LOW SERUM ADIPONECTIN AND HIGH SERUM LEPTIN LEVELS FOUND IN WOMEN WITH HYPERTENSIVE DISEASES OF PREGNANCY COMPARED TO NORMOTENSIVE PREGNANT WOMEN

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ABSTRACT

Objective: The study aimed to compare serum leptin and adiponectin levels between women with hypertensive diseases of pregnancy (HDP) and normotensive pregnant women and to evaluate their associations with Body Mass Index and blood pressure.

Methodology: A cross-sectional study was conducted at the outpatient department of Hayatabad Medical Complex, Peshawar, from 12thAugust 2024 to12th November 2024. A total of 125 participants were divided into two groups: women with hypertensive diseases of pregnancy (HDP; n = 62) and normotensive pregnant women (n = 63). Serum levels of leptin and adiponectin were measured using enzyme-linked immunosorbent assays (ELISA). Body Mass Index (BMI) and blood pressure were recorded and classified. Data were analyzed using descriptive and inferential statistics in SPSS

Results: Women with HDP had significantly elevated serum leptin levels (45.2 ± 9.6 ng/mL) and decreased adiponectin levels (3.8 ± 0.9 µg/mL) compared to the normotensive group (leptin: 27.8 ± 7.1 ng/mL; adiponectin: 5.6 ± 1.2 µg/mL). Correlation analysis revealed a positive association between leptin levels, Body Mass Index (BMI), and blood pressure (systolic and diastolic). Conversely, adiponectin levels showed a negative association with BMI and blood pressure. These findings highlight the potential role of these biomarkers in the pathophysiology of hypertension during pregnancy.

Conclusion: In conclusion, Elevated levels of leptin and reduced adiponectin are associated with hypertensive diseases during pregnancy. These biomarkers could serve as likely indicators for early detection and management of HDP.

Keywords: Hypertensive Diseases of Pregnancy, Leptin, Adiponectin, BMI, Blood Pressure, Pregnancy.

INTRODUCTION

Hypertensive diseases of pregnancy (HDP), including preeclampsia and gestational hypertension, are among the most common pregnancy complications, significantly affecting maternal and fetal health. , major significant complications that can impact maternal and fetal conditions[1 2].

These conditions are characterized by increased blood pressure and probable end-organ dysfunction. Studies suggest that metabolic markers like Leptin and Adiponectin may play a key role in the pathophysiology of HDP. Leptin, an adipokine produced by adipose tissue, is associated with inflammation, endothelial dysfunction, and increased vascular resistance, all contributing to hypertension. Conversely, adiponectin, known for its anti-inflammatory and vasodilatory properties, helps regulate vascular function and blood pressure, with its reduced levels linked to the development of hypertension in pregnancy.[3].

The global incidence of HDP ranges from 5% to 10%, with significant variation across different populations. [4 5]. In high-income countries, the occurrence is comparatively stable, whereas in low- and middle-income countries, rates can be higher due to limited access to prenatal care. HDP prevalence differs between 5% and 15%, with a higher incidence of 6 % reported in South Asian countries. In Pakistan, studies show an occurrence of around 8-12%, with notable regional differences [6].

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HDP is one of the leading causes of maternal and perinatal morbidity and mortality [7]. The pathogenesis involves interactions between genetic, environmental, and metabolic factors [8]. The hormone Leptin is linked with adipose tissue, and adiponectin, an adipokine with anti-inflammatory properties, has been involved in of regulating blood pressure and vascular function during pregnancy [9].

Elevated leptin levels and reduced adiponectin levels are believed to contribute to the development and progression of hypertension in pregnancy. These associations may improve our capacity to predict and manage HDP. cause [10].

The rationale for this study is based on the critical need to understand the role of metabolic markers, such as leptin and adiponectin, in HDP. These biomarkers are implicated in vascular and inflammatory pathways associated with hypertension. Exploring the differences in leptin and adiponectin levels between women with HDP and normotensive pregnant women may provide valuable insights into their involvement in HDP pathophysiology. Such findings can enhance our ability to develop effective screening, early detection, and management strategies for HDP, ultimately improving maternal and fetal outcomes based on adiponectin leptin and adiponectin levels.

METHODOLOGY

The study design was a cross-sectional study conducted at Hayatabad Medical Complex Peshawar OPD from 12th August 2024 to 12th November 2024. The study aimed to evaluate differences in leptin and adiponectin levels between women with HDP and normotensive pregnant women.

The sample size was calculated using G Power software to compare two independent means. The expected mean difference was set at 15 ng/mL, with a 10 ng/mL standard deviation for both groups[11]. The confidence level was 95% ($\alpha = 0.05$), and the power was 80% ($\beta = 0.20$). The required sample size per group was calculated using these parameters, which included 60 participants. To ensure robustness and account for potential dropouts, the total sample size was increased to 125 participants, with 62 in the HDP group and 63 in the normotensive group divided. The study was approved by the Institutional Review Board (IRB) of Hayatabad Medical Complex with approval no. 2047. 'Informed consent was obtained from all participants before inclusion in the study.' Procedures conducted 'in accordance' with ethical 'guidelines' for research involving human subjects.

The inclusion criteria for the study were: (1) pregnant women aged 18–40 years, (2) singleton pregnancies (to minimize confounding variables and maintain data consistency, as multiple pregnancies introduce additional physiological complexities and risks), and (3) a confirmed clinical diagnosis of either HDP or normotensive status.

The exclusion criteria included (1) women with a pre-existing diagnosis of hypertension or diabetes, (2) medical conditions known to influence leptin or adiponectin levels, and (3) women taking medications that could affect leptin or adiponectin levels. After using ethical approval, blood samples were gathered from participants using standard venipuncture techniques. For analysis, samples were processed and stored at -80°C. A proper sterilization protocol was followed for blood collection to minimize the risk of contamination.

After the blood processing was collected and processed, serum levels of leptin and adiponectin were measured using enzyme-linked immunosorbent assays (ELISA), following the industrialist's instructions. ELISA plates were read using a microplate reader at the appropriate wavelengths for each biomarker.

Body Mass Index (BMI) was calculated using height and weight measurements obtained from each participant. BMI was categorized as < 30 kg/m² (normal weight) and ≥ 30 kg/m² (obese).

Blood pressure was recorded using a calibrated sphygmomanometer. Readings were categorized as high (systolic >140 mm Hg or diastolic >90 mm Hg) or normal (systolic ≤120 mm Hg and diastolic ≤80 mm Hg).

Statistical Analysis Descriptive Statistics were used to summarize demographic and clinical data. Differences between the HDP and normotensive groups were assessed using t-tests for continuous variables and chi-square tests for categorical variables. Pearson's correlation coefficient was used to determine the relationships between leptin, adiponectin, BMI, and blood pressure. A p-value of < 0.05 was considered statistically significant.

RESULTS

The study included 125 participants, divided into the HDP group (n = 62) and the normotensive group (n = 63). Age distribution varied between the groups, with 40% of participants in the HDP group aged between 20–30 years and 60% aged 31–40 years. In the normotensive group, 68% were aged 20–30, and 32% were aged 31–40. , Demographic and Laboratory Characteristics of Study Participants (n = 125 total). Age Distribution: HDP Group (n = 62): 40% were aged 20-30, and 60% were aged 31-40, and 32% were aged 31-40 years and 32% were aged 31-40The HDP group had a higher proportion of older participants (31-40 years) than the normotensive group. This suggests that hypertension-related risks may increase with age, as indicated by the statistically significant difference ($p = 0.01$). In the HDP group, 35% of participants had a BMI below 30 kg/m², while 65% had a 30 kg/m² or higher BMI .In the normotensive group, 70% of participants had a BMI below 30 kg/m², while 30% had a BMI of 30 kg/m² or higher. A higher proportion of women with HDP were obese (BMI ≥ 30 kg/m²) compared to the normotensive group, indicating a strong association between higher BMI and HDP ($p < 0.001$). This finding supports the idea that obesity is a significant risk factor for HDP.

In the HDP group, 60% of participants were from a low socioeconomic background, 30% from a medium socioeconomic status, and 10% from a high socioeconomic status. In the normotensive group, 49% were from a low socioeconomic background, 35% from a medium socioeconomic status, and 16% from a high socioeconomic status. The difference in socioeconomic status between the two groups was not statistically significant ($p = 0.09$), suggesting that socioeconomic factors are unlikely to be a significant confounder in this study. Significant Leptin levels HDP Group: 76% had high leptin levels (>40 ng/mL), and 24% had normal levels. Normotensive Group: 24% had high leptin levels, and 76% had normal levels. A significantly higher proportion of women with HDP have elevated leptin levels than the normotensive group ($p < 0.001$). This reinforces the association between high leptin levels and HDP. In the HDP group, 76% of participants had low adiponectin levels (<4 µg/mL), compared to 21% in the normotensive group. Conversely, only 24% of participants in the HDP group had normal adiponectin levels, whereas 79% of the normotensive group had normal levels. This statistically significant difference ($p < 0.001$) highlights a marked association between reduced adiponectin levels and HDP, indicating that lower adiponectin levels were more common in women with HDP than normotensive pregnant women.

In the HDP group, 77% of participants had high systolic blood pressure (>140 mm Hg), compared to only 13% in the normotensive group ($p < 0.001$). Similarly, 76% of the HDP group had high diastolic blood pressure (>90 mm Hg), while only 11% of the normotensive group had diastolic readings above this threshold ($p < 0.001$).

It is important to note that participants classified as normotensive met strict clinical criteria for normal blood pressure at the time of the study, and the small percentage of elevated readings in this group may reflect temporary fluctuations rather than sustained hypertension. These results confirm the diagnostic distinction between the HDP and normotensive groups and highlight hypertension as a key feature of HDP.

In the HDP group, 39% of participants were in the 20–28 weeks range, 35% in the 29–36 weeks range, and 26% in the 37–40 weeks range. Similarly, in the normotensive group, 35% were in the 20–28 weeks range, 43% in the 29–36 weeks range, and 22% in the 37–40 weeks range. There was no statistically significant difference in gestational age between the two groups ($p = 0.12$), indicating that the timing of gestation does not significantly influence the observed differences in biomarkers between women with HDP and those with normotensive pregnancies.

Table 1: Demographic and Laboratory Characteristics of Study Participants (n = 125 total)

Variable	HDP Group (n = 62)	Normotensive Group (n = 63)	p-value
Age Distribution			
20–30 years	25 (40%)	43 (68%)	0.01
31–40 years	37 (60%)	20 (32%)	

BMI (kg/m²)			
< 30	22 (35%)	44 (70%)	<0.001
≥ 30	40 (65%)	19 (30%)	
Socioeconomic Status			
Low	37 (60%)	31 (49%)	0.09
Medium	19 (30%)	22 (35%)	
High	6 (10%)	10 (16%)	
Leptin Levels (ng/mL)			<0.001
High (>40 ng/mL)	47 (76%)	15 (24%)	
Normal	15 (24%)	48 (76%)	
Adiponectin Levels (µg/mL)			<0.001
Low (<4 µg/mL)	47 (76%)	13 (21%)	
Normal	15 (24%)	50 (79%)	

In Table 2: Serum Leptin Levels in HDP vs Normotensive Pregnant Women HDP Group, the HDP group exhibited significantly higher mean leptin levels compared to the normotensive group ($p < 0.001$)

Table 2: Serum Leptin Levels in HDP vs Normotensive Pregnant Women

Group	Leptin (ng/mL)	p-value
HDP Group (n = 62)	45.2 ± 9.6 (Range: 30.1–65.7)	< 0.001
Normotensive Group (n = 63)	27.8 ± 7.1 (Range: 18.2–40.6)	

In Table 3: Serum Adiponectin Levels in HDP vs Normotensive Pregnant Women HDP Group Adiponectin levels were significantly lower in the HDP group compared to the normotensive group ($p < 0.001$), emphasizing the strong association between reduced adiponectin and the development of HDP.

Table 3: Serum Adiponectin Levels in HDP vs Normotensive Pregnant Women

Group	Adiponectin (µg/mL)	p-value
HDP Group (n = 62)	3.8 ± 0.9 (Range: 2.1–5.5)	< 0.001
Normotensive Group (n = 63)	5.6 ± 1.2 (Range: 3.9–7.8)	

In Table 4: Correlation of Leptin and Adiponectin with BMI, Blood Pressure, and Gestational Age, leptin showed significant positive correlations with BMI, systolic blood pressure, and diastolic blood pressure ($p < 0.001$), highlighting its association with adiposity and hypertension in HDP. Conversely, adiponectin displayed significant negative correlations with BMI, systolic blood pressure, and diastolic blood pressure ($p < 0.001$), reinforcing its protective role against hypertension. No significant correlations were observed between either biomarker and gestational age.

Table 4: Correlation of Leptin and Adiponectin with BMI, Blood Pressure, and Gestational Age

Variable	Leptin (r-value)	Adiponectin (r-value)	p-value
BMI (kg/m²)	+0.52	-0.43	< 0.001*
Systolic BP (mm Hg)	+0.62	-0.39	< 0.001*
Diastolic BP (mm Hg)	+0.58	-0.36	< 0.001*
Gestational Age (weeks)	-0.15	+0.22	0.23

DISCUSSION

Our study highlights 'significant differences' in serum leptin and adiponectin levels 'between women with hypertensive diseases of pregnancy' (HDP) and those with 'normotensive' pregnancies. Increased levels of leptin and decreased adiponectin in women with HDP highlight the importance of these biomarkers in detecting and managing HDP. Our findings were consistent with studies suggesting that leptin and adiponectin play crucial roles in the pathophysiology of pregnancy-induced hypertension. Elevated leptin levels contribute to hypertension by promoting inflammation, endothelial

dysfunction, and increased vascular resistance. In contrast, reduced adiponectin levels impair its anti-inflammatory and vasodilatory functions, exacerbating vascular dysfunction and hypertension. These mechanisms highlight the importance of these adipokines in the progression of hypertensive disorders during pregnancy. [12-14].

The elevated leptin levels observed in our study align with findings from international research. For example, Veiga et al. (2022)[14] reported increased leptin levels in women with preeclampsia. Similarly, Lara-Barea et al. (2022)[15] highlighted variations in leptin thresholds, suggesting that while leptin is a reliable marker for HDP, population-specific factors can influence its levels. Our study supports these findings, emphasizing leptin's importance as a biomarker across diverse populations. These variations underscore the need for further research to explore how genetic, environmental, and lifestyle factors influence leptin levels.

Additionally, our results show significantly reduced adiponectin levels in women with HDP compared to normotensive controls, consistent with Jeba Malar Abraham et al. (2023), who identified decreased adiponectin levels in HDP. This supports adiponectin's known role as an anti-inflammatory and insulin-sensitizing hormone[16]. These findings highlight adiponectin's importance as a HDP biomarker and utility in regions like South Asia, where HDP prevalence is mainly high[17 18]. leptin levels, A study by Jeba Malar Abraham et al. (2023) found that Our study demonstrates a positive correlation between leptin levels and BMI, supporting the concept that leptin, a hormone produced by adipose tissue, is influenced by body fat and inflammation. Elevated leptin levels may indicate increased adiposity or inflammatory responses, both of which are associated with hypertension. Conversely, the observed negative correlation between adiponectin levels and BMI suggests that lower adiponectin levels are linked to higher body fat and diminished anti-inflammatory effects. Phoswa et al. (2021) emphasized the roles of leptin and adiponectin in adiposity and hypertension, providing further insight into their involvement in the pathogenesis of HDP[19]. A positive correlation was found in our study among levels of leptin and systolic and diastolic blood pressure. A study by Lu et al 2020 reported that the increased levels of leptin directly increased blood pressure, possibly through vascular resistance and endothelial dysfunction [18]. In contrast, the negative correlations between adiponectin and blood pressure specify that decreased levels of adiponectin are associated with higher blood pressure. This finding highlights the important role of adiponectin in alleviating hypertension through its anti-inflammatory and endothelial-protective effects.

The difference between levels of leptin and adiponectin levels among women with HDP and normotensive women underlines that such biomarkers could be valuable for screening and managing HDP [18 20]. Integrating measurements of leptin and adiponectin into prenatal care could aid in identifying women at high risk of developing HDP. This approach would enable early prediction and management strategies, potentially improving outcomes for both mothers and infants through timely therapeutic interventions. Recently it has also been confirmed by Saddaf Durrani et al in Hayatabad Medical Complex that serum adiponectin has also an inverse relation with cardiovascular diseases and insulin resistance[21]

Although our study offers important insights, its cross-sectional study restricts the ability to determine causality. Longitudinal studies are necessary to examine how variations in leptin and adiponectin levels over time are associated with the onset and progression of HDP. Moreover, future research should investigate the basic mechanisms involving these biomarkers to HDP, which could lead to targeted treatments. As highlighted by Ghazala Shams et al. that early detection of antenatal issues, HDP, allows for timely management during the early stages. This approach is highly beneficial not only for the health of the pregnant woman but also in preventing premature birth of the fetus[22].Gaining insight into the interaction between leptin, adiponectin, and other risk factors will enhance our ability to predict and manage HDP more effectively.

CONCLUSION

Our study emphasizes the potential role of leptin and adiponectin as biomarkers for HDP. The statistical significance observed in both biomarkers between women with HDP and normotensive controls underlines their importance in detecting and managing HDP. Future research is important to understand the mechanisms of these associations and explore effective interventions targeting these biomarkers. Incorporating these visions into clinical could improve early detection and management of HDP, eventually improving maternal and fetal outcomes.

DECLARATIONS

I Dr Gul Muhammad, hereby declare that this study entitled "**Low Serum Adiponectin and high serum leptin levels found in Women with hypertensive diseases of Pregnancy Compared to normotensive pregnant women"** is my work and that to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to a substantial extent has been accepted for the award of any other degree or diploma at any university or equivalent institution.
I also declare that the intellectual content of this thesis is the product of my work, except to the extent that assistance from others in the project's design and conception or style, presentation, and linguistic expression is acknowledged.

Dr Gul Muhammad
Date 21/10/2024

CONFLICT OF INTEREST

I do not consider that any of the associations present a conflict of interest. I declare that there is no conflict of interest regarding the publication of this paper

ACKNOWLEDGMENT

I am expressing our deepest gratitude and appreciation for the assistance and support of my co-authors in the department of physiology, Dr Shabnam Gul gynecologist worked hard and sorted out all the required cases of pregnancy-induced hypertensive women. We also pay thanks to the Head department of the gynae in HMC and other colleagues working there in the department for their help and support throughout this research work. I want to take this opportunity to acknowledge the contributions of Professor Dr Wajid Ali Akhunzada Professor of the psychiatry department at Hayatabad Medical Complex Peshawar for ethical approval and allowed me to do this work of research. I also want to express my heartfelt thanks to the laboratory staff of HMC for their wonderful collaboration. Without their support I couldn't complete this research project, I cordially pay thanks to all of them.

AUTHOR'S CONTRIBUTIONS

Author Name	Contribution
Dr. Shabnam Gul	Conceptualization, Study Design, Data Collection, and Manuscript Review.
Dr. Gul Muhammad	Data Analysis, and Manuscript Writing.
Dr. Muhammad Salman Khan	Study Design, Data Interpretation, and Critical Review of the Manuscript.
Dr. Sara Mariyum	Laboratory Work (ELISA Testing), Data Validation, and Manuscript Drafting.
Dr. Hijab Hashmi	Data Collection, Literature Review, and Manuscript Editing.
Dr. Syed Soban Ahmed Tirimzi	Statistical Analysis, Graph/Table Preparation, and Manuscript Formatting.

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