DOI: 10.7860/JCDR/2026/87577.24358

Review Article

Obstetrics and Gynaecology Section

From Placentation to Prediction: Modern Perspective on Emerging Biomarkers in Preeclampsia Prediction

R SAROASH ZULFISHAAN[1], R ANUSHA[2], PREET AGARWAL[3], LEENA CHAND[4]

ABSTRACT

Preeclampsia (PE), a multisystem hypertensive disorder complicating 3-8% of pregnancies worldwide, drives substantial maternal and perinatal morbidity and mortality, necessitating early predictive strategies to enable timely interventions. This narrative review synthesises evidence on galectin-7, galectin-3, galectin-13 (PP13), galectin-1, galectin-9, Carbonic Anhydrase IX (CAIX), and soluble fms-like tyrosine kinase-1 (sFlt-1)/Placental Growth Factor (PlGF) ratio. Gal-7 and Gal-13 modulate trophoblast invasion, immune tolerance, and spiral artery remodelling at the maternal foetal interface; CAIX, regulates pH under conditions of placental ischaemia; sFlt-1 antagonises proangiogenic Vascular Endothelial Growth Factor (VEGF)/PlGF, precipitating endothelial dysfunction - a PE hallmark; and Gal 3 promotes inflammation and trophoblast migration while linking to fibrosis. Prospective cohorts demonstrated presymptomatic alterations highlighting diagnostic accuracy over traditional. By elucidating these biomarkers' mechanistic roles in defective placentation, angiogenic imbalance, and hypoxic stress, this analysis underscores their potential in multi-marker panels for precision risk stratification facilitating aspirin prophylaxis and surveillance to avert preterm delivery and organ injury.

Keywords: Angiogenic factors, Placental dysfunction, Reproductive Health (SDG 3)

INTRODUCTION

The PE is characterised by an initial rise in blood pressure that usually occurs after 20 weeks of gestation during pregnancy, along with other symptoms such as proteinuria, neurological symptoms, liver dysfunction, signs of acute kidney injury, haemolysis or thrombocytopenia, and/or Foetal Growth Restriction (FGR) [1]. It affects 3-8% of pregnancies. Foetal morbidity and mortality are brought on by iatrogenic preterm delivery, placental abruption and FGR, in addition to the increase in maternal morbidity. PE causes 76,000 maternal and 500,000 child fatalities worldwide each year with patients in low-income versus high-income nations experiencing noticeably greater rates of morbidity and mortality. Between 2014 and 2017, maternal hypertension disease during pregnancy was associated with 6.6% of pregnancy-related deaths in the United States [1]. PE is a complex and multifactorial pregnancy disorder often described as a condition with diverse and overlapping pathogenic mechanisms. This is one of the well-recognised "great obstetrical syndromes" in which several pathological processes often overlapping converge on to a common pathway that ultimately leads to their clinical diagnosis [2]. PE shares certain pathophysiological features with preterm labour, including inflammatory activation, decidual dysfunction, and abnormal uteroplacental remodelling membrane and decidual activation.

The PE is diagnosed as hypertension following the twentieth week and meeting one of the following criteria as mentioned in [Table/Fig-1]. The PE and overlapping conditions occur in pregnant women with persistent hypertension. Pregnant women who exhibit persistent Systolic Blood Pressure (SBP) of 160 mm Hg or Diastolic Blood Pressure (DBP) of 110 mm Hg, or who meet any of the criteria in [Table/Fig-1], are considered to have severe PE [3].

The placenta is a vital organ in pregnancy that performs multiple essential functions, including supporting foetal growth and development through nutrient and gas exchange, waste removal, and endocrine activity [1].

Criteria	Parameters
Blood pressure	>140/90 mmHg after 20 weeks
Proteinuria	P/C ratio > 0.3; > 1.0 g/L on reagent cassette
Renal dysfunction	Creatinine > 1.02 mg/dL
Liver dysfunction	Elevated transaminase
Haematological	Thrombocytopenia/DIC
Neurological	Visual disturbances, seizures
Uteroplacental	IUGR, abnormal doppler

[Table/Fig-1]: Diagnostic criteria for Preeclampsia (PE) [3].
IUGR:Intrauterine growth restriction; DIC:Disseminated intravascular coagulation

LITERATURE SEARCH

This narrative review was conducted using a structured literature search strategy across PubMed, Scopus, Web of Science, and Google Scholar databases. Articles published in English between 2010 and 2025 were reviewed. Keywords and Mesh terms included 'preeclampsia", "biomarkers", "placental growth factor", "sFlt-1", "galectins", "PAPP-A", "NGAL", "CAIX", "placental hypoxia" and "prediction of preeclampsia".

Inclusion criteria: Original research articles, systematic reviews, meta-analyses, and clinical studies evaluating serum biomarkers associated with PE prediction or pathophysiology were included in the study.

Exclusion criteria: Studies with insufficient methodological clarity, duplicate data, or unrelated outcomes were excluded from the study. The purpose of this review was to provide a comprehensive narrative synthesis of emerging biomarkers and their potential clinical relevance in predicting PE.

Angiogenic Biomarkers

One proangiogenic factor produced by the placenta is the PlGF which contributes to angiogenesis. It enhances the function of VEGF-A, which is necessary for maintaining vascular homeostasis. Maternal blood can be tested for PlGF as early as the eighth week of pregnancy; after the second trimester of pregnancy, the level

gradually decreases until delivery. However, due to the elevated levels of soluble fms-like tyrosine kinase-1 (sFlt-1), PlGF remains persistently low in PE. An anti-angiogenic factor called sFlt-1 is elevated in the mother's circulation during a typical pregnancy, but it is elevated even further in PE [4]. By attaching to the receptor-binding domains of endothelial cell surface receptors, this protein inhibits the interaction of VEGF and PlGF, resulting in endothelial dysfunction. Because sFlt-1 binds to endothelial receptors, this will result in a decrease in the concentrations of free VEGF and PlGF in circulation. The amount of maternal sFlt-1 in circulation will rise about five weeks prior to the onset of symptoms. Hence, it was discovered that sFlt-1, sFlt-1/PlGF ratio, and maternal PlGF performed well in screening, predicting development, diagnosing, and short-term monitoring of established PE. Ultimately, it is better to measure the sFlt-1/PlGF ratio rather than the PlGF level alone because we cannot rely on the level of PlGF in PE with severe features or early in the course of the disease, whereas the sFlt-1/PlGF ratio provides a more accurate and clinically useful assessment of angiogenic imbalance and disease severity [5].

Placental Growth Factor (PlGF): PlGF serves as a pivotal biomarker in PE prediction, with low maternal serum levels reliably identifying high-risk pregnancies across numerous studies [6]. Meta-analysis demonstrates the strong predictive performance, yielding a pooled odds ratio of 9 (95% CI: 6-13) in 92,687 asymptomatic pregnant women participants, alongside high sensitivity 0.78 and specificity 0.88 for levels below 80-120 pg/mL, particularly after 14 weeks of gestation and for early-onset cases (OR: 18) [6]. Combining PlGF with sFlt-1 enhances accuracy, as evidenced by a meta-analysis of 15 studies showing 80% sensitivity and 92% specificity for the sFlt-1/PlGF ratio (>38), outperforming traditional markers and predicting onset within 7-28 days in symptomatic women [7]. First-trimester screening further supports its integration into routine protocols, reducing diagnostic delays and severe maternal events when used adjunctively, though randomised trials are warranted. PlGF is a placenta-derived angiogenic factor whose circulating levels are significantly reduced in women who subsequently develop PE, often weeks before the onset of clinical symptoms [8]. Low maternal serum PlGF, particularly in the first and early second trimester, has been shown to improve the prediction of both early and late onset PE when incorporated into multi-marker models. These findings underscore PlGF's value in personalised antenatal surveillance for PE- prone pregnancies [9]. Ng KW et al., (2024) reviewed biomarkers and point of care screening for PE management, highlighting sFlt-1/PlGF ratio >99% negative predictive value to rule out imminent disease, rapid POC assays (<15 min), and multi-marker panels with clinical factors achieving >90% preterm detection [10]. The imbalance between antiangiogenic factors like sFlt-1 and proangiogenic factors such as PlGF and VEGF correlates with PE onset and severity.

Galectins

Galectins are a family of soluble glycan-binding proteins that play a key role in pregnancy, particularly in healthy placental development [11]. Currently, 15 galectins have been identified and are being studied to determine how they may contribute to various pathogenic pathways. At the foetal-maternal interface, the galectin family members Galectin-1 (Gal-1), Galectin-3 (Gal-3), and Galectin-9 (Gal-9) are highly expressed [12]. More precisely, several investigations and published studies have shown that dysregulated expression of Gal-3 and Gal-7 is associated with impaired placental vascularisation and perfusion, placental insufficiency, and has been implicated in the development of PE [13].

Gal 3: For successful implantation and placental development, trophoblast tissue invasion and migration are critical processes in which galectin-3 is involved. Galectin-3 is essential for controlling the behaviour of trophoblast cells, as evidenced by a recent study [14]. Galectin-3 was discovered to improve trophoblast cells' migratory and invasive properties by modifying several signalling pathways and cytoskeletal dynamics. These processes are severely hampered by the lack of galectin-3 or its downregulation, which results in insufficient placentation [15]. Galectin-3 (Gal-3) is present in many organs, such as immune cells, endothelium, and epithelial cells, as well as sensory neurons. Moreover, galectin-3 expression is downregulated throughout life. Nearly all immunocompetent cells, such as mast cells, dendritic cells, neutrophils, eosinophils, basophils, monocytes, and macrophages, express galectin-3, which is essential for a number of immune functions. Galectin-3's proinflammatory characteristics have been shown in several investigations. These qualities include its ability to attract neutrophils and macrophages, facilitate phagocytosis, and improve granulocyte adherence to endothelium [14]. Comprehending the intricate processes that explain PE is essential for creating efficient diagnostic tools and therapies aimed at averting and controlling this illness. Consequently, to look into and shed light on any potential links between galectin-3 and pregnancy-related illnesses, such as PE and gestational hypertension.

Gal 7: Galectin-7 has been implicated in several processes essential for placentation, including regulation of cell adhesion, trophoblast migration, and immune modulation. Experimental studies have shown that LGALS7- deficient mice remain viable and fertile, suggesting possible compensatory biological mechanisms galectin-7 may function through both extracellular paracrine signalling and intracellular interactions involving proteins such as Ras and Bcl-2 to influence gene transcription and cellular responses [16]. Serum levels of Galectin-7 are abnormally increased in first-trimester patients who go on to develop PE [16]. Immune cells of the first-trimester placental villi and decidua, as well as STB and endothelial cells of the term placenta have all been demonstrated to have galectin-7. Decidua and endothelial cells of the term placenta express galectin-7 in addition to trophoblast. Galectin-7 represents novel, prospective serum biomarkers for PE [16]. Jovanovic´ Krivokuc´a M et al., (2021) reported that galectin-7 plays an important role in trophoblast migration, apoptosis, and immune regulation during placental development. Dysregulated galectin-7 expression has been associated with abnormal placentation and PE, suggesting its potential utility as an early biomarker of placental dysfunction and adverse pregnancy outcomes [17]. Menkhorst E et al., 2014 showed that, in contrast to pregnancies that were healthy, women who got PE had higher blood concentrations of galectin-7 in the 10-12th and 17-20th weeks of gestation [18]. Despite the fact that a bigger sample size is required to establish galectin-7 as a predictive PE biomarker, it would be significant to combine serum levels of Galectin-7 with other proteins changed in PE, as there are currently no predictive biomarker(s) available for this pregnancy-related disease. The placenta would express galectin-7, which would be found in serum. Galectin-7 was localised in syncytiotrophoblasts, extravillous trophoblasts, and glandular epithelium during the first trimester, while term placentas demonstrated expression primarily in syncytiotrophoblasts and endothelial cell. Notably, endothelial staining was absent in placentas from pregnancies complicated by PE [18]. When compared to women in healthy pregnancies, the blood concentration of galectin-7 was considerably higher in women (who later had PE) [18].

Gal 13: Placental Protein-13 (PP13), also known as galectin-13, is a placental galectin involved in trophoblast implantation, spiral artery remodelling, and regulation of inflammatory processes at the maternal-foetal interface. In pregnancies subsequently afflicted by ischaemic placental disease, its levels are lower during the first PE trimester and gradually increase during the second and third trimesters [19]. PP-13, a protein linked to cell differentiation and inflammatory processes in the placenta, seems to be an effective biomarker for PE screening. Maternal blood tests performed between

nine and 12 weeks of gestation revealed substantially lower serum levels of PP13 in women who had PE more than 15 to 25 weeks later in this prospective nested case-control research [20]. When compared to normal pregnancies, the PP13 serum levels were significantly lower in women whose pregnancies were complicated by IUGR and preterm birth; nevertheless, these levels were still much greater than in the women who ultimately developed PE [20]. On the reproductive system, especially on a set of six galectins that first became apparent in anthropoid apes along with the development of lengthy gestations and very invasive placentation. Among these six, PP 13 (also known as Gal 13) interacts with glycolipids and glycoproteins to facilitate a fruitful pregnancy [21].

Gal 1: The molecular pathogenesis is increasingly defined by the dysregulation of the galectin family, specifically the contrasting roles of Gal 1 and Gal 9 in mediating placental health. Gal 1, a 14.5 kDa homodimer protein, has been proposed as a primary angiogenic marker at the maternal-foetal interface [22]. Galectin-1 is a glycan-binding protein highly expressed at the maternal-foetal interface that supports placental development and vascular remodelling by promoting endothelial cell activation and angiogenesis [23]. Mechanistically, Gal 1 binds to the glycan structure of Neuropilin-1 (NRP-1), which serves as a combination co-receptor that stabilises the Vascular Endothelial Growth Factor Receptor-2 (VEGFR2) endothelial cells [22]. This interaction mimics the protein angiogenic signalling of VEGF, promoting robust trophoblast invasion and the expansion of the placental vascular network. Furthermore, Gal 1 is essential for establishing maternal-foetal immune tolerance by inducing the apoptosis of alloreactive maternal T cells and promoting an angiogenesis-protective T regulatory (Treg) cell environment [24].

Gal 9: Gal 9 contributes as a promising inflammatory switch that contributes to the vascular failure characteristics of the disease. While historically recognised for its role in the Tim-3 immune checkpoint pathway, recent high impact evidence has identified more deleterious mechanisms; and trophoblast derived Gal 9 binds to the CD44 receptor on decidual macrophages [25]. Li ZH et al., (2019), showed that Galectin-9 reduced blood pressure, proteinuria and placental injury in an LPS-induced preeclampsia-like rat model. It promoted decidual macrophage polarisation the proinflammatory M1 phenotype toward the anti-inflammatory M2 phenotype. Galectin-9 also improved trophoblast invasion and spiral artery remodeling, suggesting a protective role in placental development [26]. Complementing these findings, Miko E et al., (2013) found that Galectin-9/TIM-3 signalling axis appears to play a pivotal role in maintaining immune tolerance during pregnancy, and dysregulated expression of galectin-9 and TIM-3 has been associated with heightened systemic inflammation, including Th1 lymphocyte activation, in PE [27]. One of the main causes of placental insufficiency is placental hypoxia. The placental vascular network, which is essential for facilitating gas and nutrition exchange between the mother and foetus, is established during placentation when the trophoblast cells develop and enter the maternal tissues. Any interference with this mechanism may result in insufficient oxygen delivery to the placenta, which in turn may cause placental insufficiency and associated problems with pregnancy [28]. Therefore, in order to comprehend a portion of the pathophysiology of placental insufficiency, evaluating placental oxygenation or hypoxia is crucial [29].

LIPOCALIN-2/NGAL: Lipocalin-2 (LCN2), also known as Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a 25 kDa glycoprotein released by neutrophils and renal tubular epithelial cells and is recognised as a biomarker of inflammation and renal injury. Sisti G et al., (2023) [30] evaluated the association between NGAL levels and PE and found that maternal serum/plasma NGAL concentrations were significantly higher in women with PE compared with normotensive

Category/Biomarker	Study Type	Author/ Reference	Mechanism	1st Trimester	2nd Trimester	Performance/Notes
Angiogenic						
PlGF	Systematic review and meta-analysis	Agrawal S et al., [6]	Proangiogenic factors involved in placental vascular development;reduced levels indicate placental dysfunction.	Testable wk 8; low high-risk	Decreases; persistently low PE	OR 9 (CI 6-13); sens 78%, spec 88% (<80-120 pg/mL).
sFlt-1/PlGF ratio	Meta-analysis	Creswell L et al., [8]	Antiangiogenic; binds VEGF/ PlGF	Rises ~5 wks pre-symptoms	Elevated in PE	The study indicates that an elevated sFlt-1/PlGF ratio shows high specificity and negative predictive value for ruling out Preeclampsia (PE), rather than a positive predictor as mentioned..
Galectins						
Gal-3	Experimental study	Bojić-Trbojević Z et al., [14]	Trophoblast invasion; proinflammatory	Overexpressed	N/A	Downregulation → poor placentation
Gal-7	Nested case -control	Menkhorst E et al., [18]	Placental development, trophoblast apoptosis, inflammation	Elevated galectin-7 in women who later developed PE.	Further elevation before onset	Galectin-7 serum concentration was significantly elevated in women (weeks 10–12 and 17–20) who subsequently developed pre-eclampsia compared to women with healthy pregnancies.
Gal-13 (PP13)	Nested case-control study	Chafetz I et al., [20]	Implantation/remodelling	Low ischaemic disease	N/A	Lower first-trimester levels in PE, rising in second and third trimesters.
Gal 1	Experimental study in mice	Freitag N et al., [22]	Trophoblast adhesion;immune tolerance	Potentially low	Decreased in established PE	Promotes HLA-G expression: low levels link to miscarriage/PE.
Gal 9	Experimental study	Li X et al., [25]	Macrophage Polarization Suppresses remodelling	Increased levels	Elevated in decidua	Higher Gal 9 linked to CD11c+ Macrophage-driven vascular failure.
Hypoxic/Other						
NGAL	Systematic review and meta-analysis	Sisti G et al., [30]	Marker of inflammation, endothelial dysfunction and renal tubular injury	Elevated in women who developed PE later	Elevated levels associated with disease progression	Maternal blood levels of NGAL are elevated in women who subsequently develop pre-eclampsia compared with healthy controls.
CAIX	Observational study	Ozgen G and Dincgez B [32]	Hypoxia pH balance	N/A	Higher levels associated with Foetal Growth Restriction (FGR) in early-onset PE	Elevated CAIX levels may help identify pregnancies at risk of severe placental insufficiency and Foetal Growth Restriction (FGR).

[Table/Fig-2]: Summarises the biomarkers performance based on trimesters, balancing galectins with angiogenic/hypoxic markers [7,8,14,18,20,22,26,30,32].

pregnant controls. Elevated NGAL levels were observed before the clinical onset of the disease, suggesting its potential role as an early predictive biomarker. The authors concluded that NGAL reflects the inflammatory and endothelial dysfunction associated with PE and may aid in risk assessment, although further large-scale studies are required to establish its clinical utility and standardised cut-off values [30].

Carbonic Anhydrase IX (CAIX): A zinc metalloenzyme, CAIX is a member of the α carbonic anhydrase family, which catalyses the reversible conversion of carbon dioxide into bicarbonate ions and protons. For almost all biological activities requiring an acid-base balance in subcellular compartments and across the plasma membrane, this straightforward reaction is necessary [31].

Ozgen G and Dincgez B (2025) investigated the predictive value of maternal serum CAIX levels for FGR in women with early-onset PE. The study found significantly higher CAIX concentrations in preeclamptic pregnancies complicated by FGR compared with those without FGR. The authors proposed that elevated CAIX reflects increased placental hypoxia and insufficiency, which contribute to impaired foetal growth. Their findings suggest that CAIX may be a promising biomarker for identifying severe placental dysfunction and predicting adverse foetal outcomes in early-onset PE [32]. [Table/Fig-2] shows biomarkers performance based on galectins with angiogenic/hypoxic markers [7,8,14,18,20,22,26,30,32].

However, current evidence regarding CAIX remains limited by small cohort sizes and insufficient longitudinal validation studies. Further multicentre prospective studies are required to establish standardised cut-off values and determine its predictive accuracy in diverse populations before routine clinical implementation.

DISCUSSION

The PE is a multifactorial hypertensive disorder characterised by abnormal placentation, endothelial dysfunction, angiogenic imbalance, inflammation, oxidative stress, and immune dysregulation. Increasing evidence suggests that placental dysfunction precedes the onset of maternal clinical manifestations, highlighting the importance of early predictive biomarkers for timely intervention and improved maternal-foetal outcomes [33,34].

Among currently available biomarkers, the sFlt-1/PlGF ratio demonstrates the strongest clinical utility for the prediction and diagnosis of PE. Elevated circulating sFlt-1 antagonises VEGF and PlGF signalling, resulting in endothelial dysfunction and impaired angiogenesis. Meta-analyses have shown that the sFlt-1/PlGF ratio provides high sensitivity and specificity, particularly in early-onset and severe PE, making it useful for short-term prediction and clinical monitoring [6,8]. However, the predictive accuracy of isolated PlGF measurements may vary depending on gestational age, disease severity, and population characteristics supporting the use of combined biomarker strategies rather than reliance on a single marker [7].

Emerging evidence also supports the involvement of galectins in placental development and immune regulation. Galectin-1 appears to contribute to trophoblast invasion, angiogenesis, and maternal-foetal immune tolerance, whereas galectin-3 has been associated with inflammatory signalling and trophoblast migration [13,14,22]. Similarly, altered maternal serum levels of galectin-7 and galectin-13 (PP13) have been reported in pregnancies that later develop PE, suggesting their possible role in early placental maladaptation [18-20]. Nevertheless, findings related to galectins remain heterogeneous, and several studies are limited by small sample sizes, variable gestational sampling periods, and differences in laboratory methodologies. In addition, most evidence regarding galectin-7 and galectin-9 is derived from experimental or observational studies indicating that their predictive utility still requires validation through large prospective multicenter trials CAIX, a hypoxia-associated biomarker, has shown potential in identifying placental ischaemia and endothelial dysfunction in PE. Elevated maternal serum CAIX levels have been associated with early-onset PE and FGR, suggesting its possible role in predicting severe placental insufficiency. However, current evidence is limited and requires further large-scale validation studies [32]. Likewise, PAPP-A and NGAL/Lipocalin-2 reflect abnormal placentation and renal injury, respectively, and may complement angiogenic biomarkers in multi-marker prediction models [29,30]. However, the predictive performance of these biomarkers varies across studies, and standardised cut-off values have not yet been universally established.

CONCLUSION(S)

The PE remains a leading cause of maternal and perinatal morbidity, highlighting the need for effective early prediction. The sFlt-1/PlGF ratio currently has the strongest clinical value for predicting and monitoring the disease. Emerging biomarkers, including galectin-1, galectin-7, galectin-13 (PP13), PAPP-A, NGAL and CAIX, offer additional information on placental dysfunction, inflammation, immune imbalance, and hypoxia. Evidence suggests that combining multiple biomarkers with clinical and biophysical parameters improves early risk assessment. However, variability among studies and the absence of standardised cut-off values limit routine clinical application. Further large-scale prospective studies are needed to validate these biomarkers for precision obstetric care.

REFERENCES

[1] Overton E, Tobes D, Lee A. Preeclampsia diagnosis and management. Best Pract Res Clin Anaesthesiol. 2022;36(1):107-21 Doi: 10.1016/j.bpa.2022.02.003.
[2] Jung E, Romero R, Yeo L, Gomez-Lopez N, Chaemsaithong P, Jaovisidha A, et al. The etiology of preeclampsia. Am J Obstet Gynecol. 2022;226(2):S844-S866 Doi: 10.1016/j.ajog.2021.11.1356.
[3] Ramos JGL, Sass N, Costa SHM. Preeclampsia. Rev Bras Ginecol Obstet. 2017;39(9):496-512. Doi: 10.1055/s-0037-1604471.
[4] Alghifari RM, Alhusayni NI, Alyamani ZF, Sabban A, Almoghrabi Y, Bakheit KH. The role of biochemical markers in the prediction of preeclampsia. Int J Biochem Res Rev. 2023;32(8):39-47. Doi: 10.9734/ijbcrr/2023/v32i8833.
[5] Stepan H, Galindo A, Hund M, Schlembach D, Sillman J, Surbek D, et al. Clinical utility of sFlt-1 and PlGF in screening, prediction, diagnosis and monitoring of pre-eclampsia and fetal growth restriction. Ultrasound Obstet Gynecol. 2023;61(2):168-80. Doi: 10.1002/uog.26032.
[6] Agrawal S, Shinar S, Cerdeira AS, Redman C, Vatish M. Predictive performance of PlGF (placental growth factor) for screening preeclampsia in asymptomatic women: A systematic review and meta-analysis. Hypertension. 2019;74(5):1124-35. Doi: 10.1161/HYPERTENSIONAHA.119.13360.
[7] Agrawal S, Cerdeira AS, Redman C, Vatish M. Meta-analysis and systematic review to assess the role of soluble fms-like tyrosine kinase-1 and placental growth factor ratio in prediction of preeclampsia: The SaPPPhirE study. Hypertension. 2018;71(2):306-16. Doi: 10.1161/HYPERTENSIONAHA.117.10182.
[8] Creswell L, O'Gorman N, Palmer KR, da Silva Costa F, Rolnik DL. Perspectives on the use of placental growth factor (PlGF) in the prediction and diagnosis of pre-eclampsia: Recent insights and future steps. Int J Womens Health. 2023;15:255-71. Doi: 10.2147/IJWH.S368454.
[9] Mathur P, Maru L, Dave A. A prospective study of placental growth factor assay as a novel biomarker in predicting early-onset preeclampsia in high-risk patients. J Obstet Gynaecol India. 2016;66(Suppl 1):98-103 Doi: 10.1007/s13224-015-0793-7.
[10] Ng KW, Chaturvedi N, Coté GL, Fisher SA, Mabbott S. Biomarkers and point of care screening approaches for the management of preeclampsia. Commun Med. 2024;4(1):208. Doi: 10.1038/s43856-024-00642-4.
[11] Oladipo AF, Jayade M. Review of labouratory testing and biomarker screening for preeclampsia. BioMed. 2024;4(2):122-35. Doi: 10.3390/biomed4020010.
[12] Ali M, Ahmed M, Memon M, Chandio F, Shaikh Q, Parveen A, et al. Preeclampsia: A comprehensive review. Clinica Chimica Acta. 2024;2024:119922 Doi: 10.1016/j.cca.2024.119922.
[13] Potiris A, Fotiou A, Drakaki E, Potetsianaki A, Zikopoulos A, Moustakli E, et al. Bridging the gap between Galectin-3 expression and hypertensive pregnancy disorders: A narrative review. J Clin Med. 2024;13(16):4636 Doi: 10.3390/jcm13164636.
[14] Pugliese G, Iacobini C, Ricci C, Fantauzzi CB, Menini S. Galectin-3 in diabetic patients. Clin Chem Lab Med. 2014;52(10):1413-23. Doi: 10.1515/cclm-2014-0187.
[15] Bojić-Trbojević Ž, Jovanović Krivokuća M, Vilotić A, Kolundžić N, Stefanoska I, Zetterberg F, et al. Human trophoblast requires Galectin-3 for cell migration and invasion. Sci Rep. 2019;9(1):2136. Doi: 10.1038/s41598-018-38374-w.
[16] Menkhorst E, Zhou W, Santos LL, Delforce S, So T, Rainczuk K, et al. Galectin-7 impairs placentation and causes preeclampsia features in mice. Hypertension. 2020;76(4):1185-94. Doi: 10.1161/HYP.0000000000000198.

[17] Jovanović Krivokuća M, Vilotić A, Nacka-Aleksić M, Pirković A, Ćujić D, Legner J, et al. Galectins in early pregnancy and pregnancy-associated pathologies. Int J Mol Sci. 2021;23(1):69 Doi: 10.3390/ijms23010069.
[18] Menkhorst E, Koga K, Van Sinderen M, Dimitriadis E. Galectin-7 serum levels are altered prior to the onset of pre-eclampsia. Placenta. 2014;35(4):281-85. Doi: 10.1016/j.placenta.2014.01.009.
[19] Vasilache IA, Carauleanu A, Socolov D, Matasariu R, Pavaleanu I, Nemescu D. Predictive performance of first trimester serum galectin-13/PP-13 in preeclampsia screening: A systematic review and meta-analysis. Exp Ther Med. 2022;23(6):1-2. Doi: 10.3892/etm.2022.11297.
[20] Chafetz I, Kuhnreich I, Sammar M, Tal Y, Gibor Y, Meiri H, et al. First-trimester placental protein 13 screening for preeclampsia and intrauterine growth restriction. Am J Obstet Gynecol. 2007;197(1):35-e1 Doi: 10.1016/j.ajog.2007.02.025.
[21] Sammar M, Drobnjak T, Mandala M, Gizurarson S, Huppertz B, Meiri H. Galectin 13 (PP13) facilitates remodelling and structural stabilization of maternal vessels during pregnancy. Int J Mol Sci. 2019;20(13):3192. Doi: 10.3390/ijms20133192.
[22] Freitag N, Tirado-González I, Barrientos G, Herse F, Thijssen VL, Weedon-Fekjær SM, et al. Interfering with Gal-1–mediated angiogenesis contributes to the pathogenesis of preeclampsia. Proc Natl Acad Sci U S A. 2013;110(28):11451-56. Doi: 10.1073/pnas.1303707110.
[23] Xie Y, Zhao F, Freitag N, Borowski S, Wang Y, Harms C, et al. Maternal-derived galectin-1 shapes the placenta niche through Sda terminal glycosylation: Implication for preeclampsia. PNAS nexus. 2023;2(8):pgad247 Doi: 10.1093/pnasnexus/pgad247.
[24] Ramhorst RE, Giribaldi L, Fraccaroli L, Toscano MA, Stupirski JC, Romero MD, et al. Galectin-1 confers immune privilege to human trophoblast: Implications in recurrent fetal loss. Glycobiology. 2012;22(10):1374-86 Doi: 10.1093/glycob/cws104.
[25] Li Y, Sang Y, Chang Y, Xu C, Lin Y, Zhang Y et al. A Galectin-9-driven CD11chigh decidual macrophage subset suppresses uterine vascular remodeling in preeclampsia. Circulation. 2024;149(21):1670-78. Doi: 10.1161/CIRCULATIONAHA.123.064391.
[26] Li ZH, Wang LL, Liu H, Muyayalo KP, Huang XB, Mor G, et al. Galectin-9 alleviates LPS-induced preeclampsia-like impairment in rats via switching decidual macrophage polarization to M2 subtype. Front Immunol. 2019;9:3142.
[27] Miko E, Meggyes M, Bogar B, Schmitz N, Barakonyi A, Varnagy A, et al. Involvement of Galectin-9/TIM-3 pathway in the systemic inflammatory response in early-onset preeclampsia. PLoS One. 2013;8(8):e71811. Doi: 10.1371/journal.pone.0071811.
[28] Al Darwish FM, Meijerink L, Coolen BF, Strijkers GJ, Bekker M, Lely T, et al. From molecules to imaging: Assessment of placental hypoxia biomarkers in placental insufficiency syndromes. Cells. 2023;12(16):2080. Doi: 10.3390/cells12162080.
[29] Mazer Zumaeta A, Wright A, Syngelaki A, Maritsa VA, Da Silva AB, Nicolaides KH. Screening for pre-eclampsia at 11–13 weeks' gestation: Use of pregnancy-associated plasma protein-A, placental growth factor or both. Ultrasound Obstet Gynecol. 2020;56(3):400-07. Doi: 10.1002/uog.22093.
[30] Sisti G, Rubin G, Zhou C, Orth T, Schiattarella A. Neutrophil gelatinase–associated lipocalin as a predictor of pre-eclampsia: A systematic review and meta-analysis. Int J Gynaecol Obstet. 2023;163(1):63-74. Doi: 10.1002/ijgo.14777.
[31] Pastorekova S, Gillies RJ. The role of carbonic anhydrase IX in cancer development: Links to hypoxia, acidosis, and beyond. Cancer Metastasis Rev. 2019;38(1):65-77. Doi: 10.1007/s10555-019-09799-0.
[32] Ozgen G, Dincgez B. Could carbonic anhydrase IX predict fetal growth restriction in early onset preeclampsia? Rev Assoc Med Bras. 2025;71(11):e20250838. Doi: 10.1590/1806-9282.20250838.
[33] MacDonald TM, Walker SP, Hannan NJ, Tong S, Kaitu'u-Lino TU. Clinical tools and biomarkers to predict preeclampsia. EBioMedicine. 2022;75. Doi: 10.1016/j.ebiom.2021.103780.
[34] Anderson UD, Olsson MG, Kristensen KH, Åkerström B, Hansson SR. Biochemical markers to predict preeclampsia. Placenta. 2012;33:S42-S47. Doi: 10.1016/j.placenta.2011.11.021.

PARTICULARS OF CONTRIBUTORS:
1. PhD Scholar, Department of Biochemistry, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
2. Professor and Head, Department of Biochemistry, Panimalar Medical College and Research Hospital, Chennai, Tamil Nadu, India.
3. Professor, Department of Obstetrics and Gynaecology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
4. Associate Professor, Department of Biochemistry, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Leena Chand,
Associate Professor, Department of Biochemistry, Sri Ramachandra Institute of Higher Education and Research, Chennai-600116, Tamil Nadu, India.
E-mail: leena@sriramachandra.edu.in

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 31, 2026
- Manual Googling: Jun 11, 2026
- iThenticate Software: Jun 13, 2026 (1%)

ETYMOLOGY: Author Origin

EMENDATIONS: 8

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 20, 2026**
Date of Peer Review: **Mar 13, 2026**
Date of Acceptance: **Jun 15, 2026**
Date of Publishing: **Sep 01, 2026**