0.463	0.913	0.681	0.655	0.919	0.968	0.245	0.971	0.248	0.626	0.452
	BMI	Spearman rho		0.303	-0.047	-0.140	0.093	-0.147	0.101	0.110	-0.076	0.085	-0.170	0.039	-0.046
		p-value		**0.003**	0.647	0.175	0.369	0.154	0.329	0.284	0.460	0.409	0.097	0.708	0.657
	Hemoglobin	Spearman rho			-0.150	0.020	0.236	0.238	0.232	0.122	0.064	-0.048	-0.052	-0.049	0.114
		p-value			0.143	0.847	**0.021**	**0.019**	**0.023**	0.235	0.535	0.644	0.616	0.635	0.267
	PLT	Spearman rho				0.060	0.032	0.057	-0.022	0.257	-0.126	0.750	-0.189	0.195	0.124
		p-value				0.558	0.754	0.582	0.833	**0.012**	0.223	**<0.001**	0.065	0.057	0.228
	WBC	Spearman rho					-0.357	-0.426	-0.206	0.665	0.257	0.008	0.349	0.739	-0.367
		p-value					**<0.001**	**<0.001**	**0.045**	**<0.001**	**0.011**	0.939	**<0.001**	**<0.001**	**<0.001**
	Total cholesterol	Spearman rho						0.508	0.074	-0.014	0.053	0.233	-0.165	-0.274	0.477
		p-value						**<0.001**	0.471	0.889	0.608	**0.022**	0.107	**0.007**	**<0.001**
	LDL-cholesterol	Spearman rho							0.297	-0.040	0.246	0.281	-0.149	-0.488	0.627
		p-value							**0.003**	0.698	**0.016**	**0.005**	0.147	**<0.001**	**<0.001**
	HDL-cholesterol	Spearman rho								-0.266	-0.075	-0.142	-0.550	-0.710	-0.451
		p-value								**0.009**	0.469	0.168	**<0.001**	**<0.001**	**<0.001**
	Neutrophil/ lymphocyte	Spearman rho									0.430	0.580	0.223	0.710	0.061
		p-value									**<0.001**	**<0.001**	**0.029**	**<0.001**	0.552
	Monocyte/ lymphocyte	Spearman rho										0.299	0.698	0.182	0.179
		p-value										**0.003**	**<0.001**	0.075	0.081
	Platelet/ lymphocyte	Spearman rho											0.012	0.272	0.386
		p-value											0.905	**0.007**	**<0.001**
	Monocyte/HDL	Spearman rho												0.502	0.236
		p-value												**<0.001**	**0.021**
	Neutrophil/HDL	Spearman rho													0.024
		p-value													0.816

Table 4. Continued

Correlations															
Groups			BMI	Hemoglobin	PLT	WBC	Total cholesterol	LDL-cholesterol	HDL-cholesterol	Neutrophil/ Lymphocyte	Monocyte/ Lymphocyte	Platelet/ Lymphocyte	Monocyte/ HDL	Neutrophil/ HDL	LDL/ HDL
Preeclampsia	Age	Spearman rho	0.641	0.021	-0.144	-0.083	-0.184	-0.368	-0.145	-0.224	0.150	-0.085	0.157	-0.057	-0.331
		p-value	**<0.001**	0.837	0.163	0.422	0.072	**<0.001**	0.160	**0.029**	0.144	0.409	0.127	0.582	**0.001**
	BMI	Spearman rho		0.022	-0.110	0.021	-0.228	-0.428	-0.017	-0.037	0.009	-0.025	0.064	0.020	-0.403
		p-value		0.833	0.285	0.841	**0.025**	**<0.001**	0.869	0.722	0.931	0.806	0.535	0.844	**<0.001**
	Hemoglobin	Spearman rho			-0.581	0.321	0.089	0.116	0.348	0.084	0.055	-0.519	-0.048	-0.054	0.063
		p-value			**<0.001**	**0.001**	0.388	0.259	**0.001**	0.414	0.597	**<0.001**	0.640	0.602	0.543
	PLT	Spearman rho				0.121	0.246	0.133	-0.045	0.130	0.006	0.646	-0.085	0.151	0.011
		p-value				0.241	**0.016**	0.196	0.662	0.208	0.953	**<0.001**	0.412	0.143	0.912
	WBC	Spearman rho					0.018	-0.031	0.182	0.244	0.016	-0.213	0.229	0.478	-0.158
		p-value					0.862	0.764	0.075	**0.016**	0.874	**0.037**	**0.025**	**<0.001**	0.124
	Total cholesterol	Spearman rho						0.857	0.451	0.315	0.127	0.287	-0.324	-0.202	0.574
		p-value						**<0.001**	**<0.001**	**0.002**	0.219	**0.005**	**0.001**	**0.048**	**<0.001**
	LDL-cholesterol	Spearman rho							0.406	0.375	0.103	0.249	-0.376	-0.186	0.753
		p-value							**<0.001**	**<0.001**	0.317	**0.014**	**<0.001**	0.069	**<0.001**
	HDL-cholesterol	Spearman rho								0.038	-0.062	-0.017	-0.580	-0.636	-0.202
		p-value								0.711	0.549	0.871	**<0.001**	**<0.001**	**0.048**
	Neutrophil/ lymphocyte	Spearman rho									0.524	0.561	0.088	0.506	0.354
		p-value									**<0.001**	**<0.001**	0.392	**<0.001**	**<0.001**
	Monocyte/ lymphocyte	Spearman rho										0.282	0.581	0.234	0.167
		p-value										0.005	**<0.001**	**0.022**	0.104
	Platelet/ lymphocyte	Spearman rho											-0.144	0.139	0.169
		p-value											0.163	0.178	0.099
	Monocyte/ HDL	Spearman rho												0.553	0.001
		p-value												**<0.001**	0.990
	Neutrophil/ HDL	Spearman rho													0.202
		p-value													**0.049**

Table 4. Continued

Correlations															
Groups			BMI	Hemoglobin	PLT	WBC	Total cholesterol	LDL-cholesterol	HDL-cholesterol	Neutrophil/ Lymphocyte	Monocyte/ Lymphocyte	Platelet/ Lymphocyte	Monocyte/ HDL	Neutrophil/ HDL	LDL/ HDL
Severe Preeclampsia	Age	Spearman rho	-0.037	-0.099	0.041	0.012	-0.294	-0.353	-0.112	0.159	0.074	0.087	0.079	0.076	-0.309
		p-value	0.776	0.446	0.753	0.930	**0.022**	**0.005**	0.389	0.221	0.570	0.503	0.543	0.559	**0.015**
	BMI	Spearman rho		-0.096	-0.106	0.178	-0.110	-0.156	-0.189	0.069	0.118	-0.221	0.284	0.233	0.015
		p-value		0.464	0.417	0.170	0.397	0.230	0.144	0.597	0.366	0.087	**0.027**	0.071	0.911
	Hemoglobin	Spearman rho			-0.040	-0.011	0.121	0.061	0.330	-0.184	-0.095	-0.264	-0.153	-0.128	-0.126
		p-value			0.759	0.931	0.354	0.639	**0.009**	0.155	0.468	**0.040**	0.239	0.326	0.332
	PLT	Spearman rho				0.195	0.290	0.304	0.080	-0.263	-0.268	0.517	-0.077	-0.055	0.272
		p-value				0.131	**0.023**	0.017	0.538	**0.041**	**0.037**	**<0.001**	0.556	0.676	**0.034**
	WBC	Spearman rho					0.008	0.029	-0.086	0.471	0.090	0.017	0.245	0.797	0.050
		p-value					0.954	0.823	0.512	**<0.001**	0.489	0.895	0.057	**<0.001**	0.700
	Total cholesterol	Spearman rho						0.934	0.514	-0.288	-0.200	0.065	-0.395	-0.346	0.614
		p-value						**<0.001**	**<0.001**	**0.024**	0.122	0.616	**0.002**	**0.006**	**<0.001**
	LDL-cholesterol	Spearman rho							0.356	-0.316	-0.209	0.052	-0.306	-0.276	0.789
		p-value							**0.005**	**0.013**	0.107	0.693	**0.016**	**0.032**	**<0.001**
	HDL-cholesterol	Spearman rho								-0.039	-0.043	0.127	-0.632	-0.578	-0.223
		p-value								0.765	0.740	0.329	**<0.001**	**<0.001**	0.084
	Neutrophil/ lymphocyte	Spearman rho									0.653	0.437	0.189	0.577	-0.386
		p-value									**<0.001**	**<0.001**	0.145	**<0.001**	**0.002**
	Monocyte/ lymphocyte	Spearman rho										0.297	0.598	0.243	-0.257
		p-value										**0.020**	**<0.001**	0.059	**0.046**
	Platelet/ lymphocyte	Spearman rho											-0.135	0.001	-0.084
		p-value											0.298	0.995	0.521
	Monocyte/HDL	Spearman rho												0.518	0.053
		p-value												**<0.001**	0.683
	Neutrophil/HDL	Spearman rho													0.017
		p-value													0.899

BMI: Body mass index, WBC: White blood count, LDL: Low-density lipoprotein, HDL: High-density lipoprotein. Significant p values are shown in bold

Table 5. Odds ratios for preeclampsia risk calculated by multivariate regression analysis

Variables	Odds ratio	95% CI for odds ratio		p-value
		Lower	Upper	
Age	0.916	0.861	0.975	**0.006**
Monocyte/HDL ratio	1.094	1.009	1.185	**0.029**
Triglyceride	1.008	1.000	1.016	0.061
Total cholesterol	1.040	1.015	1.065	**0.001**
LDL cholesterol	0.953	0.919	0.989	**0.011**
LDL/HDL	1.564	0.507	4.823	0.437

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, CI: Confidence interval. Significant p values are shown in bold

Table 6. Odds ratios for severe preeclampsia risk calculated by multivariate regression

Variables in the equation	Odds ratio	95% CI for odds ratio		p-value
		Lower	Upper	
Age	0.906	0.801	1.024	0.114
BMI	0.953	0.850	1.070	0.417
Neutrophil/lymphocyte ratio	2.198	0.893	5.410	0.086
Monocyte/lymphocyte ratio	0.020	0.000	123.594	0.380
Platelet/lymphocyte ratio	0.996	0.976	1.017	0.734
Monocyte/HDL ratio	1.731	1.218	2.459	**0.002**
Neutrophil/HDL ratio	0.978	0.948	1.009	0.162
LDL/HDL	0.247	0.021	2.946	0.269
Triglyceride	1.022	1.007	1.038	**0.005**
Total cholesterol	1.063	1.015	1.113	**0.010**
LDL cholesterol	0.992	0.925	1.064	0.818

BMI: Body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, CI: Confidence interval. Significant p values are shown in bold

Ethics

Ethics Committee Approval: Ethical Committee approval was obtained from the Inonu University School of Medicine Clinical Research Ethics Committee for the study, and the researchers committed to comply with the World Medical Association Declaration of Helsinki (including improvements added in 2013) for the conduct of medical research on human subjects throughout the study (approval number: 2019/56).

Informed Consent: All participants gave their written informed consent prior to their inclusion in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: R.M., Design: R.M., Data Collection or Processing: Ş.Y., Analysis or Interpretation: Ş.Y., Literature Search: N.Z.Ç., H.Ö., Writing: R.M.

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

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