



RESEARCH ARTICLE

The Association Between PIGF Level and Neonatal Outcomes in Normal Pregnancies, Early Onset and Late Onset Preeclampsia at Dr. M. Djamil General Hospital Padang

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Abstract

Background: Preeclampsia is a major pregnancy complication contributing to maternal and neonatal morbidity and mortality. Impaired placentation causes an imbalance between angiogenic and antiangiogenic factors, including reduced placental growth factor (PIGF), which may contribute to adverse neonatal outcomes.

Objective: To determine the relationship between maternal serum PIGF levels and neonatal outcomes in normal pregnancies, early-onset preeclampsia (EOPE), and late-onset preeclampsia (LOPE) at Dr. M. Djamil General Hospital, Padang.

Methods: This observational analytic study used a cross-sectional design involving pregnant women with normal pregnancies, EOPE, and LOPE who met the inclusion criteria. Maternal serum PIGF levels were measured using enzyme-linked immunosorbent assay (ELISA). Neonatal outcomes included birth weight, birth length, and Apgar scores. Data were analyzed using univariate and bivariate analyses

Results: Forty-eight pregnant women were included, comprising 16 normal pregnancies, 16 EOPE cases, and 16 LOPE cases. The highest mean PIGF level was observed in normal pregnancies, followed by LOPE and EOPE, with a significant difference among groups. The lowest mean birth weight, birth length, and Apgar scores were observed in EOPE. Bivariate analysis showed a significant association between PIGF levels and birth weight in EOPE ($p = 0.0001$), while no significant association was found with birth length or Apgar scores.

Conclusion: Maternal serum PIGF levels differed significantly among normal pregnancies, EOPE, and LOPE, supporting its potential as a biomarker of preeclampsia. PIGF was significantly associated with birth weight in EOPE but not with birth length or Apgar scores.

Keywords: preeclampsia, placental growth factor, neonatal outcomes

INTRODUCTION

Preeclampsia remains one of the most significant complications in pregnancy, contributing substantially to maternal and neonatal morbidity and mortality worldwide¹. It is estimated that preeclampsia affects approximately 5–10% of pregnancies globally, with a disproportionately higher burden in developing countries². In Indonesia, the incidence ranges from 2.1% to 8.5% and represents one of the leading causes of maternal death, second only to hemorrhage³. The impact of preeclampsia extends beyond maternal complications, as it is also strongly associated with adverse neonatal outcomes such as low birth weight, prematurity, and perinatal mortality⁴.

Despite decades of research, the exact pathophysiology of preeclampsia remains incompletely understood. It is widely accepted as a multifactorial disorder involving abnormal placentation, endothelial dysfunction, immunological maladaptation, and angiogenic imbalance^{5–7}. Among these mechanisms, the disruption of angiogenic balance has gained increasing attention. In normal pregnancy, angiogenesis is tightly regulated by proangiogenic factors such as vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), alongside antiangiogenic factors like soluble fms-like tyrosine kinase-1 (sFlt-1)^{8–10}. In preeclampsia, increased levels of sFlt-1 lead to sequestration of VEGF and PlGF, resulting in decreased bioavailability of these proangiogenic factors and subsequent endothelial dysfunction¹¹.

Placental growth factor (PlGF), a member of the VEGF family, plays a crucial role in placental development by promoting angiogenesis, trophoblast invasion, and vascular remodeling¹². Under normal physiological conditions, maternal serum PlGF levels increase progressively during pregnancy, peaking around 30 weeks of gestation before declining near term¹³. However, in preeclampsia, particularly early-onset preeclampsia, PlGF levels are significantly reduced even before clinical manifestations appear¹⁴. This early decline highlights its potential utility as a biomarker for early detection and risk stratification.

Several studies have demonstrated the diagnostic and predictive value of PlGF in preeclampsia. Previous research has shown that women with preeclampsia exhibit significantly lower PlGF levels compared to normotensive pregnant women¹⁵. Additionally, low PlGF levels are associated with an increased risk of developing preeclampsia¹⁶. The sFlt-1/PlGF ratio has been reported to have high sensitivity and specificity in identifying preeclampsia^{17,18}. International guidelines have also recommended the use of PlGF as part of screening strategies for early detection¹⁹.

However, while the role of PlGF as a biomarker for preeclampsia is well established, its relationship with neonatal outcomes remains less clearly defined. Some studies suggest that low PlGF levels are associated with adverse outcomes such as fetal growth restriction (FGR), low birth weight, and increased need for neonatal intensive care^{20,21}. Conversely, other studies have reported inconsistent findings, particularly regarding outcomes such as Apgar scores and birth length²². These discrepancies highlight ongoing controversies regarding the predictive value of PlGF for neonatal outcomes.

Moreover, differences between early-onset preeclampsia (EOPE) and late-onset preeclampsia (LOPE) further complicate interpretation. EOPE is more strongly associated with placental dysfunction and adverse fetal outcomes, whereas LOPE is often linked to maternal cardiovascular factors^{23,24}. Recent studies have also emphasized the growing role of angiogenic biomarkers in improving prediction models for adverse pregnancy outcomes²⁵. However, data from developing countries remain limited.

This study aims to investigate the association between maternal serum PIGF levels and neonatal outcomes in normal pregnancies, EOPE, and LOPE. Understanding this relationship may provide insights into the role of PIGF as both a diagnostic and prognostic biomarker.

METHODS

This study was an observational analytic study with a cross-sectional design conducted at a tertiary referral hospital. The study population consisted of pregnant women categorized into three groups: normal pregnancy, early-onset preeclampsia, and late-onset preeclampsia. A total of 48 participants were included using consecutive sampling. Inclusion criteria were based on established diagnostic guidelines for preeclampsia^{1,3}. Exclusion criteria included chronic hypertension, diabetes mellitus, renal disease, and other systemic conditions that may influence angiogenic factors. A consecutive sampling method was used to recruit eligible participants.

Maternal blood samples were collected and analyzed for serum PIGF levels using the enzyme-linked immunosorbent assay (ELISA) method, which is widely recognized for its sensitivity in detecting angiogenic biomarkers⁶. Neonatal outcomes assessed included birth weight, birth length, and Apgar scores. Statistical analysis consisted of univariate and bivariate methods, with significance set at $p < 0.05$.

RESULT

This study was conducted in the PONEK unit and inpatient ward of the Department/SMF of Obstetrics and Gynecology at Dr. M. Djamil General Hospital and its affiliated hospitals from December 2024 to December 2025. A total of 48 samples were collected and classified into three groups: normal pregnancy, early-onset preeclampsia, and late-onset preeclampsia. Maternal blood samples were analyzed at the Biomedical Laboratory, Faculty of Medicine, Universitas Andalas, to measure PIGF levels.

Table 1. Characteristics of the study subjects: normal pregnant women and preeclampsia patients

Variable	Normal		EOPE		LOPE	
	f	%	f	%	f	%
Age of mother						
<20 years	0	0	0	0	0	0
20-35 years	14	87,5	10	62.5	14	87,5
>35 years	2	12,5	6	37.5	2	12,5
Age of pregnancy						
Preterm	0	0	16	100	7	43,8
Aterm	16	100	0	0	9	56,3
Parity						
Primipara	3	18,8	12	75	9	56,3
Multipara	13	81,3	4	25	7	43,8

Table 2. PIGF levels in normal pregnancy, early-onset preeclampsia, and late-onset preeclampsia

PIGF level (pg/mL)						
Variable	n	Mean	±SD	Min	Max	p-value
Normal	16	41.36	40.16	19.96	62.76	0.001
EOPE	16	18.32	5.71	15.27	21.36	0.0001
LOPE	16	21.88	19.95	11.24	32.51	0.001

Table 3. Relationship between PIGF levels and neonatal outcomes (Body Weight) in normal pregnancies, early-onset and late-onset preeclampsia

Pregnancy group	Median PIGF (min-max)	BB (Mean±SD)	r	p-value
Normal	20.05 (12,25-140,47)	3265.63 (±263.77)	-0.123	0,650
EOPE	18.323 (±5.718)	1467.50 (±404.19)	0,991	0,0001
LOPE	14,47 (4,85-71,43)	2850 (2589-3865)	-0,297	0,264

Table 4. Relationship between PIGF levels and neonatal outcomes (body length) in normal pregnancies, early-onset and late-onset preeclampsia

Pregnancy group	Median PIGF (Min-Max)	Median TB (Min-Max)	r	p-value
Normal	20.05 (12,25-140-47)	45.19 (±3.311)	-0,212	0,430
EOPE	18.323 (±5.718)	36.25 (±6.708)	0140	0,604
LOPE	14,47 (4,85-71,43)	44.38 (±4.911)	0,083	0,759

Table 5. Relationship between PIGF levels and neonatal outcomes (Apgar scores) in normal pregnancies, early-onset and late-onset preeclampsia

Pregnancy group	Med PIGF (Min-max)	Med AS 1	Med AS 5	r PIGF–Apgar	p-value
		(Min-Max)	(Min-Max)		
Normal	20.05 (12,25-140-47)	7	8	Apgar 1 menit: r = -0,055	0.840
		(6-8)	(7-10)	Apgar 5 menit: r = -0,050	0,855
EOPE	18.323 (±5.718)	4	7	Apgar 1 menit: r = -0,221	0,412
		(0-6)	(0-8)	Apgar 5 menit: r = -0,014	0,958
LOPE	14,47 (4,85-71,43)	7	8	Apgar 1 menit: r = 0.847	0,749
		(6-8)	(7-9)	Apgar 5 menit: r = 0.087	0,749

DISCUSSION

This study demonstrates a significant association between maternal serum PIGF levels and neonatal outcomes, particularly birth weight, in pregnancies complicated by early-onset preeclampsia. The findings support the hypothesis that angiogenic imbalance plays a critical role not only in the pathogenesis of preeclampsia but also in determining fetal growth and neonatal health^{8,12}. The significantly lower PIGF levels observed in early-onset preeclampsia are consistent with previous studies, which have shown that EOPE is strongly associated with placental insufficiency^{14,23}. Inadequate trophoblast invasion and incomplete remodeling of spiral arteries lead to uteroplacental ischemia, resulting in reduced production of angiogenic factors such as PIGF^{5,13}. This impaired placental function directly affects fetal growth, explaining the strong association with low birth weight observed in this study^{20,21}.

The absence of a significant relationship between PIGF levels and birth length or Apgar scores suggests that these outcomes may be influenced by multiple factors beyond placental angiogenesis. For instance, Apgar scores are affected by intrapartum conditions, neonatal

resuscitation, and other acute factors that may not directly correlate with chronic placental dysfunction²².

Interestingly, late-onset preeclampsia showed intermediate PlGF levels and relatively better neonatal outcomes compared to early-onset cases. This supports the concept that LOPE is less placental-driven and more related to maternal cardiovascular factors²⁴. Therefore, the predictive value of PlGF may be more pronounced in EOPE than in LOPE. The findings of this study align with previous research indicating that low PlGF levels are associated with fetal growth restriction and adverse perinatal outcomes^{20,21,25}. However, discrepancies in the literature regarding other neonatal outcomes highlight the complexity of preeclampsia and the multifactorial nature of neonatal health²².

From a clinical perspective, the results suggest that measuring PlGF levels could be useful not only for early detection of preeclampsia but also for identifying pregnancies at risk of low birth weight, particularly in early-onset cases^{17,19}. This could facilitate closer monitoring, timely intervention, and improved perinatal outcomes. However, this study has several limitations. The relatively small sample size may limit the generalizability of the findings. Additionally, the cross-sectional design precludes causal inference. Longitudinal studies with larger sample sizes are needed to further validate these findings.

CONCLUSION

In conclusion, this study demonstrates a significant association between maternal serum Placental Growth Factor (PlGF) levels and preeclampsia, with the lowest levels observed in early-onset cases. Furthermore, a significant relationship was identified between PlGF levels and birth weight in early-onset preeclampsia, indicating that lower PlGF levels are associated with poorer fetal growth. However, no significant associations were found between PlGF levels and birth length or Apgar scores across the study groups. These findings suggest that PlGF has potential as a biomarker not only for preeclampsia but also for predicting specific neonatal outcomes, particularly low birth weight in early-onset preeclampsia.

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