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Placental Growth Factor (PlGF) and sFlt-1 as Biomarkers for Diagnosing Preeclampsia Risk

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ABSTRACT

Background & Objective: Preeclampsia is a multisystem disorder and one of the principal causes of illness and death among mothers, fetuses, and newborns, characterized by hypertension and proteinuria. Placental growth factor (PlGF) promotes angiogenesis, whereas soluble fms-like tyrosine kinase-1 (sFlt-1), secreted primarily by the placenta, antagonizes both PlGF and vascular endothelial growth factor (VEGF), thereby contributing to endothelial dysfunction. This study aimed to evaluate maternal serum levels of PlGF and sFlt-1, and the ratio between them, in women with preeclampsia compared with normotensive pregnant controls.

Materials & Methods: This case–control study enrolled 125 pregnant women: 75 with preeclampsia and 50 normotensive controls, recruited between July 2024 and May 2025 at Bint Al-Huda Teaching Hospital and Al-Haboubi Teaching Hospital in Nasiriyah, Iraq. Blood pressure was assessed with a standard mercury sphygmomanometer. Venous blood samples were collected, processed, and stored at −20°C. Exclusion criteria included chronic hypertension, diabetes mellitus, renal disease, coagulation disorders, urinary tract infections, autoimmune diseases, or lack of informed consent.

Results: Serum PlGF concentrations were markedly reduced in the preeclampsia group (mean [SD], 5.18 [1.82]) compared with controls (14.38 [20.47]). Conversely, sFlt-1 levels were significantly elevated among women with preeclampsia (6.84 [1.60]) than in controls (3.74 [3.04]). The sFlt-1/PlGF ratio was markedly elevated in participants with preeclampsia (1.28 [0.51]) compared with controls (0.42 [0.42]).

Conclusion: Maternal obesity and advanced gestational age increase the risk of preeclampsia. Assessment of sFlt-1, PlGF, and the sFlt-1/PlGF ratio measured during the third trimester may serve as valuable diagnostic biomarkers for preeclampsia and assist in developing targeted therapeutic strategies.

Keywords: Preeclampsia, Biomarkers, Angiogenesis, Endothelial Dysfunction, Gestational Hypertension

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1. Introduction

Pregnancy is a period of physiological stress characterized by extensive hormonal, metabolic, biochemical, and psychological changes (1). It typically lasts approximately 40 weeks (2, 3). Among the potential complications, preeclampsia (PE) is one of the most clinically significant (4, 5). PE is a multisystem disorder that typically develops beyond twenty weeks' gestation and is accompanied by hypertension and proteinuria (6).

Preeclampsia affects approximately 2% to 10% of pregnancies and represents the most common hypertensive disorder during gestation (7). The diagnosis is based on the development of hypertension with concurrent proteinuria during pregnancy, whereas gestational hypertension refers to elevated BP typically defined as systolic pressure >140 mm Hg and/or diastolic pressure >90 mm Hg, arising during the latter half of gestation (8, 9).

Gestational hypertension denotes newly developed blood pressure ≥140/90 mm Hg after 20 weeks in previously normotensive women, without proteinuria (6). It is often asymptomatic and usually detected during routine prenatal evaluations. Although gestational hypertension may be associated with low birth weight or preterm delivery, these outcomes are generally less severe than those seen with preeclampsia. Preeclampsia, in

contrast, is characterized by hypertension accompanied by proteinuria or evidence of end-organ dysfunction, such as hepatic or renal impairment (6, 7). Clinical manifestations can include headache, edema (particularly of the hands and face), visual disturbances, and abdominal pain. In severe cases, preeclampsia can lead to life-threatening complications for both mother and fetus, including eclampsia, HELLP syndrome, and multiorgan injury. Management typically involves close monitoring, antihypertensive therapy, and, when necessary, early delivery to prevent adverse outcomes (6).

Although the precise etiology of preeclampsia remains unclear, placental dysfunction is considered the central pathogenic mechanism (10, 11). Abnormal placental development early in gestation may precede clinical disease. Placental growth factor, an angiogenic protein, plays a key role in vascular growth and maturation (12, 13). Its activity involves both direct effects on endothelial and trophoblastic cells and indirect effects on nonvascular cells that support vessel formation (14).

VEGFR-1 is also present as a soluble isoform, termed soluble fms-like tyrosine kinase-1 (sFlt-1), a placentally derived factor. sFlt-1 acts as a decoy receptor that sequesters PlGF and VEGF, thereby blocking their binding to membrane-bound VEGFR-1 and VEGFR-2 (15, 16). This antagonism reduces the bioavailability of angiogenic factors, leading to endothelial dysfunction—the hallmark of preeclampsia (17, 18).

Measurement of circulating PlGF and sFlt-1 levels provides valuable diagnostic and prognostic information for preeclampsia (19). These biomarkers contribute to maternal risk stratification and may guide clinical decision-making to improve maternal and fetal outcomes. Emerging evidence indicates that the placenta releases soluble angiogenic factors before the onset of clinical manifestations, suggesting their potential role in early disease prediction (20, 21).

This study sought to assess and compare the diagnostic performance of angiogenic biomarkers-PlGF and sFlt-1- and to identify optimal threshold values for diagnostic sensitivity and specificity. Improved diagnostic accuracy may support earlier identification and better management of women at risk for preeclampsia.

2. Materials and Methods

2.1 Study Design and Participants

This research enrolled 125 pregnant women, including 75 with preeclampsia and 50 normotensive controls. Participants were recruited between July 2024 and May 2025 from Bint Al-Huda Teaching Hospital and Al-Haboubi Teaching Hospital in Nasiriyah, Iraq. The study protocol received approval from the institutional ethics committees, and all participants gave written informed consent before enrollment. Blood pressure measurements were carried out using a manual mercury sphygmomanometer in a seated position. Eligible participants were 20 to 38 years of age and were divided into 2 groups.

The control group included pregnant women with normal blood pressure and no evidence of preeclampsia. The preeclampsia group included women with gestational hypertension (systolic BP ≥140 and <160 mm Hg; diastolic BP ≥90 and ≤110 mm Hg) and proteinuria, confirmed by their attending physicians.

All women were in the third trimester (beyond 30 weeks of gestation) at the time of sampling. Participants were excluded if they were under 18 or over 45 years, had chronic hypertension, gestational diabetes, autoimmune diseases, Aspirin allergy, smoked, had multiple gestations, or a history of thrombosis or coagulation disorders. Clinical and demographic information including obstetric history, thyroid function status, and family history of preeclampsia, diabetes, or hypertension was recorded. Vital signs (pulse rate, temperature, and respiratory rate) were also measured.

A 3 mL sample of maternal venous blood was aseptically collected into a red-capped vacuum tube. Blood samples from participants were left to clot at room temperature (18–25°C) for 15–30 minutes before processing. After clot formation, tubes were centrifuged, and the resulting serum was carefully transferred into Eppendorf tubes using a Pasteur pipette. When immediate analysis was not feasible, serum samples were aliquoted (0.5 mL) and stored at −20°C until batch analysis (22, 23). Serum samples were analyzed between 30 and 40 weeks of gestation to assess statistically significant differences between groups.

Determination of placental growth factor levels (PlGF)

2.2 Principle

The assay employs a sandwich enzyme-linked immunosorbent assay (ELISA) technique to quantify human PlGF (ELK Biotechnology CO, Ltd. USA). Microtiter wells were pre-coated with a monoclonal antibody specific for PlGF, and standards and serum samples were added to the designated wells, followed by the addition of a biotin-conjugated antibody specific to human PlGF. Subsequently, avidin conjugated to horseradish peroxidase (HRP) is added, and the plates are incubated.

Only wells containing human PlGF, the biotin-conjugated detection antibody, and the HRP–avidin complex will develop color upon addition of the tetramethylbenzidine (TMB) substrate solution. The enzymatic reaction was stopped by adding sulfuric acid, the resulting color change was measured at 450 nm ± 10 nm using a spectrophotometer.

The optical density (OD) values of the samples are compared with the standard curve to determine the concentration of human PlGF in each specimen.

2.3 Reagent Preparation

1. Prior to use, all kit components and samples were brought to room temperature. All reagents were confirmed to be completely dissolved and thoroughly mixed before use. When the kit was not used in its entirety, only the strips and reagents required for the current experiment were removed. Unused strips and reagents were stored according to the manufacturer's instructions.

2. The 25× Wash Buffer was diluted with double-distilled water to prepare a 1× Wash Buffer. The Standard Working Solution was centrifuged for one minute at 1000 × g. Subsequently, 1.0 mL of standard diluent buffer was added to the Standard, which was then allowed to stand at room temperature for 10 minutes before being gently mixed to avoid foaming. The resulting stock solution had a concentration of 1000 pg/mL. Seven tubes, each containing 0.5 mL of standard diluent Buffer, were prepared. A twofold serial dilution series was generated using the diluted Standard. Before transferring to the next tube, the contents of each tube were thoroughly mixed by pipetting up and down several times to ensure homogeneity.

3. The tube containing only standard diluent buffer served as the blank (0 pg/mL). Seven standard concentrations were prepared for the calibration curve: 1000, 500, 250, 125, 62.5, 31.25, and 15.63 pg/mL. A new standard solution was prepared for each experiment to ensure result accuracy. Pipette tips were replaced after each dilution step, progressing from the highest to the lowest concentration. Care was taken not to transfer any solution from the preceding tube into the final blank tube. Sequential 500-µL transfers yielded standards at 500, 250, 125, 62.5, 31.25, and 15.63 pg/mL, with the final tube containing only diluent as the 0 pg/mL blank. Each dilution was thoroughly mixed before the next transfer, and new pipette tips were used for each step to prevent cross-contamination. Before using, 1× Streptavidin-HRP and 1× Biotinylated antibody they centrifuged or span for a short time. HRP Diluent or Biotinylated Antibody Diluent was used to dilute the reagents to their respective working concentrations at a 1:100 ratio. When the TMB Substrate Solution was used, only the required amount was aspirated with sterile tips, and any remaining solution was not returned to the original vial.

2.4 Assay Procedure

1. All kit components were allowed to reach room temperature. Then, 100 µL of either the sample or the appropriately diluted Standard Working Buffer was added to each well. The plate was incubated at 37 °C for 80 minutes.

2. The liquid from each well was discarded, and the plate was washed three times with 200 µL of 1× Wash Buffer per well. The plate was gently blotted on clean absorbent paper. Subsequently, 100 µL of 1× Biotinylated Antibody Working Solution was dispensed into each well, and the plate was incubated at 37 °C for 50 minutes.

3. The liquid was removed, and the plate was washed again three times with 200 µL of 1× Wash Buffer before being gently blotted dry. Then, 100 µL of Streptavidin–HRP Working Solution (1×) was added to each well, and the plate was incubated at 37 °C for 50 minutes.

4. The liquid was discarded, and the plate was washed five times with 200 µL of 1× Wash Buffer per well, followed by gentle blotting. Next, 90 µL of TMB Substrate Solution was added to each well, and the plate was incubated in the dark at 37 °C for 20 minutes.

5. Finally, 50 µL of Stop Solution was added to each well, and the plate was shaken gently for 1 minute to ensure proper mixing. The optical density (OD) was immediately recorded at 450 nm, and the results were calculated as described.

2.5 Calculation of Results

The mean OD value of the zero standard (blank) was subtracted from the mean OD values of each standard, sample, and control. A standard curve was then constructed by plotting absorbance values on the x-axis against the corresponding human PlGF concentrations on the y-axis (Table 1). A best-fit curve was generated via the plotted data points, and the concentration of PlGF in each sample was derived from this curve. For diluted samples, the measured concentration was multiplied by the respective dilution factor. Data analysis and curve fitting were performed using specialized software (CurveExpert; Hyams Development, USA) (Figure 1).

Corrected OD values (x-axis) were plotted against corresponding concentrations of PLGF (pg/mL, y-axis). A best-fit curve was generated using serial dilutions from 1000 to 15.63 pg/mL, with a correlation coefficient (r) of 0.9999, demonstrating high linearity and assay reliability.

2.6 Principle

The assay employed a sandwich ELISA approach. Each well of the supplied microtiter plate was pre-coated with a monoclonal antibody that specifically binds human sFlt-1. Appropriate wells were loaded with either standards or samples, after which a biotin-conjugated antibody specific for human sFlt-1 was added. Subsequently, each well was incubated with avidin conjugated to HRP. Only wells containing human sFlt-1 bound to both the biotin-conjugated antibody and enzyme-labeled avidin will develop color upon addition of the TMB (3,3',5,5'-tetramethylbenzidine) substrate solution. The enzymatic reaction was stopped by the addition of sulfuric acid, and the resulting color change was measured using a spectrophotometer at 450 nm ± 10 nm. The OD values readings were evaluated against the standard curve to quantify human sFlt-1 levels in each sample.

2.7 Reagent Preparation

1. Equilibration**:** Prior to starting the assay, all kit components and samples were allowed to equilibrate to room temperature. We were ensured all reagents were completely dissolved and thoroughly mixed before starting the assay.

2. Partial Use of Kit: If the entire kit will not be used at once, only the required number of strips and reagents were used for the current experiment. The remaining strips and reagents were stored according to the manufacturer's instructions.

3. Wash Buffer Preparation: The 25× Wash Buffer was diluted with double-distilled water to prepare the 1× Wash Buffer.

4. Standard Working Solution preparation: The Standard Working Solution was centrifuged for 1 minute at 1000 × g. Then 1.0 mL of Standard Diluent Buffer was added to the Standard, and allowed it to stand at room temperature for 10 minutes, and gently mixed (avoid foaming). The stock standard solution had a concentration of 10 ng/mL.

Seven tubes, each containing 0.5 mL of Standard Diluent Buffer was prepared. Using the stock solution, a twofold serial dilution was performed as shown in the example below. Each dilution was up and down by pipetting several times to ensure complete mixing before proceeding to the next dilution. The final EP tube containing only Standard Diluent Buffer served as the Blank (0 ng/mL). Seven points of diluted standards were prepared as follows: 10 ng/mL, 5 ng/mL, 2.5 ng/mL, 1.25 ng/mL, 0.63 ng/mL, 0.32 ng/mL, and 0.16 ng/mL. A fresh standard series was prepared for each experiment to ensure accuracy and reliability. Pipette tips were replaced after each dilution step, proceeding from the highest to the lowest concentration. The solution from the previous dilution was not pipetted into the final blank tube to prevent cross-contamination.

2.8 Procedure

1. After all reagents were allowed to reach room temperature, 100 µL of either the appropriately diluted Standard Working Buffer or the sample was added to each well. The plate was incubated at 37 °C for 80 minutes.

2. The wells were emptied, rinsed three times with 200 µL of 1× Wash Buffer, and gently blotted on clean absorbent paper. Then, 100 µL of Biotinylated Antibody Working Solution (1×) was added to each well, followed by incubation at 37 °C for 50 minutes.

3. The liquid was discarded, and each well was washed again three times with 200 µL of 1× Wash Buffer and blotted dry. Then, 100 µL of Streptavidin–HRP Working Solution (1×) was added to each well, and the plate was incubated at 37 °C for 50 minutes.

4. The washing step was repeated five times with 200 µL of 1× Wash Buffer, and the plate was dried on absorbent paper. Subsequently, 90 µL of TMB Substrate Solution was added to each well, and the plate was incubated in the dark at 37 °C for 20 minutes.

5. The reaction was stopped by adding 50 µL of Stop Solution to each well. The plate was gently shaken for 1 minute to ensure thorough mixing. The optical density (OD) was read immediately at 450 nm, and the results were calculated as described.

2.9 Calculation of Results

The mean OD of the zero standard was subtracted from the mean duplicate OD readings of each standard, control, and sample. A standard curve was constructed by plotting absorbance values on the x-axis against the corresponding human sFlt-1 concentrations on the y-axis. A best-fit curve was generated to determine the concentration of sFlt-1 in each sample. For diluted samples, the measured concentration obtained from the standard curve was corrected by applying the corresponding dilution factor. Data analysis and curve fitting were performed using CurveExpert software (Table 2, Figure 2).

PlGF levels were measured using the Demerited ELISA Kit. This assay was based on a sandwich-type solid-phase enzyme-linked immunosorbent assay (ELISA) (24). A monoclonal antibody targeting a specific antigenic epitope of the PlGF molecule was coated onto the microtiter wells. An aliquot of the patient sample containing endogenous PlGF was then incubated in the coated wells. Following the washing step, a biotin-conjugated polyclonal antibody specific for PlGF was added to the wells. After further washing to remove any unbound antibody, the streptavidin–HRP enzyme complex was introduced. The unbound enzyme complex was subsequently removed by washing after incubation. The concentration of PlGF in each sample was directly proportional to the amount of bound peroxidase. Upon addition of the substrate solution, a color reaction developed, and the intensity of the color was directly proportional to the PlGF concentration in the patient sample. Statistical analyses were performed using SPSS version 23. Numerical data were expressed as medians and ranges or as means ± standard deviations, as appropriate. Categorical data were summarized as percentages.

Table 1. Optical density (OD) values and corrected readings for the ELISA standard curve.

Concentration (pg/ml)	OD	Corrected
1000	1,952	1.867
500	1.625	1.54
250	1.227	1.142
125	0.892	0.807
62.5	0.585	0.5
31.25	0.342	0.257
15.63	0.248	0.163
0	0.085	0.000

Table 2. Optical density (OD) values and corrected readings for the ELISA standard curve.

Concentration (ng/ml)	OD	Corrected
10	2.054	1.973
5	1.594	1.513
2.5	1.116	1.035
1.25	0.897	0.816
0.63	0.559	0.478
0.32	0.365	0.284
0.16	0.226	0.145
0	0.081	0.000

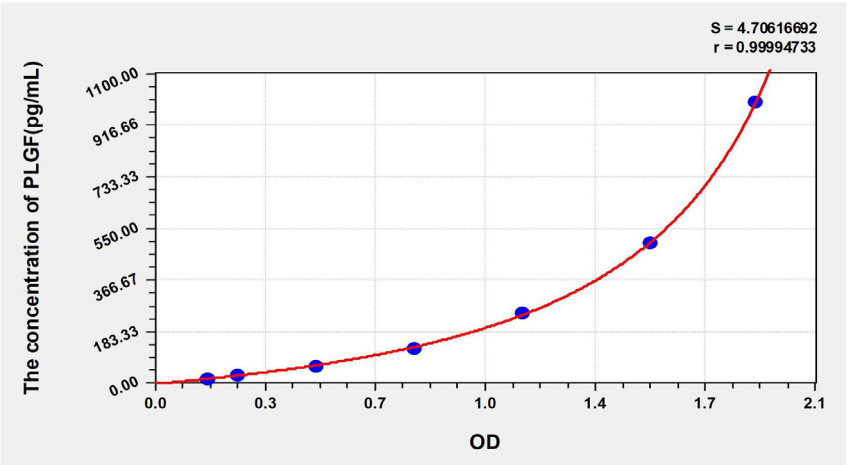


Figure 1. Standard curve for human PLGF concentrations measured by ELISA (**Prepared by Authors, 2025**).

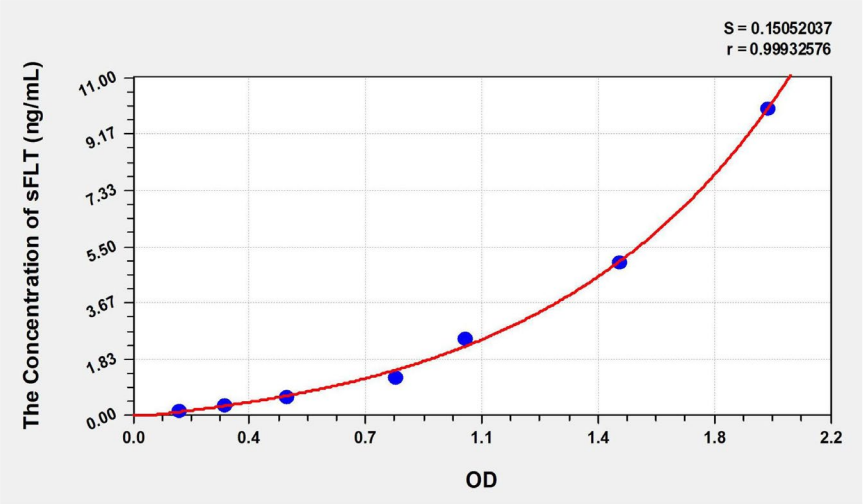


Figure 2. Standard curve for human PLGF concentrations measured by ELISA. Corrected OD values (x-axis) were plotted against corresponding concentrations of PLGF (pg/mL, y-axis). A best-fit curve was generated using serial dilutions from 1000 to 15.63 pg/mL, with a correlation (**Prepared by Authors, 2025**).

3. Result

Maternal demographic characteristics and clinical parameters are summarized in Table 3. A significant difference in maternal age was observed between the preeclampsia and control groups, as illustrated in Figure 3A.

There was a statistically significant increase in BMI among women with preeclampsia compared with the controls (Figure 3B). In contrast, gestational age did not differ significantly between the two groups (Table 3). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were markedly elevated in the preeclampsia group compared with the control group (Table 3). These differences are demonstrated in Figures 3C and 3D, respectively, and reflect the hypertensive profile associated with the onset of preeclampsia. Serum concentrations of pro- and anti-angiogenic markers are presented in Table 4. PlGF level was significantly lower in the preeclampsia group than in the control group (Figure 3E). In contrast, sFlt-1 concentrations were significantly higher in the preeclampsia group (Figure 3F).

The sFlt-1/PlGF ratio was also markedly elevated in women with preeclampsia compared with the control group (Table 4, Figure 3G), further supporting the diagnostic value of this biomarker ratio in identifying preeclampsia. The results presented in Table 5 and Figure 4 highlight the diagnostic performance of SFIT, PlGF based on ROC curve analysis across control, moderate, and severe groups. All parameters demonstrated statistically significant discriminative ability with $p < 0.001$, confirming their diagnostic value. However, their predictive power varied in terms of sensitivity, specificity, and area under the curve (AUC).

SFIT showed outstanding diagnostic accuracy, with an AUC of 0.998, indicating near-perfect discrimination. Although the sensitivity was relatively modest (70.2%), the high specificity (82.39%) reflects its reliability in ruling out false positives. This suggests that SFIT may serve as a robust biomarker in identifying disease severity, particularly when combined with other diagnostic markers. Recent studies have similarly emphasized the potential of novel functional indices as reliable indicators of oxidative stress and metabolic dysfunction (7). PlGF demonstrated excellent diagnostic capacity with an AUC of 0.974, coupled with both high sensitivity (92.87%) and specificity (98.45%). These results suggest that PlGF could be a highly effective biomarker for differentiating between severity groups. PlGF has been increasingly recognized in recent years as a regulator of angiogenesis and vascular health, with growing evidence supporting its use in clinical diagnostics for inflammatory and metabolic disorders.

The ROC curves shown in Figure 4 demonstrate the diagnostic ability of SFIT and PlGF across all study groups. The steep rise of the curves toward the upper left corner indicates strong discriminatory ability for most criteria, with SFIT showing near-perfect separation between groups. PlGF also achieved a high level of specificity with consistently increasing sensitivity across a wide range of characteristics, although its discriminatory ability was relatively lower compared to other biomarkers. Overall, these ROC profiles confirm that the markers have valuable diagnostic potential, with some criteria showing greater accuracy than others in distinguishing disease severity.

Table 3. Features of the research population Preeclampsia Factor.

Factors	Preeclampsia group (N =75)	Control group (N =50)	P
Age (years)	29.43± 6.61	25.68± 5.67	0.007
BMI (Kg/m^2)	33.40± 5.71	28.24 ± 3.15	0.001
Gestational age (weeks)	34.11 ± 3.02	35.48 ± 4.50	0.090
SBP (mmHg)	154.58 ± 14.88	120.42 ± 4.79	0.001
DBP (mmHg)	96.32 ± 7.95	80.17 ± 8.07	0.001
Data are presented as mean ± standard deviation (SD)			

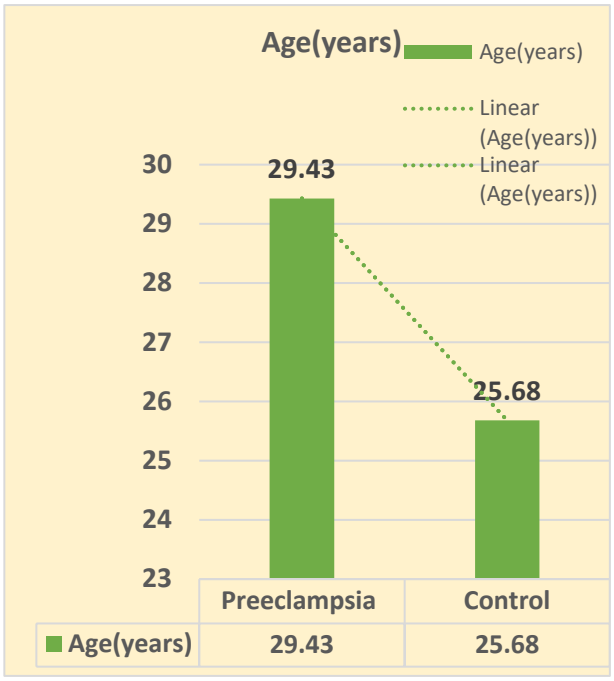
Table 4. PlGF and sFlt-1 levels and their ratios in the control and preeclamptic groups.

Parameters	Preeclampsia group (N =75)	Control group (N =50)	P
PlGF (Pg/mL)	5.18 ± 1.82	14.38 ± 20.47	0.003
sFlt-1(Pg/mL)	6.84 ± 1.60	3.74 ± 3.04	0.001
sFlt-1/PlGF	1.28 ± 0.51	0.42 ± 0.42	0.001
Data represent mean ± standard deviation (S.D)			

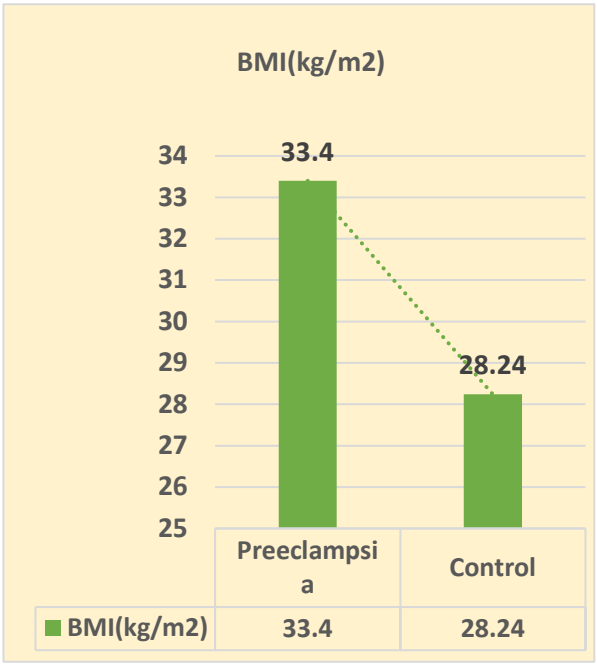
Table 5. Diagnostic Performance of sFlt-1, PlGF Based on ROC Curve Analysis.

Parameters	Sensitivity	Specificity	Cut-off value	Area	Std. Error	P value	Asymptotic 95% Confidence Interval	
							Lower Bound	Upper Bound
SFlT	70.2%	82.39%	≥ 4.93	0.998	0.002	<0.001*	0.995	1.000
PlGF	92.87%	98.45%	≤ 596.17	0.974	0.017	<0.001*	0.913	0.973

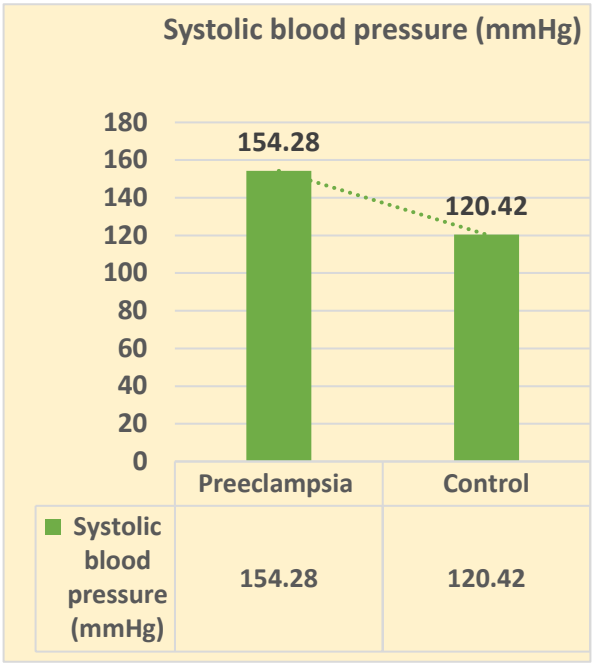
A



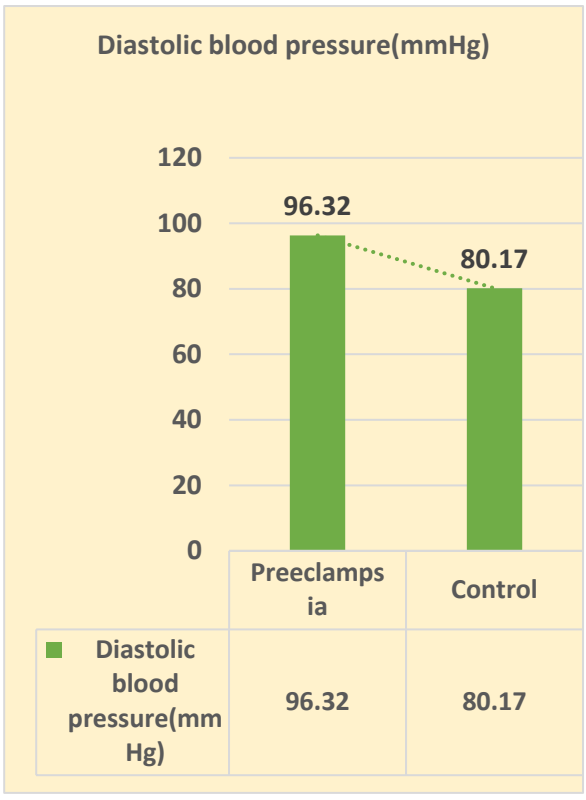
B


BMI(kg/m2)
34
33
32
31
30
29
28
27
26
25
33.4
28.24
Preeclampsia
Control
BMI(kg/m2)
33.4
28.24

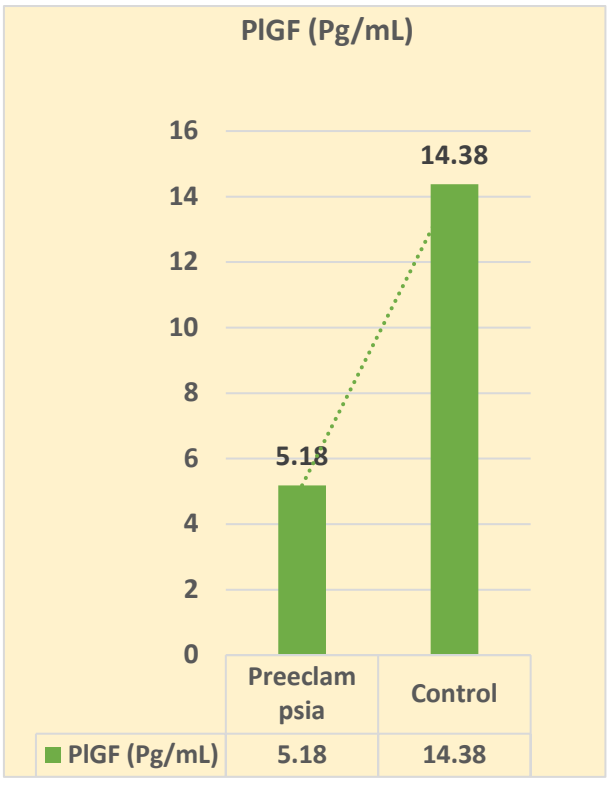
C


Systolic blood pressure (mmHg)
180
160
140
120
100
80
60
40
20
0
154.28
120.42
Preeclampsia
Control
Systolic blood pressure (mmHg)
154.28
120.42

D


Diastolic blood pressure(mmHg)
120
100
80
60
40
20
0
96.32
80.17
Preeclampsia
Control
Diastolic blood pressure(mmHg)
96.32
80.17

E


PlGF (Pg/mL)
16
14
12
10
8
6
4
2
0
14.38
5.18
Preeclampsia
Control
PlGF (Pg/mL)
5.18
14.38

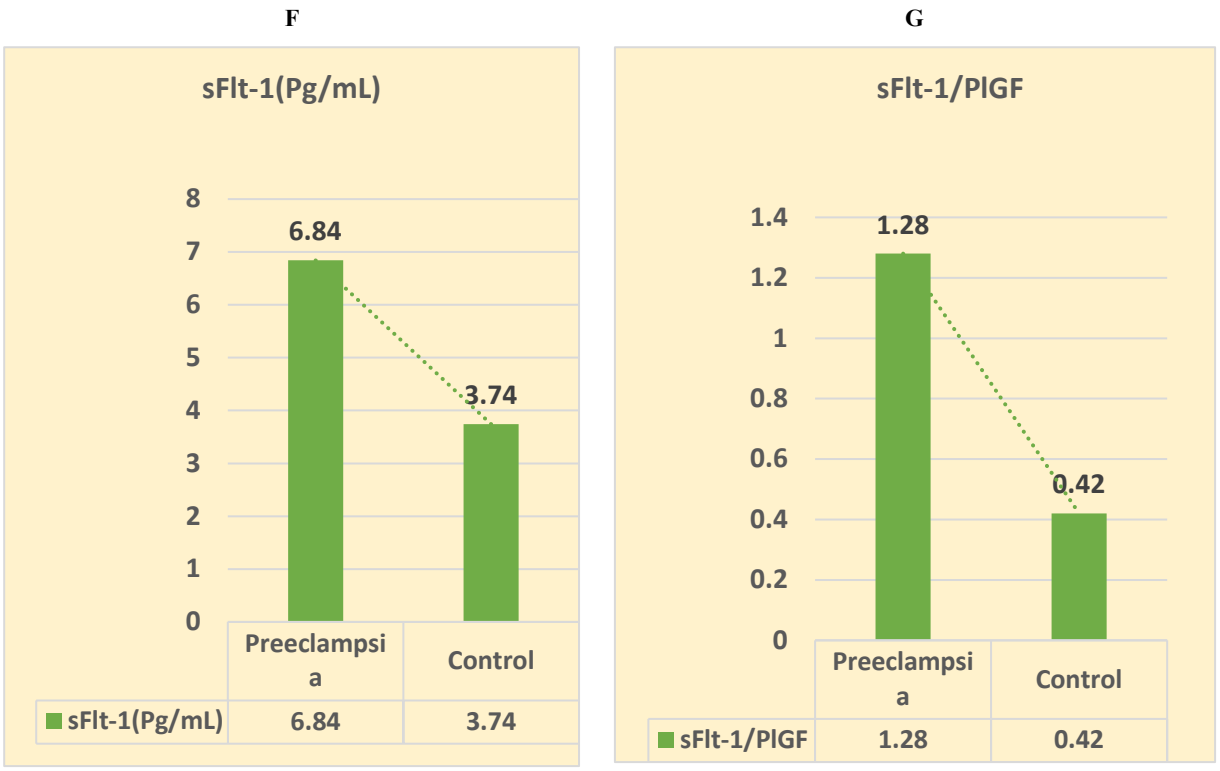


Figure 3. Comparison of maternal clinical parameters between the preeclampsia and control groups: (A) Maternal age. (B) Body mass index (BMI), (C) Systolic blood pressure (SBP), (D) Diastolic blood pressure (DBP), (E) Placental growth factor (PlGF), (F) Soluble fms-like tyrosine kinase-1 (sFlt-1), (G) sFlt-1/PlGF ratio (**Prepared by Authors, 2025**).

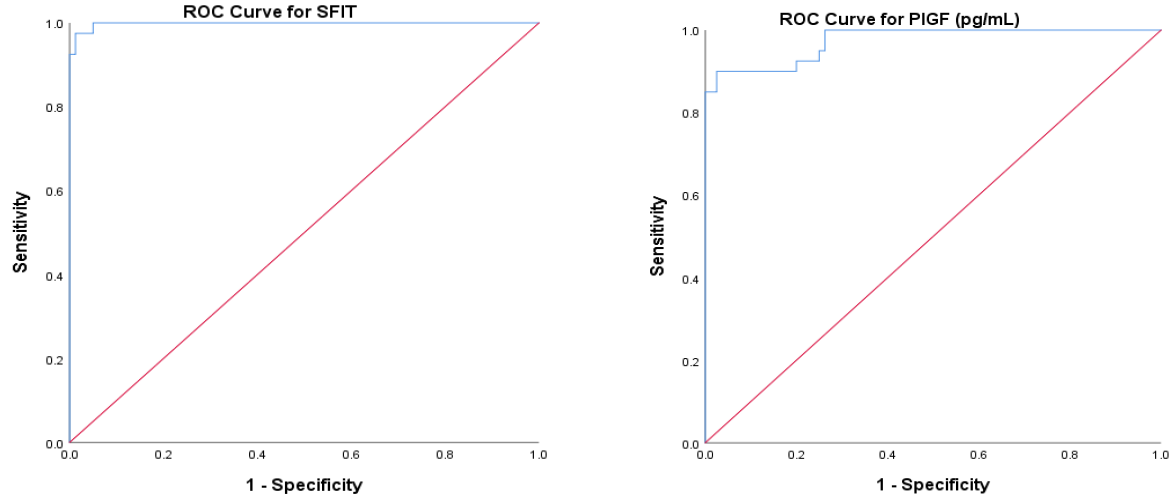


Figure 4. Analysis using ROC curves of SFIT, PlGF for Differentiating Study Groups (**Prepared by Authors, 2025**).

4. Discussions

Preeclampsia remains a major contributor to maternal and fetal morbidity and mortality worldwide, affecting approximately 2–8% of all pregnancies and accounting for nearly 18% of maternal deaths globally equivalent to about 70,000 fatalities annually, most of which occur in low- and middle-income countries (26).

The clinical presentation of preeclampsia can vary widely (27), and accurate and timely diagnosis is crucial for optimizing maternal and fetal outcomes. This study aimed to evaluate the predictive value of placental growth factor (PlGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) levels, as well as their ratio, in the early detection of preeclampsia. Additionally, the potential effects of maternal body mass index (BMI) and gestational age were examined.

The mean maternal age differed significantly between the groups: 29.43 ± 6.61 years in the preeclampsia group and 25.68 ± 5.67 years in the control group. BMI also

varied significantly between the groups (P = 0.007), consistent with findings from previous studies (28). Specifically, the mean BMI was higher in the preeclampsia group (33.40 ± 5.71 kg/m²) than in the control group (28.24 ± 3.15 kg/m²). However, gestational age did not differ significantly, in line with earlier reports (29). These findings suggest that higher BMI may contribute to the risk of preeclampsia and gestational hypertension. Indeed, this study supports previous evidence indicating that women with normal BMI are less likely to develop preeclampsia than those who are overweight or obese prior to pregnancy (30). Systolic blood pressure and diastolic blood pressure were markedly higher in the preeclampsia group (SBP = 154.58 ± 14.88 mmHg; DBP = 96.32 ± 7.95 mmHg) compared with the control group (SBP = 120.42 ± 4.79 mmHg; DBP = 80.17 ± 8.07 mmHg). Regarding angiogenic biomarkers, the serum levels of PlGF were significantly reduced in the preeclampsia group (5.18 ± 1.82 pg/mL) compared with the control group (14.38 ± 20.47 pg/mL). Conversely, sFlt-1 levels were markedly elevated in the preeclampsia group (6.84 ± 1.60 pg/mL) relative to the control group (3.74 ± 3.04 pg/mL). These findings indicate that preeclamptic women exhibited significantly higher circulating levels of antiangiogenic factors and reduced levels of proangiogenic factors, consistent with previous research (31, 32).

It has been established that preeclampsia is more likely to occur when serum levels of proangiogenic factors, such as PlGF, are reduced, while antiangiogenic factors, such as sFlt-1, are elevated. The ratio of sFlt-1 to PlGF has therefore been recognized as a valuable diagnostic and predictive biomarker for preeclampsia (28). In the present study, the mean sFlt-1/PlGF ratio was significantly higher in the preeclampsia group (1.28 ± 0.51) than in the control group (0.42 ± 0.42; P=0.007), further supporting its potential clinical utility in identifying and predicting preeclampsia.

5. Conclusion

The findings of this study indicate a strong association between preeclampsia and elevated BMI and the risk of preeclampsia. Increasing obesity is likely to increase the risk of preeclampsia. Therefore, the potential benefits of pre-pregnancy weight loss programs should be considered. The risk of preeclampsia may increase with advancing gestational age and increasing maternal BMI. PlGF, tyrosine kinase-1, and sflt-1/plGF ratio in the third trimester may significantly contribute to the diagnostic potential of preeclampsia.

6. Declarations

6.1 Acknowledgments

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6.2 Ethical Considerations

The study was approved by the Ethical Approval Committee. Ethical approval was obtained from the Institutional Review Board (IRB) of University of Dhi-Qar (Approval No. REC201/2024, dated September 11, 2024). Written informed consent was obtained from all participants prior to their inclusion in the study.

6.3 Authors' Contributions

Ali Ghazi Faisal: Sample collection and preparation for testing, as well as statistical analysis. Raed M. H. Al-Saleh: Performing some of the required analyses and measuring the samples. Wasan Rahim Mubarak: Performing the remaining required analyses and measurements.

6.4 Conflict of Interest

The authors have no conflict of interest.

6.5 Fund or Financial Support

This research received no external funding.

6.6 Using Artificial Intelligence Tools (AI Tools)

The authors declare that artificial intelligence (AI) tools were used solely for minor language editing and grammar improvement. The authors take full responsibility for the content of the manuscript.

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