DOI: https://doi.org/10.54393/pjhs.v5i11.2398

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 11 (November 2024)

Systematic Review

OPEN ACCESS

Clinicopathological Role of Adiponectin in Preeclampsia: Linkage with Placental Function and Maternal Health

Mohammedelfateh Adam[1], Sarfaraz Khan[2], Memona Zia[3], Anum Iftikhar[4], Sajid Hussain Sherazi[5], Naveed Ahsan[6] and Ehsan Ul Haq[7*]

[1]Department of Obstetrics and Gynaecology, Galway University Hospital, Ireland
[2]Department of Medicine and Endocrinology, Mercy Teaching Hospital, Peshawar, Pakistan
[3]Department of Pathology, Abu Umara Medical and Dental College, Lahore, Pakistan
[4]Department of Pathology, Bahawalpur Medical and Dental College, Bahawalpur, Pakistan
[5]Department of Pediatric, Niazi Medical and Dental College, Sargodha, Pakistan
[6]Department of Biochemistry, Bhitai Dental and Medical College, Mirpurkhas, Pakistan
[7]Department of Allied Health Sciences, University of Health Sciences, Lahore Pakistan

ARTICLE INFO

Keywords:
Adiponectin, Preeclampsia, Placental Gene Expression, Maternal Health

How to Cite:
Adam, M., Khan, S., Zia, M., Iftikhar, A., Sherazi, S. H., Ahsan, N., & Haq, E. U. Clinicopathological Role of Adiponectin in Preeclampsia: Linkage with Placental Function and Maternal Health: Clinical-pathology of Adiponectin in Preeclampsia: Placental and Maternal Outcomes. Pakistan Journal of Health Sciences, 5(11), 270-277. https://doi.org/10.54393/pjhs.v5i11.2398

Corresponding Author:
Ehsan Ul Haq
Department of Allied Health Sciences, University of Health Sciences, Lahore Pakistan
ehsanulhaqkhan33@gmail.com

Received Date: 12th October, 2024
Acceptance Date: 23th November, 2024
Published Date: 30th November, 2024

ABSTRACT

Preeclampsia is a hypertensive, multisystem disease in pregnancy, associated with dysfunction of the placenta. Emerging studies point toward the possibility that adiponectin, a hormone with anti-inflammatory and vasodilator properties, may contribute to the development of preeclampsia. **Objectives:** To systematically review the role of adiponectin in the pathophysiology of preeclampsia with limited evidence on the role of placental gene expression, providing clinicopathological insights into its role in maternal and fetal health. **Methods:** A comprehensive literature search was conducted across PubMed, Science Direct, and Google Scholar for articles published between 2017 and 2024. Included studies explored the relationship between Adiponectin levels and preeclampsia in relevance to placental pathology, and hormonal levels. Studies analyzed adiponectin's role in modulating insulin resistance, hypertension, placental growth, and vascular health in preeclampsia. Data from multiple regions, including Asia, Europe, and America, provided global perspectives. **Results:** An association between reduced adiponectin levels and increased severity of preeclampsia and its potential role in impaired placental physiology and adverse pregnancy outcomes were reviewed. **Conclusions:** It was concluded that adiponectin plays a crucial role in the pathophysiology of preeclampsia, affecting both maternal health and placental function. Understanding these mechanisms may offer insights for therapeutic interventions in managing preeclampsia and improving fetal outcomes.

INTRODUCTION

Preeclampsia is a pregnancy hypertension complication that occurs in the second half of pregnancy, usually after 20 weeks of pregnancy, and is associated with blood pressure and protein levels. Incidence of 2–8% in pregnancy across the globe makes it a cause of significant maternal and peripartum mortalities and morbidities especially in developing countries [1]. The significance of assessing preeclampsia is based on its serious consequences which include placental insufficiency, fetal birth restriction, preterm birth, pregnancy termination, and maternal or fetal fatalities [2]. It is therefore important to understand the processes involved in affecting the overall progress in the well-being of both the mother and her baby. In different countries, the occurrence differs, but it is high in Africa, Asia, and Latin America most likely attributed to economic reasons and poor health facilities [3]. In European countries and America, the prevalence of preeclampsia is relatively low, but remains a major public health problem, as 2-5% of pregnancies are affected by it [4]. The condition has been linked to internal derangement characterized by

DOI: https://doi.org/10.54393/pjhs.v5i11.2398

endothelial dysfunction, oxidative stress, immune maladaptation, poor placental development with resultant poor perfusion, and compromised fetal status [5]. The cause of preeclampsia is still not clear; however, both genetic and immunological factors as well as environmental predisposing factors are involved. Specific risk factors include chronic hypertension, diabetes, obesity, and an older maternal age, which predispose to internal pathophysiological derangements leading to this condition [6]. Adiponectin, a hormone secreted mainly by adipose tissue, is a potential novel biochemical marker related to preeclampsia, which has been discovered in recent years. Adiponectin has been characterized as an anti-inflammatory, insulin-sensitizing, and vasodilation agent indispensable for the regulation of maternal metabolism and vasculature [7,8,9]. It has been proposed that weight loss or a change in the percentage of body fat can be used to predict the onset of mild and severe preeclampsia because adiponectin has a role in regulating insulin signalling and inflammation and its circulating levels were linked to preeclampsia [10]. Adiponectin modulation of placental function and its potential implications for preeclampsia is the focus of our primary review. Placental dysfunction is well established in preeclampsia, although recent work has implicated adiponectin, which regulates pathways necessary for trophoblast invasion, angiogenesis, and nutrient transport, in preeclampsia mechanisms based on placental maladaptation [11]. Adiponectin is shown to regulate key signalling pathways: Mitogen-activated protein kinase/Signal transducer and activator of transcription 5 (MAPK/STAT5) and Vascular endothelial growth factor (VEGF) axes, critical for trophoblast proliferation and vascular development, as well as placental structure integrity [12]. We further categorized the adiponectin's signalling pathways documented to impact placental gene expression and function to provide a clearer understanding of preeclampsia clinical relevance although this information remains limited to one study in our systematic review. Recent findings of regional and ethnic variation in adiponectin and its ability as a biomarker for adiponectin are reviewed and predictions are made about future performance in different populations. We also adjusted for confounders among maternal health factors including BMI, gestational diabetes, and other factors to clarify adiponectin's independent role in preeclampsia. Based on this synthesis of recent studies, adiponectin's regulatory mechanisms and signalling pathways may potentially become targets for early diagnosis and therapeutic intervention in preeclampsia to improve maternal and foetal health outcomes.

This study aims to systematically review the role of Adiponectin in the pathophysiology of preeclampsia with limited evidence on the role of placental gene expression, providing clinicopathological insights into its role in maternal and fetal health.

METHODS

The PRISMA guidelines for reporting were followed throughout the conduct of this study. It included 87 articles in English from the last 7 years (2017-2024). The papers included the following information, which was arranged systematically according to the inclusion criteria of PRISMA guidelines 2020: author name followed by year, country, sample population, factors and variables, study design, and references. Several search engines and public libraries were taken for fetching articles for our study. The names included are PubMed, Science Direct, Springer Link, and search engine includes Google Scholar. The search was conducted using phrases such as Adiponectin, preeclampsia, placental gene expression, maternal health, fetal development, vascular function, and insulin resistance. We conducted a literature search using key phrases such as "Preeclampsia and adiponectin", "mechanistic role of adiponectin in preeclampsia" and "clinical studies on the role of adiponectin in preeclampsia". This search was conducted in abstracts and duplicate entries which were then filtered systematically using specific inclusion and exclusion criteria. If the article was not pointing out the relation between adiponectin and preeclampsia, was not appropriate from a clinical or a pathophysiological aspect of preeclampsia and did not adhere to the appropriate methodologies such as clinical studies like prospective, randomized controlled trials (RCT), and cohort were excluded. Studies directly investigating the influence of adiponectin on preeclampsia pathophysiology, especially on placental function, fetal outcomes, and to some extent gene expression were emphasized as the inclusion criteria. Other considerations included BMI, gestational diabetes, or ethnic or regional differences. As a result of this rigorous selection, fifteen studies were selected for detailed analysis. 87 articles in total were downloaded from databases, 6 duplicates were removed and 81 were left for further study analysis. A total of 66 articles from the systematic review after full-text review and 15 were left which were sorted and used. PRISMA Work Flow for Filtering Out Articles Focusing On Inclusion and Exclusion Method. Initially, 87 Studies were taken according to abstract and title and relevancy. Total of 6 duplicates were eliminated. only full-text articles that can be downloaded and read were screened. Finally, 15 studies were taken and sorted according to study type (Figure 1).

DOI: https://doi.org/10.54393/pjhs.v5i11.2398

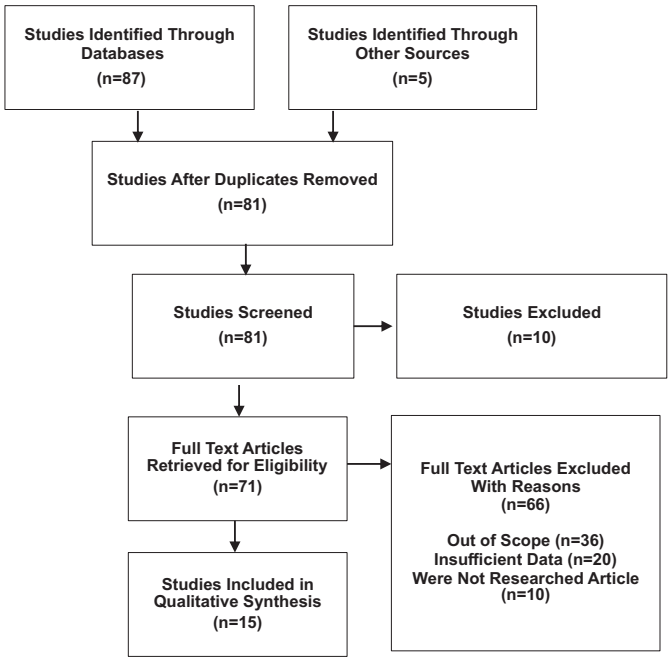

Figure 1: Filtering Out Articles Focusing on Inclusion and Exclusion Method

RESULTS

This study mainly reviewed papers that were cohort studies, prospective studies, controlled trials and preclinical trials (one study only) because these type of studies helps in understanding disease patterns, their risk factors, unique insights about conditions and potential and optimum treatments. The studies in this review are taken from well-known public libraries for scientific research and search engines such as Google Scholar (80%), PubMed (10%) and Science Direct (10%), in line with PRISMA guidelines. Confounders like BMI, gestational diabetes, age of mother, and lifestyle characteristics including smoking, physical activity and socioeconomic status are found in most studies and were controlled in this study as well. These include prospective, cohort, case-control, RCTs and preclinical design to provide a substantial level of evidence regarding the association of Adiponectin in preeclampsia. The table presents the consideration of the effects of Adiponectin on placental function, gene expression, fetal outcome physical activity, and socioeconomic status) which are common in most studies and were adjusted to ensure accurate findings. The table reflects a focus on how Adiponectin levels impact placental function, gene expression, and fetal outcomes. Results suggest that adiponectin and leptin levels as well as total antioxidant status (TAS) are pathologically significant biomarkers of preeclampsia severity and adverse maternal outcomes. Consistently, elevated leptin levels and lower adiponectin/leptin ratio were associated with increased oxidative stress, markers of inflammatory responses and endothelial dysfunction all associated with placental insufficiency. Reduced adiponectin levels had a specific effect on trophoblasts thus limiting placental development and fetal growth. In many cases, though 'elevated' for compensatory purposes in response to oxidative stress, TAS levels were insufficient to quell the inflammation-driving complications such as Hemolysis, Elevated Liver-enzymes, and Low Platelet-count (HELLP) syndrome and eclampsia. Together, these findings underscore the important roles of adipokines and oxidative balance in preeclampsia pathogenesis and could provide possible molecular and biomarker tools to aid early detection, and targeted treatment. Results of these studies [13-27] are shown (Table 1).

Table 1: A Systematic Review of the Literature for Articles

Reference	Study Design	Population	Key Findings	Confounders	Conclusions
[13]	Case-control	70 pregnant women (32 with PIH,38 healthy controls)	Adiponectin levels were lower in the Pregnancy-induced hypertension (PIH) group,but not significantly different from controls. Adiponectin /Leptin levels were significantly higher.	Body Mass Index (BMI(, gestational age, number of pregnancies, delivery method	High Adiponectin/ leptin levels in PIH women may predict the need for a caesarean section, while adiponectin levels were not a significant marker.
[14]	Case-control	Pregnant women: Control (n=59), Gestational Hypertension (n=55), Late (n=68) & Early (n=66) Preeclampsia groups	Elevated adiponectin, Malondialdehyde MDA, and Total antioxidant status (TAS) levels were associated with adverse outcomes (e.g.,Hemolysis, Elevated Liver enzymes, Low Platelet count (HELLP) syndrome, eclampsia) in preeclampsia. Adiponectin plays a protective role by counterbalancing inflammation and endothelial dysfunction.	BMI, gestational age, renal function, pre-existing conditions like hypertension and diabetes	Elevated adiponectin and TAS are linked to adverse maternal outcomes in preeclampsia, possibly as compensatory mechanisms to inflammation, oxidative stress, and endothelial damage.

DOI: https://doi.org/10.54393/pjhs.v5i11.2398

[15]	Prospective Study	50 pre-eclampsia patients, 50 normotensive controls	Lower adiponectin/leptin ratio and higher leptin levels in pre-eclamptic women. Predictive value of adiponectin/leptin ratio and leptin levels for pre-eclampsia diagnosis.	BMI, Obesity, Hypertension,Diabetes	Adiponectin/leptin ratio < 0.153 and leptin> 24.1 ng/ml serve as potential biomarkers for pre-eclampsia diagnosis.
[16]	Case-control Study (Cohort)	126 pre-eclampsia patients,297 controls	Reduced adiponectin/leptin (A/L) ratio in the first trimester correlates with pre-eclampsia . The A/L ratio serves as a better predictor of pre-eclampsia than either hormone individually.	BMI, Maternal metabolic syndrome	A lower A/L ratio in early pregnancy predicts pre-eclampsia; more effective than using adiponectin or leptin alone.
[17]	Prospective Cohort	1,776 Pregnant women (multi-ethnic)	Decreased adiponectin levels lead to increased inflammation and impaired metabolic pathways, linked with higher preeclampsia risk (AOR 1.45)	BMI, age, smoking, ethnicity	Dysregulation in adiponectin levels early in pregnancy increases preeclampsia risk, especially in certain ethnic groups.
[18]	Prospective Cohort	1012 Preterm and term new-borns	Low cord adiponectin in preterm infants is linked to adipose tissue dysfunction and metabolic dysregulation, which may be associated with maternal preeclampsia	GA, birth weight, Black race, DM	Low adiponectin in new-borns, particularly in preterm births,may signal future metabolic dysfunction related to maternal preeclampsia.
[19]	Prospective, Case-control Study	166 pregnant women divided into groups based on BMI and Gestational diabetes mellitus (GDM) status	Serum adiponectin levels were lower in obesity and higher in preeclampsia, suggesting a role in its pathogenesis.	Obesity, GDM, hypertension	Adiponectin does not significantly differentiate between pregnant women with or without GDM, but obesity complicates outcomes. Adiponectin's role in preeclampsia is suggested by its anti-inflammatory effects.
[20]	Prospective Study	60 preeclampsia women and 60 normotensive controls	Adiponectin levels were insignificantly higher in the preeclampsia group. However, the leptin/adiponectin ratio was significantly lower in preeclampsia women, suggesting an imbalance in adipokines.	Obesity, hypertension, diabetes	Adiponectin and leptin ratios can serve as biomarkers for preeclampsia, with altered ratios indicating adipose tissue dysfunction and inflammatory processes.
[21]	Case-control Study	90 Preeclampsia,100 normotensive pregnant women	Adiponectin levels were significantly lower in Preeclampsia pregnancies. Adiponectin, leptin, resistin, and visfatin are predictors of PE.	BMI, family history of diabetes, hypertension	Adiponectin and other adipokines are significant predictors of PE. Controlling for confounders, adiponectin was the best predictor.
[22]	Cohort Study	2503 pregnancies, including 93 Preeclampsia pregnancies, with normal, moderate, and severe obesity	In severely obese women, Preeclampsia is associated with lower adiponectin levels. Leptin was inversely associated with PE in severe obesity.	BMI, maternal age, smoking	Adiponectin is a significant predictor of PE in obese women. Leptin levels are predictive only in severe obesity.

DOI: https://doi.org/10.54393/pjhs.v5i11.2398

[23]	Retrospective Study	118 severe pre-eclampsia patients and 90 controls	Serum adiponectin levels were negatively correlated with umbilical artery resistance/pulsatility indexes; lower adiponectin levels in severe pre-eclampsia may indicate poor placental function and adverse outcomes	Maternal age, body mass index, history of hypertension, kidney disease, diabetes	Umbilical artery Doppler combined with serum adiponectin levels can predict adverse pregnancy outcomes in severe pre-eclampsia.
Studies on Gene Profile Analysis					
[24]	Case-control Study	52 pre-eclampsia patients, 30 normal pregnancies	Adiponectin downregulates p38 MAPK, activates STAT5, and controls trophoblast function in preeclampsia. Decreased adiponectin in pre-eclampsia correlates with abnormal placental function.	Age, Gestational age(GA), BMI, Urinary protein	Adiponectin regulates trophoblast function via the MAPK-STAT5 pathway, playing a crucial role in the pathogenesis of pre-eclampsia.
[25]	Case-control	First-trimester pregnant women (126 PE cases, 297 controls)	Lower adiponectin/leptin ratio suggests impaired insulin sensitivity,contributing to metabolic disturbances that can lead to preeclampsia	BMI, maternal insulin resistance (IR)	Adiponectin/leptin ratio is a predictive marker for preeclampsia, reflecting underlying metabolic imbalances such as insulin resistance.
[26]	Cohort Study	Pregnant women with GDM, Preeclampsia, and combined Preeclampsia + GDM	Adiponectin levels were lower in Preeclampsia compared to controls, and higher in PE + GDM. PR3 and placental proteins altered in PE and GDM.	Age, BMI, fasting glucose	Adiponectin is lower in PE and GDM,with placental changes showing systemic inflammatory involvement.

DISCUSSION

Preeclampsia is a hypertensive disorder and a new onset of hypertension and proteinuria after 20 weeks of gestation. According to WHO, preeclampsia is a leading cause of maternal (and perinatal) mortality and morbidity worldwide, with higher incidence and lower access to healthcare in developing regions, and contributes to 10 to 15% of maternal deaths worldwide. The prevalence is 2–8 per cent of pregnancies, with the highest prevalence in sub-Saharan Africa and South Asia. This disorder appears to be severe for both mother and fetus and may complicate with eclampsia, placental abruption, preterm birth, intrauterine growth restriction (IUGR) and mortality [27]. This review aimed to assess systematically the role of adiponectin in the pathophysiology of preeclampsia based on available supplemental evidence regarding the clinical and pathologic effects of adiponectin on fetal health. The review evaluated adiponectin's involvement in clinical and metabolic aspects of preeclampsia and its potential contribution to prevention and diagnosis while controlling for BMI and gestational diabetes. A variety of internal and external factors are inherent to the development and degree of preeclampsia. Within the context of the cell, oxidation stress, impairment of endothelium, and immunological dysfunction have been pointed out as the key players in this pathogenesis of the disease [28]. Human endothelium is central to the regulation of vascular resistance and its derangement results in some of the key pathophysiological features observed in preeclampsia: vasoconstriction, inflammation, and increased endothelial permeability [29]. Moreover, the distribution of preeclampsia by geographic location, race, and ethnicity shows that women of African origin are more likely to develop preeclampsia than white women [30]. Adiponectin is a hormone mainly secreted from adipocytes with insulin-sensitizing, anti-inflammatory, and vasodilator properties important for pregnancy-associated metabolic and vascular control [31]. Adiponectin, in the pathway of preeclampsia management, shows a protective effect regulating several actions which support the maintenance of placenta function as well as the effective and safe functioning of the maternal circulation. Despite this, many investigations have shown that adiponectin concentration is decreased in women with preeclampsia compared to normotensive pregnant women [32]. Such a decrease in adiponectin levels results in enhancing inflammatory response, endothelial dysfunction and inhibition of angiogenesis, these processes provoke placental insufficiency and adverse pregnancy outcomes in preeclampsia [33]. Adiponectin exerts most of its regulatory mechanistic function via two receptors, the AdipoR1 and AdipoR2, which in turn stimulate various signalling pathways that lessen inflammation, improve cellular energy, fatty acid oxidation and glucose utilization through the AMP-activated protein

DOI: https://doi.org/10.54393/pjhs.v5i11.2398

kinase (AMPK) pathway and enhance the insulin-sensitizing Peroxisome proliferator-activated receptor (PPAR) pathway and the anti-inflammatory MAPK pathway [34]. Stimulation of these pathways also increases insulin tolerance, improves oxidative stress and has anti-inflammatory effects which are essential to compensate for altered-looking placental function. In preeclampsia, these pathways fail due to low adiponectin leading to dysfunction of trophoblasts and improper development of the placenta leading to restrictive fetal growth [35]. From the literature used, our review focuses on several works that investigate adiponectin on preeclampsia, as described in Table 1, many case-controls, cohort, as well as, prospective-based studies have shown a significant inverse relationship between the levels of adiponectin and the probability and severity of preeclampsia. For example, a study identified that low adiponectin concentrations were associated with severe preeclampsia and placental dysfunction [36], while one study established that although adiponectin was lower in women with Pregnancy-induced hypertension (PIH), leptin had better effectiveness index in predicting adverse outcomes [37]. In tandem, a study, also showed that a low ratio of adiponectin/leptin in the first trimester predicted preeclampsia in the second and third trimesters [38]. These results imply that it would be effective to screen adiponectin and leptin as biomarkers for preeclampsia in women and intervene before complications occur. This paper, however, has some limitations despite providing useful information on adiponectin mechanisms for preeclampsia diagnosis and review. First, the studies investigated in the current review have a wide variety of designs, sample sizes, and population characteristics. Some analyses involved selected ethnic groups or geographical areas, and thus could not be generalized to other communities. Moreover, not all contained the same comparison factors such as BMI, gestational diabetes and other metabolic problems while doing correlation analysis of adiponectin levels and preeclampsia risk. One more significant drawback is that most data originated from observational or case-control trials; such research does not allow for establishing causality because of their susceptibility to bias. Cross-sectional designs also restrict the examination of the temporal association between adiponectin and preeclampsia occurrence. Last, it is also essential to mention that, although this review discusses several signaling pathways connected with adiponectin, there is a deficiency of more extensive and focused investigations on the molecular mechanisms responsible for linking adiponectin with the dysfunction of the placenta. Lastly, this review gives a comprehensive understanding of how adiponectin modulates preeclampsia's pathophysiology by regulating placental gene expression and maternal blood vessel function. The information based on these pathways should be explored further; additionally, new approaches to using the properties of adiponectin should be sought in the future. In the same regard, there is a requirement for large sample, multi-ethnic cohort studies to confirm the predictive utility of adiponectin and, the accompanied biomarkers across ethnic groups.

CONCLUSIONS

It was concluded that this review emphasizes the important pathophysiological role of adiponectin in preeclampsia and its relevance for maternal health and placentae function. The regulation of insulin sensitivity, inflammation, and vascular health by adiponectin is thus an attractive biomarker for the early detection and potential therapeutic targeting of preeclampsia. Biomarkers such as the adiponectin/leptin ratio have predicted value and suggest that future interventions may be guided by these markers and improve pregnancy outcomes. Despite these promising associations, however, more research is required to clarify the molecular mechanisms by which adiponectin affects placental gene expression and to understand its broader implications in disparate populations. In addition, confirmation of the utility of adiponectin-based diagnostics and treatments will depend on large-scale cohort studies involving multi-ethnic participants. Such an advance could considerably accelerate the management of preeclampsia and thus improve the health, and survival, of both mothers and their children.

Authors Contribution

Conceptualization: MA, SK, MZ
Methodology: MA, SK, MZ, AI, SHS. NA, EUH
Formal analysis: MA, SK, MZ
Writing review and editing: AI, SHS, NA, EUH

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

DOI: https://doi.org/10.54393/pjhs.v5i11.2398

REFERENCES

[1] Harrison MS, Betrán AP, Suresh K, Vogel JP, Goldenberg RL, Gülmezoglu AM. Risk Factors Associated with Adverse Maternal Outcomes Following Intrapartum Cesarean Birth: A Secondary Analysis of the WHO Global Survey On Maternal and Perinatal Health, 2004–2008. BioMed Central Pregnancy and Childbirth.2020 Dec; 20: 1-1. doi: 10.1186/s12884-020-03390-0.

[2] Overton E, Tobes D, Lee A. Preeclampsia Diagnosis and Management. Best Practice and Research Clinical Anaesthesiology.2022 May; 36(1): 107-21. doi: 10.1016/j.bpa.2022.02.003.

[3] Metcalfe A, Ahmed SB, Nerenberg K. Age-Period-Cohort Effects in Pre-Existing and Pregnancy-Associated Diseases Amongst Primiparous Women. Biology of Sex Differences.2020 Dec; 11: 1-9. doi: 10.1186/s13293-020-00293-9.

[4] Chang KJ, Seow KM, Chen KH. Preeclampsia: Recent Advances in Predicting, Preventing, and Managing the Maternal and Fetal Life-Threatening Condition. International Journal of Environmental Research and Public Health.2023 Feb; 20(4): 2994. doi:10.3390/ijerph20042994.

[5] Chappell LC, Cluver CA, Tong S. Pre-eclampsia. The Lancet.2021 Jul; 398(10297): 341-54. doi: 10.1016/S0140-6736(20)32335-7.

[6] Mészáros B, Kukor Z, Valent S. Recent Advances in the Prevention and Screening of Preeclampsia. Journal of Clinical Medicine. 2023 Sep; 12(18): 6020. doi: 10.3390/jcm12186020.

[7] Bawah AT, Yeboah FA, Nanga S, Alidu H, Ngala RA. Serum Adipocytokines and Adiposity as Predictive Indices of Preeclampsia. Clinical Hypertension. 2020 Dec; 26: 1-1. doi: 10.1186/s40885-020-00152-0.

[8] Gutaj P, Sibiak R, Jankowski M, Awdi K, Bryl R, Mozdziak P *et al.* The Role of the Adipokines in the Most Common Gestational Complications. International Journal of Molecular Sciences.2020 Dec; 21(24): 9408. doi: 10.3390/ijms21249408.

[9] Ali EA, Helmi ZR, Nori W. What Do We Know about Adiponectin in Preeclampsia? A Comprehensive Review. Libyan Medical Journal.2022 Mar; 14(1): 15-20. doi: 10.4135/9781529756647.n3

[10] Adu-Gyamfi EA, Fondjo LA, Owiredu WK, Czika A, Nelson W, Lamptey J et al. The Role of Adiponectin in Placentation and Preeclampsia. Cell Biochemistry and Function. 2020 Jan; 38(1): 106-17. doi: 10.1002/cbf.3458.

[11] Lappas M, Permezel M, Rice GE. Leptin and Adiponectin Stimulate the Release of Proinflammatory Cytokines and Prostaglandins from Human Placenta and Maternal Adipose Tissue Via Nuclear Factor-Kb, Peroxisomal Proliferator-Activated Receptor-Γ and Extracellularly Regulated Kinase 1/2. Endocrinology.2005 Aug; 146(8): 3334-42. doi:10.1210/en.2005-0406

[12] Tan L, Ouyang Z, Chen Z, Sun F, Guo H, Wang F *et al.* Adipokine Chemerin Overexpression in Trophoblasts Leads to Dyslipidemia in Pregnant Mice: Implications for Preeclampsia. Lipids in Health and Disease. 2023 Jan; 22(1): 12. doi: 10.1186/s12944-023-01777-4.

[13] Golańska-Wróblewska M, Fryczak J, Siejka A. Serum Levels of Sirtuins, Leptin and Adiponectin in Women with Pregnancy-Induced Hypertension. Cytokine. 2024 Jul; 179: 156612. doi: 10.1016/j.cyto.2024.156612.

[14] Abraham AJ, Bobby Z, Chaturvedula L, Vinayagam V, Jacob SE, Habeebullah S. Maternal Adverse Outcomes in Hypertensive Disorders of Pregnancy and Their Association with Serum Adiponectin and Redox Markers. Fetal and Pediatric Pathology.2022 Feb; 41(1): 1-7. doi: 10.1080/15513815.2020.1745973.

[15] Ullah Z, Bashir F, Kalsum Fatima SA, Tahir BH, Irshad F. Changes in Serum Adiponectin and Serum Leptin Levels Can Predict Pre-Eclampsia in Pregnant Women: A Prospective Study. Pakistan Journal of Medical and Health Sciences.2022; 16(12): 610-. doi: 10.53350/pjmhs20221612610.

[16] De Knegt VE, Hedley PL, Eltvedt AK, Placing S, Wøjdemann K, Shalmi AC *et al.* Adiponectin/Leptin Ratio-A Marker of Insulin Sensitivity in Pre-Eclampsia and Fetal Growth.MedRxiv.2022Oct:2022-10.doi:10.1101/2022.10.13.22281056.

[17] Lomakova YD, Chen X, Stein TP, Steer RA. Decreased Adiponectin Levels in Early Pregnancy Are Associated with High Risk of Prematurity for African American Women. Journal of Clinical Medicine. 2022 Jun; 11(11): 3213. doi: 10.3390/jcm11113213.

[18] Makker K, Zhang M, Wang G, Hong X, Aziz KB, Wang X. Maternal and Fetal Factors Affecting Cord Plasma Leptin and Adiponectin Levels and Their Ratio in Preterm and Term Newborns: New Insight On Fetal Origins of Metabolic Dysfunction. Precision Nutrition. 2022 Nov; 1(2): e00013. doi: 10.1097/PN9.0000000000000013.

[19] Mihai M, Vladut S, Sonia-Teodora L, Mihaela SL, Victoria N, Elena MI *et al.* Correlation between Overweight, Obesity, Gestational Diabetes Mellitus, Adipokines (Adipolin and Adiponectin), and Adverse Pregnancy Outcomes: A Pilot Study. Medicina.2024 Sep; 60(9): 1544. doi: 10.3390/medicina60091544.

[20] Rao S, Kumari A, Sharma M, Kabi BC. Predicting Maternal Serum Adiponectin and Leptin Level as Biomarkers of Pre-Eclampsia: A Prospective Study.

DOI: https://doi.org/10.54393/pjhs.v5i11.2398

The Journal of Obstetrics and Gynecology of India.2021 Feb; 71: 58-65. doi: 10.1007/s13224-020-01378-6.

[21] Tijani BA, Agyemang YF, Salifu N, Huseini A. Serum Adipocytokines and Adiposity as Predictive Indices of Preeclampsia. Clinical Hypertension. 2021 Jan; 27(1): 8-18. doi: 10.1186/s40885-020-00152-0.

[22] Thagaard IN, Hedley PL, Holm JC, Lange T, Larsen T, Krebs L *et al*. Leptin and Adiponectin as Markers for Preeclampsia in Obese Pregnant Women, A Cohort Study. Pregnancy Hypertension.2019 Jan; 15: 78-83. doi: 10.1016/j.preghy.2018.12.002.

[23] Zhang Z, Liu F, Zhang Q, Li D, Cai L. Umbilical Artery Ultrasound Haemodynamics Combined with Serum Adiponectin Levels Can Aid in Predicting Adverse Pregnancy Outcomes in Patients with Severe Pre-Eclampsia.Journal of Obstetrics and Gynaecology.2023Dec;43(2):2232656.doi:10.1080/01443615.2023.2232656.

[24] Dimitriadis E, Rolnik DL, Zhou W, Estrada-Gutierrez G, Koga K, Francisco RP *et al*. Pre-eclampsia. Nature Reviews Disease Primers.2023 Feb; 9(1): 8. doi: 10.1038/s41572-023-00417-6.

[25] Gaoxia DO, Ying TI, Xinqin LI. Adiponectin Participates in Preeclampsia by Regulating the Biological Function of Placental Trophoblasts Through P38 MAPK-STAT5 Pathway. Iranian Journal of Public Health. 2018 Dec; 47(12): 1838.

[26] Pheiffer C, Dias S, Jack B, Malaza N, Adam S. Adiponectin as a Potential Biomarker for Pregnancy Disorders. International Journal of Molecular Sciences.2021 Jan; 22(3): 1326. doi:10.3390/ijms22031326.

[27] Adu-Gyamfi EA, Fondjo LA, Owiredu WK, Czika A, Nelson W, Lamptey J *et al*. The Role of Adiponectin in Placentation and Preeclampsia. Cell Biochemistry and Function. 2020 Jan; 38(1): 106-17. doi: 10.1002/cbf.3458

[28] Mazaki-Tovi S, Romero R, Vaisbuch E, Kusanovic JP, Erez O, Gotsch F *et al*.Maternal Serum Adiponectin Multimers in Preeclampsia.2009;37: 349-363. doi:10.1515/JPM.2009.085

[29] Daskalakis G, Bellos I, Nikolakea M, Pergialiotis V, Papapanagiotou A, Loutradis D. The Role of Serum Adipokine Levels in Preeclampsia: A Systematic Review. Metabolism.2020 May; 106: 154172. doi:10.1016/j.metabol.2020.154172.

[30] Tejera E, Sánchez ME, Henríquez-Trujillo AR, Pérez-Castillo Y, Coral-Almeida M. A Population-Based Study of Preeclampsia and Eclampsia in Ecuador: Ethnic, Geographical and Altitudes Differences. BioMed Central Pregnancy and Childbirth.2021 Dec; 21: 1-0. doi: 10.1186/s12884-021-03602-1

[31] Pheiffer C, Dias S, Jack B, Malaza N, Adam S. Adiponectin as a Potential Biomarker for Pregnancy Disorders. International Journal of Molecular Sciences. 2021 Jan; 22(3): 1326. doi: 10.3390/Ijms22031326.

[32] Gök S, Gök BC, Enli Y. Evaluation of the Adipokine Levels of Pregnant Women with Preeclampsia. Journal of Obstetrics and Gynaecology Research.2023 Jan; 49(1): 154-63. doi: 10.1111/jog.15463.

[33] Hafiane A. Adiponectin-mediated Regulation of the Adiponectin Cascade in Cardiovascular Disease: Updates. Biochemical and Biophysical Research Communications.2023Dec; 694: 149406. doi:10.1016/j.bbrc.2023.149406.

[34] Karrasch T, Höpfinger A, Schäffler A, Schmid A. The Adipokine C1q/TNF-related Protein-3 (CTRP-3) Inhibits Toll-Like Receptor(TLR)-Induced Expression of Cathelicidin Antimicrobial Peptide (CAMP) in Adipocytes.Cytokine.2021Dec;148:155663.doi:10.1016/j.cyto.2021.155663.

[35] Stefaniak M and Dmoch-Gajzlerska E. Maternal Serum and Cord Blood Leptin Concentrations at Delivery in Normal Pregnancies and in Pregnancies Complicated by Intrauterine Growth Restriction.Obesity Facts.2022Jan;15(1):62-9. doi: 10.1159/000519609.

[36] Chen X, Liu Z, Cui J, Chen X, Xiong J, Zhou W. Circulating Adipokine Levels and Preeclampsia: A Bidirectional Mendelian Randomization Study. Frontiers in Genetics.2022 Aug; 13: 935757. doi:10.3389/fgene.2022.935757.

[37] Nugrahani AD, Aziz MA, Santoso DP, Siddiq A, Pramatirta AY, Irianti S *et al*. Adiponectin and Leptin Profiles among Obese Pregnant Women with Preeclampsia Vs. Non-Preeclampsia: A Systematic Review and Meta-Analysis. European Review for Medical and Pharmacological Sciences. 2024 Jul; 28: 3922-33 doi: 10.1016/j.clinbiochem.2024.110778.

[38] de Knegt VE, Hedley PL, Eltvedt AK, Placing S, Wøjdemann K, Shalmi AC *et al*. First-Trimester Maternal Serum Adiponectin/Leptin Ratio in Pre-Eclampsia and Fetal Growth. Life. 2023 Jan; 13(1): 130. doi: 10.3390/life13010130.