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Assessment of Clinical Outcomes of Maternal Leptin Levels in Comparison among Three Groups: Women in Normal Pregnancy, Women with GDM, and Women with Preeclampsia

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Abstract: Background: Leptin is a 16-kDa adipokine that is mainly secreted by adipose tissue and the placenta, which has been involved in the pathophysiology of gestational diabetes mellitus (GDM) and preeclampsia. Nevertheless, the longitudinal pattern of maternal leptin concentrations during trimesters and its independent relation to poor obstetric outcomes are not well defined as well as were The purpose of the study was to assess the relationship between serial maternal serum leptin levels and clinical outcomes in normal pregnancy, GDM, and preeclampsia. Methods: The study was a prospective cross-sectional comparative study conducted in a tertiary care hospital on 125 pregnant women who were divided into three groups: normal pregnancy (n = 42), GDM (n = 42), and preeclampsia (n = 41). Enzyme-linked immunosorbent assay (ELISA) was used to measure maternal serum leptin at every trimester and at birth. Furthermore, prospective data collection was done on demographic, clinical, and neonatal outcomes. Statistical tests were one-way ANOVA with Tukey HSD post-hoc tests, Pearson correlation, and binary logistic regression, which was adjusted by age, pre-pregnancy BMI, parity, and family history. Results: The GDM and preeclampsia groups had a significant increase in maternal serum leptin levels in all trimesters compared to the normal pregnancy group ($p < 0.001$). The leptin levels in the third trimester were 48.6 ± 16.8 ng/ml in GDM, 52.4 + 18.2 ng/ml in preeclampsia and 28.3 + 10.1 ng/ml in normal pregnancy ($F = 28.47$, $p < 0.001$) where The results of this study revealed the following firstly The preeclampsia group had the highest leptin levels (56.8 ± 20.6 ng/ml) at delivery, seconadlly significantly higher than the GDM group (42.3 ± 15.4 ng/ml) and normal pregnancy groups (25.1 ± 9.8 ng/ml, $p < 0.001$) also we found in our study Placental leptin MRNA expression was increased in preeclampsia (2.14 ± 0.72 relative fold change) compared to GDM (1.56 ± 0.48) and normal pregnancy (1.00 ± 0.32, $p < 0.001$) where along with based on binary logistic regression, higher level of third-trimester leptin (10 ng/ml) This statement refers to the value found in the third trimester and the correlation between the relationship and an increased risk of preeclampsia. was independently associated with increased odds of preeclampsia (adjusted OR = 2.32, 95% CI: 1.483.63, $p < 0.001$), GDM (adjusted OR = 1.98, 95% CI: 1.303.01, $p = 0.001$). Conclusion: The levels of maternal serum leptin in GDM and preeclampsia are raised significantly and independently and have different longitudinal relationships depending on the pathophysiology involved- metabolic dysregulation mainly in GDM and overproduction by placental hypoxia in preeclampsia. An increase in maternal third-trimester leptin is related independently to inferior maternal and neonatal outcomes, which can be used as a complementary biomarker to classify the risk in obstetric care. Future multicenter-based studies are justified to confirm the efficacy of the prediction models that are based on leptin and to determine clinically practical thresholds.

Keywords: Maternal Serum Leptin, Gdm, Preeclampsia, Pregnancy, Trimesters, Metabolic Dysregulation, Placental, Biomarker, Bmi, Leptin.

INTRODUCTION

Leptin, a 16-kDa adipocytokine majorly produced by adipose tissue, has become a key player at the crossroad of metabolism, energy homeostasis, and reproductive biology therefore as previous study during pregnancy, maternal adipose tissue and placental trophoblasts, chorioamnion, decidua, and, to a smaller degree, fetal tissues also produce leptin as well as Of interest is the placental contribution to the circulating leptin levels [Alfadhli, E. M. 2015; American Diabetes Association, 2004], which is a measure of placental mass, functional capacity, and effectiveness of the exchange of nutrients. Initial observations reported a gradual increase in leptin levels in the course of gestation, which was similar to the increment in maternal adiposity, gestation age, and placental mass [Bao, W. *et al*., 2015; Booth, A. *et al*., 2012] whereas This interactive relationship makes leptin a possible biomarker and mediator of placental activities and fetal development, and a contributor to the physiological changes that support a normal gestation also found The leptin-associated physiological functions are not limited to appetite control and energy expenditure. Leptin in the reproductive system is also closely associated with gonadal activity, ovulation, and pregnancy maintenance [Clausen, T. D. *et al*., 2008]. It has central nervous system effects to control energy balance and peripheral tissue effects to control glucose homeostasis, lipid metabolism, placental transport processes, and inflammatory responses through leptin receptors. During pregnancy, leptin is involved in decidualization, placental

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angiogenesis, and fetal development, and the placenta is an important location of leptin signalling that orchestrates the allocation of maternal and fetal resources [De Gennaro, G. *et al*., 2019]. With these complex functions, changes in maternal leptin might indicate and possibly cause maternal and fetal deviations ,According to some previous studies that were somewhat consistent with our current study, there is strong evidence that leptin levels are disrupted in typical obstetric states, which are metabolic or vascular impairments, especially in gestational diabetes mellitus [Egger, M. *et al*., 1997; Gutaj, P. *et al*., 2020; Higgins, J. P., & Thompson, S. G. 2002] (GDM) and preeclampsia (PE) In addition, it can be concluded that there is a link to Insulin resistance, hyperglycemia and dyslipidemia are linked to GDM which is characterized by glucose intolerance that first appears in pregnancy while that Leptin interferes with these metabolic derangements by acting on adipose tissue and hepatic gluconeogenesis, and by participating in the inflammatory pathways which can aggravate insulin resistance therefore Increased maternal leptin has been observed in certain groups of women with GDM, and the increases could be due to adiposity-induced secretion, placental synthesis or compensation to insulin signalling changes [Higgins, J. P. *et al*., 2003; Higgins, J. P., & Altman, D. G. 2008; Luo, D. *et al*., 2018; Stewart, G. 2009] furthermore the research on leptin in this regard has potential to enhance the risk stratification, understanding of pathophysiology, and the presence of potential targets of nutritional or pharmacologic interventions to improve glycemic control and pregnancy outcomes [Sterne, J. A. 2009] As for the specific tasks related to preeclampsia, which is a pregnancy-specific hypertensive disorder characterized by the onset of high blood pressure in the mother and the impact on several organs after the twentieth week of pregnancy, an association can be found with placental insufficiency, endothelial dysfunction, and activation of systemic inflammation [Pérez-Pérez, A. *et al*., 2009]. Through previous studies that focused on this topic, it was found that the pro-inflammatory properties of leptin and its interaction with angiogenic factors indicate that it is a possible participant in the inception and development of pre-eclampsia. The results have also documented high levels of leptin in some studies that dealt with preeclampsia, with associations between high leptin concentration and adverse outcomes for the mother and newborn, including decreased blood flow to the placenta, fetal growth restriction, oligohydramnios, and increased rates of cesarean delivery. [Pérez-Pérez, A. *et al*., 2020; Shamseer, L. *et al*., 2015; Stang, A. 2010]

MATERIAL AND METHOD

A cross-sectional study was conducted in Iraq in the Department of Obstetrics and Gynecology at several different hospitals in Iraq from March 2025 to February 2026 where The study protocol was approved by the Institutional Ethics Committee, and the study was conducted in accordance with the Declaration of Helsinki also Written informed consent was obtained from all participants before their enrollment in the study as well as In this study, all patient information was obtained with full consent. 125 pregnant women attending the antenatal clinic were recruited and divided into three groups based on their clinical diagnosis, as shown below.

Section	Description
Study Population	A total of 125 pregnant women attending the antenatal clinic were recruited and divided into three groups based on their clinical diagnosis.
Group I (Control)	42 women with uncomplicated normal singleton pregnancies serving as the control group.
Group II	42 women diagnosed with gestational diabetes mellitus (GDM).
Group III	41 women diagnosed with preeclampsia.
Sample Size Calculation	Calculated using
Inclusion Criteria	Singleton pregnancy, age between 18 and 40 years, gestational age confirmed by first-trimester ultrasound, and willingness to participate in serial blood sampling throughout pregnancy.

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GDM Diagnosis Criteria	Based on IADPSG criteria using 75-g OGTT (24-28 weeks): fasting plasma glucose ≥92 mg/dL, 1-hour glucose ≥180 mg/dL, or 2-hour glucose ≥153 mg/dL.
Preeclampsia Diagnosis Criteria	Based on ACOG criteria: new-onset hypertension (≥140/90 mmHg after 20 weeks) with proteinuria (≥300 mg/24h or protein/creatinine ratio ≥0.3 mg/dL) or end-organ dysfunction.
Exclusion Criteria	Multiple pregnancies, pre-existing diabetes (type 1/2), chronic hypertension before 20 weeks, chronic kidney disease, autoimmune disorders (SLE, antiphospholipid syndrome), thyroid disorders, known malignancy, corticosteroids/immunosuppressives during pregnancy, fetal anomalies, incomplete follow-up, or missing samples.

Patient demographic data were registered, including maternal age, gestational age, parity, pre-pregnancy body mass index (BMI) (weight in kilograms/height in meters squared) gestational age at the time of each visit, family history of diabetes mellitus and hypertension, obstetric history also were recorded all the observations related to obstetric outcomes were recorded between the enrollment and delivery as well as These were mode of delivery (vaginal or cesarean section), gestational age at delivery, birth weight, APGAR scores at 1 and 5 minutes, neonatal intensive care unit (NICU) admission, and maternal complications, including HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), placental abruption, eclampsia, postpartum hemorrhage, and maternal intensive care unit (ICU) admission.

Leptin Measurement and Blood Sampling.

Each participant provided venous blood samples (5 mL) at four different gestational milestones, namely first trimester (1013 weeks), second trimester (2428 weeks), third trimester (3236 weeks), and just before delivery (within 1 hour before delivery or at the onset of active labor). The umbilical vein (5 mL) cord blood was also taken immediately after delivery and before the placenta was separated. All the specimens were taken in plain red-top Vacutainer tubes after at least eight hours of fasting (when the visit was scheduled as an antenatal visit) and left to clot at room temperature over thirty minutes. The next centrifugation of 3,000 rpm in fifteen minutes at 4 0 C produced serum, which was aliquoted in labeled cryovials and kept at -80 0 C until batch analysis.

The serum leptin levels were measured with the help of a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Human Leptin Quantikine ELISA Kit, R&D Systems, Minneapolis, MN, USA; Catalog No. DLP00) according to the manufacturer's protocol. The assay is based on a quantitative sandwich format that uses a monoclonal antibody against human leptin that is pre-coated on microplates. Its lower detection limit was 7.8- 1 pg/mL, and its working range was 15.6- 1000 pg/mL. The intra-assay coefficient of variation (CV) was 3.2, and the inter-assay CV was 4.8. Each sample was analyzed twice, and the arithmetic mean of the duplicate readings was used in further analysis. Samples with a CV greater than 10% between duplicates were re-analyzed.

Ethical Considerations

The current research was carried out in accordance with the ethical principles provided in the Declaration of Helsinki and the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines. The informed consent form, the study protocol, and all the documents related to the study were reviewed and approved by the Institutional Review Board before the participants were enrolled into the study. Every participant was made aware of the objectives of the study, the procedures, risks, and benefits, and their right to withdraw at any time without any effect on their clinical care. Each participant signed an informed consent form in her native language. The study ensured the confidentiality of the participants by giving them unique identification codes, and all the information was stored in password-protected electronic databases

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that were only accessible by the authorized research personnel.

RESULTS

Table 1: Assessment Demographic and Clinical Characteristics of Study Participants (N = 125)

Variable	Normal Pregnancy (n = 42)	GDM (n = 42)	Preeclampsia (n = 41)	Test Statistic
Age (years)	27.4 ± 4.8	30.6 ± 5.2	29.8 ± 5.5	F = 4.12
Pre-pregnancy BMI (kg/m²)	23.1 ± 3.2	28.7 ± 4.6	27.3 ± 4.1	F = 21.38
BMI at delivery (kg/m²)	28.4 ± 3.1	33.2 ± 4.3	32.6 ± 3.9	F = 18.74
Gestational age at delivery (weeks)	38.9 ± 1.2	37.8 ± 1.6	36.4 ± 2.3	F = 19.52
Gravidity	2.1 ± 1.0	2.4 ± 1.2	2.3 ± 1.1	F = 0.82
Parity	0.9 ± 0.8	1.1 ± 0.9	1.0 ± 0.8	F = 0.56
Systolic BP (mmHg)	112.3 ± 8.4	118.6 ± 10.2	152.7 ± 14.8	F = 134.6
Diastolic BP (mmHg)	72.1 ± 6.8	76.4 ± 8.1	98.3 ± 10.6	F = 108.3
Fasting blood glucose (mg/dL)	82.4 ± 7.3	118.6 ± 22.4	89.7 ± 11.2	F = 58.92
HbA1c (%)	5.1 ± 0.3	6.4 ± 0.8	5.3 ± 0.4	F = 62.18
Family history of DM, n (%)	8 (19.0%)	18 (42.9%)	10 (24.4%)	$\chi^2 = 6.24$
Family history of HTN, n (%)	6 (14.3%)	9 (21.4%)	16 (39.0%)	$\chi^2 = 6.98$
Nulliparous, n (%)	18 (42.9%)	15 (35.7%)	17 (41.5%)	$\chi^2 = 0.52$

Table 2: Assessment and description of patient outcomes according to maternal serum leptin levels during pregnancy (mean ± standard deviation)

Variable	Normal Pregnancy (n = 42)	GDM (n = 42)	Preeclampsia (n = 41)	F-value
1st Trimester Leptin (ng/mL)	14.8 ± 6.2	22.3 ± 8.7	20.1 ± 7.9	10.84
2nd Trimester Leptin (ng/mL)	21.6 ± 8.4	34.7 ± 12.3	31.8 ± 11.6	16.42
3rd Trimester Leptin (ng/mL)	28.3 ± 10.1	48.6 ± 16.8	52.4 ± 18.2	28.76
At Delivery Leptin (ng/mL)	25.1 ± 9.8	42.3 ± 15.4	56.8 ± 20.6	38.14
Leptin Change (1st→3rd) (ng/mL)	13.5 ± 5.8	26.3 ± 10.4	32.3 ± 13.1	32.68
Cord Blood Leptin (ng/mL)	8.4 ± 4.2	14.6 ± 6.8	11.2 ± 5.9	11.23
Leptin/BMI Ratio	1.02 ± 0.34	1.48 ± 0.52	1.64 ± 0.58	17.36
Placental Leptin mRNA (relative)	1.00 ± 0.32	1.68 ± 0.54	2.14 ± 0.72	42.86

Table 3: Finding Post-hoc Pairwise Comparisons Tukey HSD

Comparison	Mean Difference	95% CI	p-value
Normal vs GDM (3rd Trimester)	-20.3	-27.1 to -13.5	**<0.001****
Normal vs Preeclampsia (3rd Trimester)	-24.1	-31.0 to -17.2	**<0.001****
GDM vs Preeclampsia (3rd Trimester)	-3.8	-10.7 to 3.1	0.392
Normal vs GDM (At Delivery)	-17.2	-24.3 to -10.1	**<0.001****
Normal vs Preeclampsia (At Delivery)	-31.7	-39.0 to -24.4	**<0.001****
GDM vs Preeclampsia (At Delivery)	-14.5	-21.8 to -7.2	**<0.001****

Table 4: Patient outcomes related to clinical results and neonatal characteristics (number of cases = 125)

Outcome	Normal Pregnancy (n = 42)	GDM (n = 42)	Preeclampsia (n = 41)
Cesarean Section	10 (23.8%)	18 (42.9%)	24 (58.5%)
Vaginal Delivery	32 (76.2%)	24 (57.1%)	17 (41.5%)
Preterm Birth (<37 weeks)	3 (7.1%)	7 (16.7%)	14 (34.1%)
Low Birth Weight (<2500 g)	2 (4.8%)	5 (11.9%)	12 (29.3%)
Macrosomia (>4000 g)	1 (2.4%)	6 (14.3%)	1 (2.4%)
Birth Weight (g), Mean ± SD	3284 ± 412	3468 ± 524	2876 ± 618
APGAR Score <7 at 1 min	2 (4.8%)	4 (9.5%)	8 (19.5%)

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APGAR Score <7 at 5 min	0 (0.0%)	2 (4.8%)	5 (12.2%)
NICU Admission	3 (7.1%)	8 (19.0%)	13 (31.7%)
Neonatal Hypoglycemia	1 (2.4%)	7 (16.7%)	3 (7.3%)
Respiratory Distress Syndrome	1 (2.4%)	3 (7.1%)	6 (14.6%)
Intrauterine Growth Restriction	1 (2.4%)	2 (4.8%)	8 (19.5%)
Stillbirth	0 (0.0%)	0 (0.0%)	1 (2.4%)

Table 5: Describe the final results according to maternal complications by study group (number of participants = 125)

Complication	**Normal Pregnancy (n = 42)**	**GDM (n = 42)**	**Preeclampsia (n = 41)**	**χ^2**	**p-value**
Gestational Hypertension	0 (0.0%)	4 (9.5%)	41 (100%)	108.4	**<0.001****
Severe Preeclampsia	0 (0.0%)	0 (0.0%)	14 (34.1%)	32.68	**<0.001****
Proteinuria (≥300 mg/24h)	0 (0.0%)	2 (4.8%)	38 (92.7%)	98.72	**<0.001****
Peripheral Edema (Grade ≥2)	8 (19.0%)	12 (28.6%)	32 (78.0%)	34.16	**<0.001****
HELLP Syndrome	0 (0.0%)	0 (0.0%)	4 (9.8%)	8.24	**0.016***
Placental Abruption	0 (0.0%)	1 (2.4%)	3 (7.3%)	3.42	0.181
Eclampsia	0 (0.0%)	0 (0.0%)	2 (4.9%)	4.12	0.128
Postpartum Hemorrhage	2 (4.8%)	4 (9.5%)	7 (17.1%)	3.38	0.184
Gestational Diabetes (any)	0 (0.0%)	42 (100%)	6 (14.6%)	102.8	**<0.001****
Insulin Requirement	0 (0.0%)	16 (38.1%)	3 (7.3%)	24.86	**<0.001****
Oligohydramnios	1 (2.4%)	3 (7.1%)	6 (14.6%)	3.92	0.141
Polyhydramnios	0 (0.0%)	5 (11.9%)	1 (2.4%)	5.82	0.054
Maternal ICU Admission	0 (0.0%)	1 (2.4%)	5 (12.2%)	6.48	**0.039***

Table 6: Assessment Pearson Correlation Coefficients Between 3rd Trimester Leptin Levels and Clinical Parameters

Variable	**All Patients (N = 125)**		**Normal (n = 42)**		**GDM (n = 42)**		**Preeclampsia (n = 41)**	
	r **r ranges from –1 to +1 and measures the strength and direction of a linear relationship between two variables (here: leptin vs each clinical parameter).**	**P** **p tests the statistical significance of the correlation**	**r**	**p**	**r**	**p**	**r**	**p**
Pre-pregnancy BMI	0.524	**<0.001****	0.412	**0.007***	0.486	**0.001***	0.398	**0.010***
BMI at Delivery	0.568	**<0.001****	0.438	**0.004***	0.512	**<0.001****	0.424	**0.006***
Systolic Blood Pressure	0.482	**<0.001****	0.186	0.238	0.264	0.091	0.518	**<0.001****
Diastolic	0.446	**<0.001****	0.142	0.370	0.218	0.166	0.486	**0.001***

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Blood Pressure								
Fasting Blood Glucose	0.398	**<0.001****	0.124	0.434	0.542	**<0.001****	0.186	0.244
HbA1c	0.374	**<0.001****	0.098	0.538	0.518	**<0.001****	0.162	0.312
Birth Weight	-0.186	**0.038***	-0.082	0.606	0.214	0.174	-0.384	**0.013***
Gestational Age at Delivery	-0.312	**<0.001****	-0.124	0.434	-0.198	0.208	-0.462	**0.002***
APGAR Score (5 min)	-0.218	**0.015***	-0.068	0.668	-0.142	0.370	-0.348	**0.026***
Cord Blood Leptin	0.682	**<0.001****	0.614	**<0.001****	0.724	**<0.001****	0.596	**<0.001****
Placental Leptin mRNA	0.718	**<0.001****	0.586	**<0.001****	0.648	**<0.001****	0.692	**<0.001****

Table 7: Logistic Regression Analysis: Binary to assessment finding with Predictors of Adverse Outcomes

Outcome	**Predictor**	**B**	**SE**	**OR**	**95% CI**	**p-value**
GDM	3rd Trimester Leptin (per 10 ng/mL)	0.682	0.214	**1.98**	1.30–3.01	**0.001***
	Pre-pregnancy BMI	0.348	0.098	**1.42**	1.17–1.72	**<0.001****
	Age	0.124	0.058	**1.13**	1.01–1.27	**0.032***
	Family History of DM	0.896	0.412	**2.45**	1.09–5.49	**0.030***
Preeclampsia	3rd Trimester Leptin (per 10 ng/mL)	0.842	0.228	**2.32**	1.48–3.63	**<0.001****
	Pre-pregnancy BMI	0.268	0.092	**1.31**	1.09–1.56	**0.004***
	Family History of HTN	1.124	0.448	**3.08**	1.28–7.41	**0.012***
	Nulliparity	0.586	0.384	**1.80**	0.85–3.81	0.127
Preterm Birth	3rd Trimester Leptin (per 10 ng/mL)	0.548	0.198	**1.73**	1.17–2.55	**0.006***
	Preeclampsia Diagnosis	1.486	0.524	**4.42**	1.58–12.34	**0.005***
	GDM Diagnosis	0.642	0.486	**1.90**	0.73–4.94	0.187
Cesarean Section	3rd Trimester Leptin (per 10 ng/mL)	0.386	0.168	**1.47**	1.06–2.04	**0.021***

Table 8: Association of Maternal Leptin Levels with Gestational Age, Mode of Delivery, and Neonatal Outcomes

Subgroup	**Category**	**n**	**Leptin (ng/mL)**	**Category**	**n**	**Leptin (ng/mL)**	**t-value**	**p-value**
Gestational Age	Term (≥37 wks)	101	34.2 ± 16.4	Preterm (<37 wks)	24	52.8 ± 19.6	-4.62	**<0.001****
Mode of Delivery	Vaginal	73	32.6 ± 15.8	Cesarean	52	44.8 ± 18.2	-4.08	**<0.001****
Birth Weight	Normal (2500–4000 g)	99	35.4 ± 16.2	LBW (<2500 g)	19	54.6 ± 20.8	-4.28	**<0.001****
Birth Weight pls explain	Normal (2500–4000 g)	99	35.4 ± 16.2	Macrosomia (>4000 g)	8	42.1 ± 14.6	-1.12	0.268
NICU Admission	No	101	34.8 ± 16.1	Yes	24	49.2 ± 19.4	-3.68	**<0.001****
APGAR <7 (5 min)	No	118	36.4 ± 17.2	Yes	7	56.8 ± 18.6	-3.02	**0.003***

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IUGR	No	114	36.2 ± 17.0	Yes	11	52.4 ± 18.8	-2.86	**0.005***
Postpartum Hemorrhage	No	112	36.8 ± 17.4	Yes	13	43.6 ± 16.8	-1.32	0.190
Maternal ICU Admission	No	119	36.4 ± 17.0	Yes	6	62.4 ± 16.2	-3.82	**<0.001****
Neonatal Hypoglycemia	No	114	36.8 ± 17.2	Yes	11	44.2 ± 18.4	-1.34	0.184

DISCUSSION

In our research, women with GDM had much higher leptin levels than the normal pregnancy group during gestation, and third-trimester levels were 48.6 ± 16.8 ng/mL and 28.3 ± 10.1 ng/mL ($p < 0.001$), respectively. This observation is in line with the study by Pérez-Pérez *et al*. (2020), which indicated that hyperleptinemia in GDM is a condition of leptin resistance similar to insulin resistance that defines this condition. The hypothesis that leptin dysregulation is closely associated with glucose homeostasis in pregnancy is supported by the strong positive correlation between leptin and fasting blood glucose ($r = 0.542$, $p < 0.001$) in the GDM group only. Kautzky-Willer *et al*. (2001) also showed that high leptin levels in GDM women were linked with insensitivity to insulin, implying that leptin could be a marker and a cause of the metabolic disturbances underlying GDM. [Sterne, J. A. *et al*., 2011; Stroup, D. F. *et al*., 2000; Sweeting, A. N. *et al*., 2019]

The increased prevalence of macrosomia in the GDM group (14.3% vs. 2.4% in normal pregnancy, $p = 0.047$) is a well-known effect of fetal hyperinsulinism caused by maternal hyperglycemia, as the Pedersen hypothesis explains. Interestingly, the GDM group also had the highest cord blood leptin (14.6 ± 6.8 ng/mL), which could be indicative of greater fetal adiposity and has been postulated as an early biomarker of metabolic programming of offspring obesity as proposed by Catalano *et al*. (2009) and the HAPO Study Cooperative Research Group A phrase that is linked to the following sentence as well as The preeclampsia group showed the highest level of leptin at delivery (56.8 ± 20.6 ng/mL), which was significantly higher than the normal pregnancy (25.1 ± 9.8 ng/mL) and the GDM (42.3 ± 15.4 ng/mL, $p < 0.001$). Moreover, the expression of placental leptin mRNA was significantly increased in preeclamptic placentas (2.14 ± 0.72 relative fold change), which is in agreement with the results of Mise *et al*. (1998) and Laivuori *et al*. (2006), who showed that hypoxia and hypoxia-inducible factor 1-alpha (HIF-1) activation in response to hypoxia induce leptin gene expression. Instead of maternal adipose tissue, the placenta seems to be the main source of excess leptin in preeclampsia, as the maternal serum leptin and placental leptin mRNA are strongly correlated ($r = 0.692$, $p < 0.001$) in this group [Thompson, S. G., & Higgins, J. P. 2002].

The high correlation between leptin and systolic blood pressure ($r = 0.518$, $p < 0.001$) and diastolic blood pressure ($r = 0.486$, $p = 0.001$) in the preeclampsia group, but not in the normal pregnancy group, indicates that leptin might have a direct role in the hypertensive pathophysiology of preeclampsia. It has been demonstrated that leptin activates the sympathetic nervous system, endothelial dysfunction by increasing oxidative stress, and endothelin-1 production, which leads to vasoconstriction and high blood pressure where the fact that leptin was an independent predictor of preeclampsia (or = 2.32 per 10 ng/ml increase, 95% ci: 1.483.63, $p < 0.001$) even after the confounding factors were controlled also supports the possibility that leptin is a causal factor of preeclampsia, but the cross-sectional nature of the study does not allow conclusive causation [Wan, X. *et al*., 2014] as well as the highest rates of adverse maternal and neonatal outcomes were observed in the preeclampsia group (caesarean section 58.5% preterm birth 34.1% low birth weight 29.3% NICU admission 31.7% intrauterine growth restriction 19.5%). The observed negative correlation between leptin and birth weight ($r = -0.384$, $p = 0.013$) and gestational age at birth ($r = -0.462$, $p = 0.002$) in the preeclampsia group only is the result of the effect of placental insufficiency on fetal growth and the common necessity of iatrogenic preterm birth to avoid maternal complications. A significant result of this study was the difference in the pattern of leptin elevation between GDM and preeclampsia. Although the levels of leptin in both groups were significantly elevated compared to normal pregnancy, the

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pattern of leptin rise was different [Xu, J. *et al*., 2014]. The levels of leptin were always high in GDM since the first trimester, which is indicative of the underlying metabolic dysfunction and insulin resistance that defines the condition.

It is important to note that the levels of leptin in the third trimester did not differ significantly between GDM and preeclampsia (post-hoc p = 0.392), but the levels of leptin at delivery were significantly lower in GDM than in preeclampsia (mean difference = -14.5, 95% ci: -21.8 to -7.2, p < 0.001) as well as in our study found this delivery deviation could be indicative of the acute stress response and endothelial activation that accompany the clinical deterioration commonly observed in preeclampsia in the peripartum period in addition to the correlation analysis also revealed the different pathophysiological roles of leptin in each condition: in GDM, leptin was most strongly correlated with metabolic parameters (fasting glucose, r = 0.542; hba1c, r = 0.518), whereas in preeclampsia, leptin was most strongly correlated with hemodynamic parameters (systolic bp, r = 0.518; diastolic bp, r = 0.486) and fatal compromise parameters , where this study has a number of clinical implications. To begin with, the steady rise of leptin in all trimesters of GDM and preeclampsia indicates that serial leptin assay may be used as a complementary biomarker to detect women at risk of these conditions early also the leptin levels of the first trimester were already highly elevated in both pathological groups (22.3 ± 8.7 ng/ml in gdm and 20.1 ± 7.9 ng/ml in preeclampsia vs. 14.8 ± 6.2 ng/ml in normal pregnancy, p < 0.001), which makes the idea of early pregnancy leptin screening as an addition to the already existing first-trimester risk assessment algorithms with the already known biomarkers second, the high independent correlation between leptin and adverse outcomes in the logistic regression models indicates that leptin could be a prognostic factor other than diagnosis. Women who had high levels of leptin in the third trimester were much more likely to give birth prematurely (OR = 1.73), deliver via caesarean section (OR = 1.47), be admitted to the NICU (OR = 1.59), and have low birth weight (OR = 1.67), regardless of the underlying diagnosis. The clinical implications of this finding are that it has identified a subgroup of women who might require increased antenatal surveillance, such as increased fatal growth checks, biophysical profile checks, and planning of delivery.

STRENGTHS AND LIMITATIONS

- This study has many strengths. The most important of them is the prospective design, which includes serial leptin measurements in all trimesters and at delivery, thus enabling a temporal evaluation of leptin dynamics during gestation.
- The fact that both gestational diabetes mellitus and preeclampsia cohorts are included allows making a direct comparison between these two different but similar endocrine and cardiovascular diseases. In addition, the research has conducted a thorough analysis of maternal and neonatal outcomes, thus covering both maternal and fetal outcomes. Lastly, the multivariate regression analysis used to define independent associations, but strictly controlling salient confounders, offers a strong inferential framework.
- The fact that a well-validated commercial ELISA kit with proven low intra- and inter-assay variability was used also contributes to the reliability of leptin
- quantification and enhances the validity of the results.
- The research was carried out in one tertiary care facility, which may not be generalizable to other populations and health care environments.
- The regression models controlled a number of confounders, but it is not possible to exclude the possibility of residual confounding due to unmeasured variables, including dietary intake, physical activity, socioeconomic status, and inflammatory markers. Lastly, the fact that the leptin levels overlap between the groups suggests that leptin is not necessarily a diagnostic biomarker on its own; its clinical utility is likely to be improved when it is used as a component of a multiparametric predictive model in combination with other biomarkers.

CONCLUSION

we conclude finally this study demonstrates that maternal serum leptin levels are significantly elevated in both GDM and preeclampsia compared to normal pregnancy while with distinct patterns of elevation reflecting the different pathophysiological mechanisms underlying each condition also can conclude Leptin was independently associated with increased odds of GDM, preeclampsia, and several adverse maternal and neonatal outcomes after adjustment for

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confounders where The strong correlations between leptin and metabolic parameters in GDM, and between leptin and hemodynamic parameters in preeclampsia, suggest that leptin plays condition-specific roles in these pregnancy complications

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