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MATERNAL SERUM ADIPONECTIN, LEPTIN, AND ADIPONECTIN/LEPTIN RATIO AS BIOMARKERS FOR PREECLAMPSIA

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ABSTRACT

Background: Preeclampsia (PE) is still one of the major causes of both maternal and fetal morbidity and mortality. Prevention, prediction, and effective management are therefore a major pillar in reducing these complications. Many hypotheses suggest that serum adiponectin and leptin may play a role in the pathogenesis of preeclampsia, and this study evaluates the possibility of predicting preeclampsia by these biomarkers. **Objective of the Study:** To assess the level of maternal serum leptin, adiponectin, and the adiponectin/leptin ratio as biomarkers for prediction of preeclampsia. **Patients and Methods:** A prospective case-control study of one hundred pregnant women with singleton pregnancies in their second or third trimester, aged above 18 years, with normal or overweight body mass index, was conducted at Al-Khanssa and Al-Batool Teaching Hospitals in Mosul City, Iraq, from 7th January to 1st December 2023. The case group consisted of fifty pregnant women with PE, and the control group consisted of fifty normotensive pregnant women. Maternal serum leptin and adiponectin were measured and compared, along with the ratio between the study and control groups, and the results were analyzed statistically. **Results:** The mean age and BMI of cases were significantly higher than those of controls ($p = 0.018$, $p < 0.001$, respectively). The mean levels of serum leptin and adiponectin were significantly higher among cases than controls ($p < 0.001$, $p = 0.002$, respectively), while no significant difference was detected between them regarding the adiponectin/leptin ratio. The area under the curve (for leptin and adiponectin as predictors of PE) was 0.759 (95% CI 0.663–0.855) and 0.679 (95% CI 0.575–0.783), respectively. The validity indicators of leptin and adiponectin as predictors of PE were as follows: sensitivity (72%, 54%), specificity (76%, 78%), PPV (75%, 71.1%), NPV (73.1%, 62.9%), and total agreement (74%, 66%), respectively. No significant difference was detected between the leptin and adiponectin test values and the real diagnosis of PE ($p = 0.845$ and 0.058, respectively). **Conclusions:** Maternal serum adiponectin, leptin, and the adiponectin-leptin ratio could serve as predictors for PE.

KEYWORDS: Leptin, Adiponectin, Adiponectin/Leptin Ratio, Preeclampsia, Pregnancy.

1. INTRODUCTION

Preeclampsia is a pregnancy-specific syndrome. It affects 2–8% of pregnancies globally and is progressive, unpredictable, and serious. It is associated with substantial maternal and fetal morbidity and mortality.[1], [2]

Preeclampsia is defined as gestational hypertension (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg at ≥20 weeks of gestation) accompanied by one or more of the following new-onset conditions at ≥20 weeks of gestation: (A) proteinuria; (B) other maternal end-organ dysfunction, such as renal insufficiency or acute kidney injury, hematological involvement (thrombocytopenia, hemolysis, or disseminated intravascular coagulation), liver involvement, neurological involvement (eclampsia, hyperreflexia with sustained clonus, persistent new headache, persistent visual disturbances, altered mental status, or stroke), and pulmonary edema; or (C) uteroplacental dysfunction (e.g., placental abruption,

angiogenic imbalance, fetal growth restriction, abnormal umbilical-artery Doppler waveform analysis, or intrauterine fetal death).[3], [4], [5]

Appearance of proteinuria remains an important objective marker and reflects the system-wide endothelial leak that distinguishes severe PE syndrome; repeated urine analyses to screen for the condition are part of standard antenatal care, especially for risk groups.[6] Early detection of pregnancy-related disorders is a major challenge that not only affects pregnancy health in low- and middle-income countries, but shortfalls of the currently available screening or diagnostic methods also contribute to delayed detection and management of high-risk pregnancies in high-income countries.[7]

Impending or active preeclampsia can be detected by circulating biomarkers or Doppler ultrasound assessment of the utero-placental circulation, which is useful for the early-onset but not the late-onset form of the syndrome; circulating biomarkers may be placental or maternal.[8], [9] Ideally, diagnosis should be made early in pregnancy, when interventions could begin before clinical features are manifest, and combinations of demographic and clinical factors with maternal blood pressure, uterine artery Doppler measurements, and blood biomarker assessments have been assembled to improve predictive efficiency.[10]

Adipokines are a vast group of signaling proteins and mediators secreted primarily from adipose tissue. Pro-inflammatory adipokines such as leptin correlate positively with the amount of adipose tissue and obesity, suggesting an accompanying chronic, low-grade inflammation; in an analogous manner, anti-inflammatory adipokines such as adiponectin, though fewer, have been found to be decreased in overweight individuals, and the role of adipokines in pregnancy and even in various pregnancy complications appears to be key to clarifying these metabolic processes.[11] Adipocytes release hundreds of signaling molecules that are responsible for the regulation of local and systemic cellular activities through their autocrine, paracrine, and endocrine activity.[12]

The abnormal leptin-to-adiponectin ratio is often observed in individuals with impaired glucose tolerance, dyslipidemias, and high blood pressure[13], conditions that lead directly to the development of metabolic syndrome.[14] The foremost source of leptin is adipose tissue; however, it may also be produced through the placenta (syncytiotrophoblast), ovaries, skeletal muscle, bone marrow, and pituitary gland.[15] In pregnant women, leptin is created in and secreted from placental trophoblast into the maternal circulation in substantial quantity and has been implicated in platelet aggregation and arterial thrombosis.[16] Leptin protein and mRNA levels are increased in the placenta of PE women compared with healthy pregnant controls.[17], with peaks occurring around 28 weeks of gestation before decreasing to pre-gravid concentrations immediately after delivery.[1] The increased levels of leptin in PE may be due to a number of reasons: even during normal pregnancy, the placenta secretes leptin similar in size and immunoreactivity to that derived from adipose tissue, contributing to increased levels[18]; elevation may also be due to placental stress caused by hypoxia present in the pre-eclamptic placenta[19],[20]; and as leptin has a strong angiogenic effect, its levels may be elevated in PE to increase placental blood supply by neovascularization.[21]

Adiponectin reduction plays a significant role in diseases associated with excessive weight, as it counteracts insulin resistance and inflammation.[22] Adiponectin receptor mRNA and protein are upregulated in preeclampsia, while the adipokine itself shows downregulation in placental tissue.[23] These levels were also found to correlate positively with the expression of p-STAT5 and inversely with p-p38 (both factors affecting the function of placental trophoblasts), implicating a role for adiponectin in preeclampsia.[24] Moreover, a recent study concluded that adiponectin levels were the best prognostic factor (compared with visfatin, resistin, and leptin) when corrected for BMI, age, parity, and family history of PE and diabetes.[25]

2. SUBJECTS AND METHODS

2.1 Study Design, Setting, Population, and Sampling

A prospective case-control study was conducted between January and December 2023. A convenience sample was collected over a period of five months from Al-Khansaa and Al-Batool Teaching Hospitals in Mosul City, Iraq, among patients seeking medical counseling or admitted for elective or emergency cesarean sections. The study was conducted on one hundred women: fifty cases (pregnant women with PE) and fifty controls (pregnant women without chronic hypertension or pregnancy-induced hypertension).

2.2 Inclusion Criteria

For case and control groups: singleton pregnant women in their second or third trimester, above 18 years of age, with first-trimester body mass index greater than 18.5 kg/m² but less than 30.0 kg/m². For the case group: pregnant women with high blood pressure (≥140/90 mmHg) on two occasions four hours apart, with visible dipstick proteinuria (≥"+"), with or without headache, epigastric pain, blurring of vision, nausea and/or vomiting, right hypochondrial pain, and generalized edema. For the control group: healthy normotensive women enrolled as controls.

2.3 Exclusion Criteria

For case and control groups: multiple gestation, diabetes mellitus, history of pre-gestational (chronic) hypertension, history of heart or renal problems, history of previous or recent cancer, autoimmune disease and collagen tissue disease such as rheumatoid arthritis,

systemic lupus erythematosus, and inflammatory bowel disease, and history of smoking.

2.4 Collection, Preservation, and Biochemical Analysis of Blood Samples

Blood samples were collected from each eligible participant at the time of enrollment. Leptin and adiponectin levels were measured in preeclamptic and normal pregnant women to determine whether the free components of leptin and adiponectin are increased during pregnancy and further increased in preeclampsia. Blood samples were introduced into serum separator tubes, centrifuged, and aliquots of serum were pipetted into CryoPure tubes and stored at -20°C in a refrigerator. Total serum adiponectin and leptin were quantified using the Quantikine® human adiponectin immunoassay and the Quantikine® human leptin immunoassay (R&D Systems, USA), respectively, according to the manufacturers' instructions.

2.5 Data Management and Statistical Analysis

Data coding and tabulation were performed using Microsoft Excel 2010, and data were analyzed using the Statistical Package for Social Sciences (SPSS, version 26). Descriptive statistics included mean ± standard deviation (SD) for measurable variables and frequencies and percentages for categorical variables. The independent-samples t-test was used for comparison between quantitative parameters, and the chi-square test of association was used to compare proportions; Fisher's exact test was used when the expected count in more than 20% of the cells of the table was less than 5. McNemar's test was used when the results of the leptin (or adiponectin) test were compared with the diagnosis of preeclampsia in the same patients. Youden's index was used to assign the cut-off point of leptin (or adiponectin) positivity, choosing the value that gave the highest sensitivity and specificity.

2.6 Ethical Considerations

The study population participated after verbal and written consent was obtained from each participant, and the data were used exclusively for research purposes and held on a password-protected computer, with access limited to research team members only.

3. RESULTS

Around one quarter (24%) of the cases were aged ≥35 years, compared with 4% of the control group ($p = 0.004$). More than one third (46%) of cases had an overweight BMI compared with only 12% of the control group ($p < 0.001$). The mean age of cases (27.8 years) was significantly ($p = 0.018$) higher than that of controls (24.8 years), and the mean BMI of cases (24.5 kg/m²) was also significantly ($p < 0.001$) higher than that of controls (23.1 kg/m²). The majority (94%) of women in the whole sample were housewives, but the difference was not significant ($p = 0.204$) (Table 1).

Table 1: Maternal characteristics of the study population.

Variable	Case No. (%)	Control No. (%)	P-value
Maternal age (years)			
18–34	38 (76.0)	48 (96.0)	0.004*
≥35	12 (24.0)	2 (4.0)	
Mean (SD)	27.88 (7.15)	24.82 (5.49)	0.018‡
BMI (kg/m²)			
Normal weight	27 (54.0)	44 (88.0)	<0.001*
Overweight	23 (46.0)	6 (12.0)	
Mean (SD)	24.53 (1.85)	23.16 (1.49)	<0.001‡
Occupation			
Housewife	45 (90.0)	49 (98.0)	0.204**
Employee	5 (10.0)	1 (2.0)	
Total	50 (100.0)	50 (100.0)	

*By chi-square test. **By Fisher's exact test. ‡By unpaired t-test.

No significant difference was detected between the two groups regarding gravidity ($p = 0.519$). One third (33%) of the whole sample were nulliparous, and 11% were grand multiparous, with no significant difference between the two groups ($p = 0.131$). One quarter of the study population had a history of abortion, with no significant difference between the two groups ($p = 0.171$). No significant differences (in means) were detected between cases and controls regarding gravidity ($p = 0.775$), parity ($p = 0.560$), abortion ($p = 0.572$), gestational age ($p = 0.809$), or gestational age by ultrasound ($p = 0.169$). Around two thirds (64%) of the women attended primary health care centers completely, with no significant difference between the two groups ($p = 0.677$) (Table 2).

Table 2: Obstetric determinants of the study population.

Variable	Case No. (%)	Control No. (%)	P-value
Gravidity			
Primigravida (G1)	19 (38.0)	14 (28.0)	0.519*
Multigravida (G2-4)	20 (40.0)	25 (50.0)	
Grand multigravida (G≥5)	11 (22.0)	11 (22.0)	
Mean (SD)	3.20 (2.71)	3.06 (2.15)	0.775‡
Parity			
Nulliparous (P0)	19 (38.0)	14 (28.0)	0.131*
Primiparous (P1)	9 (18.0)	17 (34.0)	
Multiparous (P2-4)	14 (28.0)	16 (32.0)	
Grand multiparous (P≥5)	8 (16.0)	3 (6.0)	
Mean (SD)	1.90 (2.31)	1.66 (1.75)	0.560‡
Abortion: Yes	10 (20.0)	16 (32.0)	0.171*
Abortion: No	40 (80.0)	34 (68.0)	
Mean (SD)	0.32 (0.77)	0.40 (0.64)	0.572‡
Gestational age (wks), mean (SD)	36.27 (3.11)	36.08 (3.54)	0.809‡
GA by US (wks), Mean (SD)	35.51 (3.67)	36.48 (3.21)	0.169‡
ANC complete (≥4 visits)	33 (66.0)	31 (62.0)	0.677*
ANC not complete (<4 visits)	17 (34.0)	19 (38.0)	
Total	50 (100.0)	50 (100.0)	

*By Chi-square test. ‡By unpaired t-test.

The following means were significantly higher among cases than controls: systolic blood pressure ($p < 0.001$) and diastolic blood pressure ($p < 0.001$) (Table 3). No significant difference was detected between cases and controls regarding mean hemoglobin ($p = 0.058$), while the following means were significantly higher among cases than controls: blood urea ($p < 0.001$), serum creatinine ($p < 0.001$), serum uric acid ($p < 0.001$), total serum bilirubin ($p = 0.019$), AST ($p < 0.001$), ALT ($p = 0.015$), and alkaline phosphatase ($p < 0.001$), while platelet count and serum calcium were significantly lower among cases than controls ($p < 0.001$) (Table 4).

Table 3: Blood pressure readings among cases and controls.

Variable	Case Mean±SD	Control Mean ± SD
Systolic BP (mmHg)	151.60±12.62	109.60±7.81
Diastolic BP (mmHg)	98.92±6.58	65.50±5.08

P-value < 0.001 for both by unpaired t-test.

Table 4: Laboratory parameters of study groups.

Variable	Case Mean±SD	Control Mean ± SD	P-value
Hb (g/dl)	11.00±1.54	11.50±0.99	0.058
Platelets ($\times 10^9$/L)	206.26±68.29	252.62±58.55	<0.001
S. calcium	7.88±0.97	8.48±0.38	<0.001
Blood urea (mg/dl)	24.31±12.23	16.69±4.92	<0.001
S. creatinine	0.71±0.26	0.50±0.12	<0.001
S. uric acid	5.67±1.81	3.58±0.58	<0.001
TSB	0.79±1.25	0.36±0.16	0.019
AST	37.98±26.23	13.62±3.78	<0.001
ALT	24.80±27.73	14.72±5.13	0.015
Alkaline phosphatase	118.16±59.75	76.86±21.70	<0.001

By unpaired t-test.

It is evident that the following means were significantly higher among cases than controls: serum leptin ($p < 0.001$) and serum adiponectin ($p = 0.002$), while no significant difference was detected regarding the adiponectin-leptin ratio ($p = 0.252$) between the two groups (Table 5).

Table 5: Means of serum biomarkers of cases and controls.

Variable	Case Mean±SD	Control Mean ± SD	P-value
Serum leptin (ng/ml)	14.29±6.84	7.38±6.72	<0.001
Serum adiponectin (ng/ml)	30.54±20.40	18.74±15.89	0.002
Adiponectin-leptin ratio	3.16±4.22	4.31±5.66	0.252

By unpaired t-test.

The area under the curve (for leptin and preeclampsia) was 0.759 (95% CI 0.663–0.855), as presented in Table 6 and Figure 1.

Table 6: ROC curve analysis of leptin as a predictor for preeclampsia.

Variable	Area	SE	95% CI (P-value)
Serum leptin (ng/ml)	0.759	0.049	0.663–0.855 (<0.001)

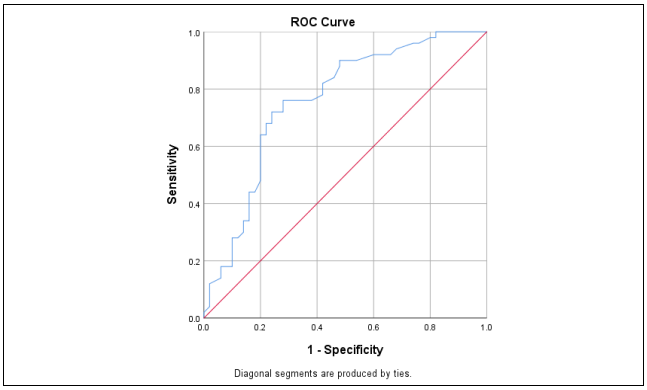

Figure 1: ROC curve of serum leptin as a predictor of preeclampsia.

The validity indicators of leptin as a predictor of preeclampsia were as follows: sensitivity (72%), specificity (76%), PPV (75%), NPV (73.1%), and agreement (74%). The cut-off value was estimated at 11.15 ng/ml. No significant difference (p = 0.845) was detected between leptin test values and the real diagnosis (Table 7).

Table 7: Validity of leptin as a predictor for preeclampsia.

Leptin (11.15 ng/ml cut-off)	Case	Control	Total
Positive (≥11.15)	36	12	48
Negative (<11.15)	14	38	52
Total	50	50	100

Sensitivity 72%, specificity 76%, PPV 75.0%, NPV 73.1%, and agreement 74% (P = 0.845 by McNemar test).

The area under the curve (for adiponectin and preeclampsia) was 0.679 (95% CI 0.575–0.783), as presented in Table 8 and Figure 2.

Table 8: ROC curve analysis of adiponectin as a predictor for preeclampsia.

Variable	Area	SE	95% CI (P-value)
Serum adiponectin (ng/ml)	0.679	0.053	0.575–0.783 (0.002)

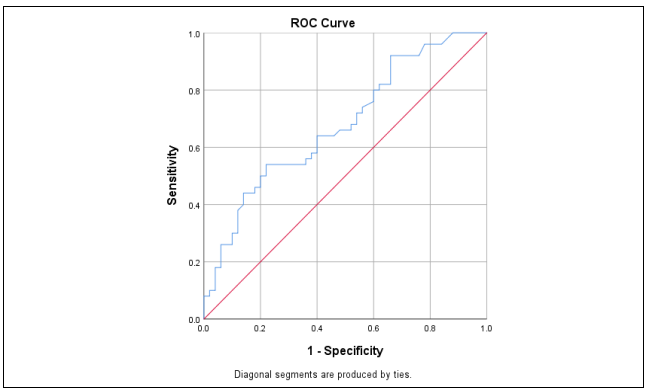

Figure 2: ROC curve of serum adiponectin as a predictor of preeclampsia.

Values of adiponectin ≥28.3 ng/ml were considered a positive test. No significant difference was detected between the adiponectin test results and the real diagnosis of preeclampsia (p = 0.06). The indicators of validity were as follows: sensitivity (54%), specificity (78%), PPV (71.1%), NPV (62.9%), and total agreement (66%), as presented in Table 9.

Table 9: Validity of adiponectin as a predictor for preeclampsia.

Adiponectin (28.3 ng/ml cut-off)	Case	Control	Total
Positive (≥28.3)	27	11	38
Negative (<28.3)	23	39	62
Total	50	50	100

Sensitivity 54%, specificity 78%, PPV 71.1%, NPV 62.9%, and agreement 66% (P = 0.06 by McNemar test).

Youden's index (sensitivity + specificity − 1) was calculated; the leptin value of 11.15 ng/ml gave the highest value of the index, yielding the highest combined sensitivity and specificity (noting that increasing sensitivity decreases specificity and vice versa). The same approach was applied for adiponectin, where the cut-off value was 28.3 ng/ml.

4. DISCUSSION

The study revealed that the mean age of cases was significantly higher than that of the control group (27.8 vs. 24.8 years, p = 0.018). In a study in India, the mean age of preeclamptic patients was 24.51 ± 3.70 years (p < 0.05)[26], while studies in Iran and Ghana found no significant age difference between groups.[27], [28] A study in Central China showed that advanced maternal age (AMA) was significantly associated with the risk of PE (p < 0.001).[29] Over recent decades, socio-economic shifts and increased use of assisted reproductive technology have led to a rise in the rate of pregnancies at an AMA, usually defined as age >35 or >40 years.[30], [31]

Increased maternal inflammatory status and oxidative stress associated with excess adipose tissue are considered the main biological triggers of abnormal early placentation among obese subjects; placental defects can increase resistance in the maternal-fetal circulation, triggering the development of preeclampsia.[32] According to previous studies, there is sufficient evidence that excess BMI is significantly associated with increased risk of PE. The current study revealed that the mean BMI of cases (24.5 kg/m²) was significantly (p < 0.001) higher than that of controls (23.1 kg/m²); a study in Iran similarly showed a significant correlation (p = 0.007)[33], while a study in Ghana found comparable BMI between normotensive and preeclamptic women.[27]

In the present study there was no significant difference between groups regarding occupation; although the association between occupational risk factors and hypertensive disorders of pregnancy has been studied for decades, definitive information is not yet available. There was no significant difference in gravidity or parity (p = 0.775 and p = 0.560, respectively) between groups, whereas a study in Ghana found gravidity differed significantly between normotensive and PE women, while parity did not differ significantly, in agreement with the present study.[27] Regarding why nulliparity is consistently found to be the most prevalent predisposing factor for PE, one theory holds that the immune system of nulliparous individuals has had limited exposure to paternal antigens, and this lack of desensitization may play a role in disease pathogenesis.[34], [35]

The present study revealed that history of previous abortion did not differ significantly between cases and controls, in contrast to a study in Sudan that found previous abortion reduced the risk of preeclampsia by 59.0%.[36] The comparison between groups in this study was not significant regarding gestational age, while a study in Japan evaluating the relationship between gestational week and PE incidence found that the incidence of PE increases exponentially with gestational age, explained by a theoretical correlation between monotonic increases of serum markers sFlt-1 or PlGF with gestational age and PE development.[37], [38]

Antenatal care (ANC) coverage is an indicator of access to and use of health care during pregnancy, and receiving ANC at least four times increases the likelihood of receiving effective maternal health interventions.[39] Around two thirds (64%) of women in this study attended primary health care centers completely, with no significant difference between groups (p = 0.677), whereas a study in northwest Ethiopia among women attending antenatal care and delivery services at Bahir Dar public hospitals showed a significant difference regarding ANC follow-up.[40]

In the current study, mean systolic and diastolic blood pressure were significantly higher among cases than controls (p < 0.001), consistent with studies in Ghana and Latin America showing that preeclamptic women had higher blood pressures than normotensive pregnant women.[27], [41] Hemoglobin did not differ significantly between cases and controls (p = 0.058), consistent with a study in Indonesia.[42] Platelet count was significantly lower among cases than controls (p < 0.001), consistent with a study in India showing significantly decreased platelet count in the PE group[43] and a study in Saudi Arabia showing significantly higher platelet count in controls.[44]

Blood urea, serum creatinine, and serum uric acid were significantly higher among cases than controls (p < 0.001) in this study, compatible with a study in India

showing significantly higher serum creatinine and uric acid in PE compared with controls[45] and with studies in Iraq (Kirkuk) showing significantly elevated serum creatinine and uric acid in PE compared with normotensive pregnant women.[46] Regarding liver enzymes, TSB, AST, ALT, and alkaline phosphatase were significantly higher among cases than controls, indicating unstable liver function, in line with a study in India showing elevated AST and ALT.[47] Serum calcium was significantly lower among cases than controls ($p < 0.001$), consistent with a study in Korea showing lower serum calcium levels in women with PE.[48]

Serum leptin was significantly higher in cases than controls (14.29 ± 6.84 vs. 7.38 ± 6.72 ng/ml, $p < 0.001$), consistent with a study in Ghana showing leptin significantly higher among PE women (18.22 ± 2.01 ng/ml) than normotensive women (13.36 ± 3.11 ng/ml, $p = 0.010$)[27], and a study in Brazil showing significantly higher leptin in PE ($p < 0.0002$)[49]; however, a study in Denmark found no association between leptin concentration and PE ($p = 0.175$).[50] ROC analysis in this study showed a cut-off value of 11.15 ng/ml, with no significant difference ($p = 0.845$) between leptin test values and the real diagnosis; the validity of leptin as a predictor of preeclampsia was sensitivity 72%, specificity 76%, PPV 75%, NPV 73.1%, and agreement 74%, noting that women of any BMI were not excluded, whereas a study in India found sensitivity, specificity, PPV, and NPV of 90%, 88.3%, 88.5%, and 89.8%, respectively, with a cut-off of >23.3 and significant accuracy ($p < 0.0001$) in a population restricted to BMI 18.5–23.[35]

Regarding adiponectin, several mechanisms could account for higher levels in PE, which is characterized by hypertension, proteinuria, inflammation, and endothelial dysfunction. Significantly higher serum adiponectin was observed in the case group than the control group (30.54 vs. 18.74 ng/ml, $p = 0.002$) in the present study, while an Indian study observed slightly higher but not statistically significant adiponectin levels in the PE group ($p = 0.089$).[35] Khosrowbeygi et al., Fondjo et al., Abd-Aaleem et al., and Aloush et al., from Iranian, Ghanaian, and Egyptian (two studies) populations, respectively, also reported elevated adiponectin levels in PE women compared with controls, with statistically significant differences in all studies ($p < 0.05$)[27, 35]; however, Mazaki-Tovi et al. and Ouyang et al. reported significantly lower adiponectin levels in PE women compared with normotensive women.[35, 51]

Values of adiponectin ≥28.3 ng/ml were considered positive in this study, with no significant difference between test results and the real diagnosis of preeclampsia ($p = 0.058$); validity indicators were sensitivity 54%, specificity 78%, PPV 71.1%, NPV 62.9%, and total agreement 66%. A study in Denmark reported the validity of adiponectin as sensitivity 72.9% and specificity 49%.[49]

This study revealed that the adiponectin-leptin ratio was lower in the case (PE) group (3.16) than the control group (4.31), with no significant difference between them ($p = 0.252$), while a study in India showed the ratio was significantly lower in the study group than controls ($p < 0.0001$)[52]; a Ghanaian study reported a significantly higher A/L ratio in PE women compared with normotensive controls, and a study from Denmark found no association between A/L ratio and PE.[53, 35, 54] The variance in the A/L ratio across studies suggests dysregulation of adipokines in PE, probably reflecting increased insulin resistance and an exaggerated systemic inflammatory and anti-angiogenic state known to be present in PE. Alteration in A/L ratio in pregnancy may therefore be a biomarker of PE and associated adipose tissue dysfunction, and its estimation could be part of the diagnostic work-up for PE, as adiponectin has anti-diabetic, anti-inflammatory, and angiogenic properties; the above-mentioned features of PE are associated with reduced adiponectin levels, which may also explain the low A/L ratio.[30, 35, 54–57]

5. CONCLUSIONS AND RECOMMENDATIONS

In the current study we concluded that higher maternal age and maternal BMI were observed among the PE group than the normotensive group. Platelet count and serum calcium level were lower among PE than normotensive women, while other renal and liver function tests were higher among PE. Levels of leptin and adiponectin were higher among the PE group, while the ratio of both was not significantly different. Validity of leptin showed 72% sensitivity and 76% specificity; validity of adiponectin showed 54% sensitivity and 78% specificity. Future prospective cohort studies with larger sample sizes are recommended to compare levels of these and other biomarkers between pregnant women who have risk factors for preeclampsia and those who do not. Counseling of health care providers and institutions is also necessary to prevent and treat PE, thereby decreasing maternal and neonatal morbidity and mortality.

Declaration

This thesis is submitted in partial fulfillment of the requirements for the Iraqi Board for Medical Specializations in Obstetrics and Gynecology.

REFERENCES

1. Eiland E, Nzerue C, Faulkner M. Preeclampsia. J Pregnancy, 2012; 2012: 586578.
2. Adu-Gyamfi EA, Fondjo LA, Owiredu WK, et al. The role of adiponectin in placentation and preeclampsia. Cell Biochem Funct, 2020; 38(1): 106-17.
3. Roberts JM, August PA, Bakris G, et al. American College of Obstetricians and Gynecologists; task force on hypertension in pregnancy. Hypertension in pregnancy. Report of the ACOG task force on hypertension in pregnancy. Obstet Gynecol, 2013; 122(5): 1122-31.

4. Brown MA, Magee LA, Kenny LC, et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension, 2018; 72(1): 24-43.
5. Steegers EA, Von Dadelszen P, Duvekot JJ, et al. Pre-eclampsia. Lancet, 2010; 376(9741): 631-44.
6. Sobh SM, Sanad SA, Abdelazeem HM, et al. Microalbuminuria during midpregnancy in the prediction of preeclampsia. Evid Based Womens Health J, 2016; 6(2): 47-50.
7. Dias S, Pheiffer C, Rheeder P, et al. Screening and diagnosis of gestational diabetes mellitus in South Africa: What we know so far. S Afr Med J, 2019; 109(7): 457-62.
8. Velauthar L, Plana MN, Kalidindi M, et al. First trimester uterine artery Doppler and adverse pregnancy outcome: a meta-analysis involving 55,974 women. Ultrasound Obstet Gynecol, 2014; 43(5): 500-7.
9. O'Gorman N, Wright D, Poon LC, et al. Accuracy of a competing-risks model in screening for pre-eclampsia by maternal factors and biomarkers at 11-13 weeks' gestation. Ultrasound Obstet Gynecol, 2017; 49(6): 751-5.
10. McLaughlin K, Zhang J, Lye SJ, Parker JD, Kingdom JC. Phenotypes of pregnant women who subsequently develop hypertension in pregnancy. J Am Heart Assoc, 2018; 7(14): e009595.
11. Kabbani N, Blüher M, Stepan H, et al. Adipokines in pregnancy: A systematic review of clinical data. Biomedicines, 2023; 11(5): 1419.
12. Makki K, Froguel P, Wolowczuk I. Adipose tissue in obesity-related inflammation and insulin resistance: cells, cytokines, and chemokines. Int Sch Res Notices, 2013; 2013.
13. Frühbeck G, Catalán V, Rodríguez A, Gómez-Ambrosi J. Adiponectin-leptin ratio: A promising index to estimate adipose tissue dysfunction. Relation with obesity-associated cardiometabolic risk. Adipocyte, 2018; 7: 57-62.
14. Supriya R, Tam BT, Yu AP, et al. Adipokines demonstrate the interacting influence of central obesity with other cardiometabolic risk factors of metabolic syndrome in Hong Kong Chinese adults. PLoS One, 2018; 13(8): e0201585.
15. Briffa JF, McAinch AJ, Romano T, Wlodek ME, et al. Leptin in pregnancy and development: a contributor to adulthood disease? Am J Physiol Endocrinol Meta b, 2015; 308(5): E335-50.
16. Manuel-Apolinar L, López-Romero R, Zarate A, et al. Leptin-mediated ObRb receptor increases expression of adhesion intercellular molecules and cyclooxygenase 2 on murine aorta tissue inducing endothelial dysfunction. Int J Clin Exp Med, 2013; 6(3): 192.
17. Sitras V, Paulssen RH, Gronaas H, et al. Differential placental gene expression in severe preeclampsia. Placenta, 2009; 30: 424-33.
18. Pérez-Pérez A, Toro A, Vilariño-García T, et al. Leptin action in normal and pathological pregnancies. J Cell Mol Med, 2018; 22(2): 716-27.
19. Thagaard IN, Hedley PL, Holm JC, et al. Leptin and adiponectin as markers for preeclampsia in obese pregnant women, a cohort study. Pregnancy Hypertens, 2019; 15: 78-83.
20. Chrelias G, Makris GM, Papanota AM, et al. Serum inhibin and leptin: risk factors for pre-eclampsia? Clin Chim Acta, 2016; 463: 84-7.
21. E. Davies J, Pollheimer J, Yong HE, et al. Epithelial-mesenchymal transition during extravillous trophoblast differentiation. Cell Adh Migr, 2016; 10(3): 310-21.
22. Fang H, Judd RL. Adiponectin regulation and function. Compr Physiol, 2018; 8: 1031-1063.
23. Adu-Gyamfi EA, Fondjo LA, Owiredu WK, et al. The role of adiponectin in placentation and preeclampsia. Cell Biochem Funct, 2020; 38: 106-117.
24. Dong G, Tian Y, Li X. Adiponectin participates in preeclampsia by regulating the biological function of placental trophoblasts through P38 MAPK-STAT5 pathway. Iran J Public Health, 2018; 47: 1838-1844.
25. Bawah AT, Yeboah FA, Nanga S, et al. Serum adipocytokines and adiposity as predictive indices of preeclampsia. Clin Hypertens, 2020; 26: 19.
26. Yadav BS, Jain SK, Toppo NA, Dehariya C. A case control study on s. uric acid and s. creatinine level in pre-eclampsia patients of a tertiary care hospital in Jabalpur district of Central India. Int J Res Med Sci, 2018; 6(5): 1519.
27. Fondjo LA, Gyamfi EA, Owiredu WK, et al. Maternal serum adiponectin, leptin and adiponectin-leptin ratio as possible biomarkers of preeclampsia. Edorium J Gynecol Obstet, 2016; 2: 41-7.
28. Khosrowbeygi A, Lorzadeh N, Ahmadvand H. Lipid peroxidation is not associated with adipocytokines in preeclamptic women. Iran J Reprod Med, 2011; 9(2): 113.
29. Sun M, Luo M, Wang T, et al. Effect of the interaction between advanced maternal age and pre-pregnancy BMI on pre-eclampsia and GDM in Central China. BMJ Open Diabetes Res Care, 2023; 11(2): e003324.
30. Khalil A, et al. Maternal age and adverse pregnancy outcome: a cohort study. Ultrasound Obstet Gynecol, 2013; 42(6): 634-43.
31. Swiercz G, Zmelonek-Znamirowska A, Szwabowicz K, et al. Navigating uncertain waters: first-trimester screening's role in identifying neonatal complications. J Clin Med, 2024; 13(7): 1982.
32. Mayrink J, Costa ML, Cecatti JG. Preeclampsia in 2018: revisiting concepts, physiopathology, and prediction. ScientificWorldJournal, 2018; 20: 18.
33. Noori N, Nurzadeh M, Arbabzadeh T, et al. Comparing serum leptin levels between pregnant women with preeclampsia and normal pregnant women. Med Sci, 2020; 24(104): 2273-9.

34. Bartsch E, Medcalf KE, Park AL, et al. High risk of pre-eclampsia identification group. Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies. BMJ, 2016; 353.
35. Rao S, Kumari A, Sharma M, Kabi BC. Predicting maternal serum adiponectin and leptin level as biomarkers of pre-eclampsia: A prospective study. J Obstet Gynecol India, 2021; 71: 58-65.
36. Mohamedain A, Rayis DA, AlHabardi N, et al. Association between previous spontaneous abortion and preeclampsia: a case-control study. BMC Pregnancy Childbirth, 2022; 22(1): 715.
37. Kumasawa K. Evaluation of the relationship between gestational week and the incidence of preeclampsia. Hypertens Res, 2023; 46(3): 790-1.
38. Zeisler H, et al. Predictive value of the sFlt-1:PlGF ratio in women with suspected preeclampsia. N Engl J Med, 2016; 374(1): 13-22.
39. Ajong AB, Kenfack B, Ali IM, et al. Ionised and total hypocalcaemia in pregnancy: An analysis of prevalence and risk factors in a resource-limited setting, Cameroon. PLoS One, 2022; 17(5): e0268643.
40. Tesfa E, Munshea A, Nibret E, et al. Determinants of pre-eclampsia among pregnant women attending antenatal care and delivery services at Bahir Dar public hospitals, northwest Ethiopia: A case-control study. Health Sci Rep, 2023; 6(7): e1440.
41. Vigil-De Gracia P, Olaya-Garay SX, Hernández CM, et al. Blood pressure changes in adolescents with preeclampsia: a multicentre, case-control study in Latin American hospitals. J Obstet Gynaecol Can, 2021; 43(1): 50-7.
42. Nanda AW, Semarawisma A. Association between anemia and preeclampsia: a case control study in Gorontalo region, Indonesia. Int J Res Med Sci, 2021; 10(1): 31.
43. Annam V, Srinivasa K, Yatnatti SK. Evaluation of platelet indices and platelet counts and their significance in pre-eclampsia and eclampsia. Int J Biol Med Res, 2011; 2(1): 425-8.
44. AlSheeha MA, Alaboudi RS, Alghasham MA, et al. Platelet count and platelet indices in women with preeclampsia. Vasc Health Risk Manag, 2016; 477-80.
45. Yadav BS, Jain SK, Toppo NA, Dehariya C. A case control study on s. uric acid and s. creatinine level in pre-eclampsia patients of a tertiary care hospital in Jabalpur district of Central India. Int J Res Med Sci, 2018; 6(5): 1519.
46. Mohammed Jumaah IA. Estimation of uric acid, urea, creatinine and creatinine clearance in the serum of preeclamptic women. Karbala J Pharm Sci, 2013; 4(4): 183-9.
47. Rajoria L, Code Q. A prospective study of association of deranged liver function tests and renal function tests with severity of preeclampsia. Int J Biomed Adv Res, 2018; 9(3): 100-2.
48. Kim J, Kim YJ, Lee R, et al. Serum levels of zinc, calcium, and iron are associated with the risk of preeclampsia in pregnant women. Nutr Res, 2012; 32(10): 764-9.
49. Veiga EC, Korkes HA, Salomão KB, et al. Association of leptin and other inflammatory markers with preeclampsia: A systematic review. Front Pharmacol, 2022; 13: 966400.
50. Thagaard IN, Hedley PL, Holm JC, et al. Leptin and adiponectin as markers for preeclampsia in obese pregnant women, a cohort study. Pregnancy Hypertens, 2019; 15: 78-83.
51. Mazaki-Tovi S, Romero R, Vaisbuch E, et al. Maternal serum adiponectin multimers in preeclampsia. J Perinat Med, 2009; 73(1): 60-5.
52. Brown MA, Magee LA, Kenny LC, et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension, 2018; 72(1): 24-43.
53. Miehle K, Stepan H, Fasshauer M. Leptin, adiponectin and other adipokines in gestational diabetes mellitus and pre-eclampsia. Clin Endocrinol (Oxf), 2012; 76(1): 2-11.
54. Ouyang Y, Chen H, Chen H. Reduced plasma adiponectin and elevated leptin in pre-eclampsia. Int J Gynaecol Obstet, 2007; 98(2): 110-4.
55. Tan KC, Xu A, Chow WS, et al. Hypoadiponectinemia is associated with impaired endothelium-dependent vasodilation. J Clin Endocrinol Metab, 2004; 89(2): 765-9.
56. Ouchi N, Ohishi M, Kihara S, et al. Association of hypoadiponectinemia with impaired vasoreactivity. Hypertension, 2003; 42(3): 231-4.
57. Robinson K, Prins J, Venkatesh B. Clinical review: adiponectin biology and its role in inflammation and critical illness. Crit Care, 2011; 15(2): 1-9.