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Maternal Serum Leptin Levels in Early Pregnancy as a Predictor of Gestational Diabetes Mellitus

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a significant pregnancy complication that affects a wide percentage of pregnant women worldwide. It is crucial to identify predictive markers of GDM such that it can be treated at an early stage and pregnancy outcomes are improved. This study investigated the predictive role of maternal serum leptin level in early pregnancy as an indicator of GDM.

Methods: It was a prospective observational study in 100 antenatal women with singleton pregnancy at 11-13 weeks gestation. Maternal serum leptin was assayed after an overnight fast, and the women were subsequently screened for GDM using the DIPSI test at 24-28 weeks gestation. Statistical analysis, including ROC curve analysis, was performed to assess the predictive potential of leptin for GDM.

Results: The study included 100 antenatal women, with a mean age of 21.45 years and a mean BMI of 23.26 kg/m². At a gestational age of 12.08 weeks, the mean pre-leptin level was 6.4 ng/mL. GDM developed in 17% of participants, with a leptin threshold of 7.1 ng/mL showing high predictive power (AUC = 0.847). The sensitivity and specificity were 70.59% and 75.90%, respectively, with a PPV of 37.50% and NPV of 92.65%. The overall test accuracy was 75.00%.

Conclusion: Maternal serum leptin levels during early pregnancy are consistent predictors of GDM. The incorporation of leptin tests into routine prenatal screening can enhance the early detection and management of GDM and result in improved maternal and foetal outcomes

Keywords: *Gestational diabetes mellitus, Leptin, Predictive biomarker, Early pregnancy, Prenatal screening*

1. INTRODUCTION

Gestational diabetes mellitus (GDM) is a significant pregnancy complication that affects approximately 14.7% of pregnant women globally [1]. GDM is characterized by glucose intolerance that develops or is first recognized during pregnancy, leading to high blood sugar levels, with potential negative impacts on both fetal and maternal health. Several factors contribute to the development of GDM, including obesity, being an older mother, a family history of diabetes, and certain ethnic backgrounds. Identifying predictive markers for GDM is crucial for early intervention and management, ultimately leading to improved pregnancy outcomes. [2]

Leptin is a polypeptide hormone that is primarily produced by adipocytes and plays a key role in regulating energy balance, appetite, and metabolism. It is involved in negative feedback between the adipose tissue and the hypothalamic satiety centre, which helps in body weight regulation. Human plasma leptin is strongly related to body fat mass, potentially reflective of obesity-associated leptin resistance [3]. Insulin and glucocorticoids are the primary regulators of leptin secretion and

synthesis, both of which increase in pregnancy to augment plasma leptin, concurrent with increases in maternal lean and fat mass and pronounced changes in glucose metabolism [4].

Maternal serum leptin concentrations are higher during pregnancy, indicating alterations in maternal fat reserves and placental secretion. Leptin rises to a peak at approximately 28 weeks of gestation, remains stable afterwards, drops slightly before delivery, and then drops precipitously after delivery. Nonetheless, the effect of pregnancy and glucose metabolism on plasma leptin and its physiological role in pregnancy, particularly the variation in plasma leptin concentration between diabetic and non-diabetic pregnant women, remains incomplete. Recent data indicate that hyperleptinemia during early pregnancy is associated with the pathogenesis of GDM. This potential correlation emphasizes the importance of determining the role of leptin in pregnancy and its utility as a predictive biomarker for GDM.[5]

The pathophysiology of GDM is multifactorial coupling between β-cell dysfunction and insulin resistance. During pregnancy, natural insulin resistance will naturally rise to ensure the provision of glucose to the growing foetus. Natural insulin resistance, in some women, however, becomes pathologic and leads to GDM. Leptin, with its regulatory effect on glucose metabolism and insulin sensitivity, may be involved. Elevated levels of maternal serum leptin during early pregnancy could represent a primary metabolic derangement that predisposes the women to GDM.[6]

Early identification of women at risk for GDM allows timely implementation of lifestyle modification and pharmacologic interventions to decrease adverse outcomes. Current screening for GDM, typically performed between 24- and 28-weeks' gestation, may be missing the opportunity for early intervention [7]. Including maternal serum leptin concentrations in early pregnancy screen tests may enhance predictive value for GDM, allowing earlier diagnosis and treatment. [8]

Understanding the function of maternal serum leptin level during early pregnancy as a predictor for GDM is likely to contribute to improved maternal and foetal health outcomes. Leptin measurement inclusion into early pregnancy screening would enable doctors to detect risk in women early enough to intervene proactively in preventing the onset and complications of GDM. The objective of this longitudinal study was to quantify plasma leptin levels in women with gestational diabetes during delivery and relate these levels with those in normal pregnant women.[9]

2. MATERIALS AND METHODS

This Prospective observational study aimed to determine whether serum leptin level can be used as a predictor of gestational diabetes. The study included expectant mothers with a single fetus, less than 13 weeks of gestational age who have not been diagnosed as GDM or known comorbidities. Women with confirmed diabetes (Type 1 or Type 2), receiving metformin for polycystic ovary syndrome, Pregnancies involving multiple foetuses, or a history of diabetes in pregnancy were excluded from the study. Approval was obtained from the Institutional Human Ethics Committee. A total of 100 women with singleton pregnancies presenting in early gestation, specifically between 11-13 weeks, at the antenatal clinic, were included in the study. Written informed consent was obtained from all participating patients.

Blood specimens were obtained from all participants after overnight fasting. Serum samples were preserved at -80 °C for subsequent examination. All screened women were requested to return for repeat assessment at 24-28 weeks of gestation to undergo a DIPSI test for the detection of GDM. For those identified with GDM, previously frozen samples were examined for serum leptin levels. Additionally, samples from healthy pregnant women were analysed for leptin levels to determine any potential elevation.

3. RESULTS

The data presented in Table 1 describes the baseline characteristics of pregnant women who were screened for GDM. Majority of the patients were of age group 21-23 years (39%) followed by 18-20 years (37%) and least were of age group 27-28 years (4%). Among the patients, 78.0% were primigravidas and 22.0% were multigravidas. 83.0% did not develop GDM, while 17.0% did. For BMI, 7% were underweight, 63% were normal weight, and 30% were overweight. Among the patients, 77.0% reported no family history of diabetes mellitus, while 23.0% had a family history of the condition.

Table 1: The baseline characteristics of pregnant women who were screened for GDM.

Baseline characteristics		**Number of patients**	**Percentage**
Age	18 - 20 yrs.	37	37%
	21 - 23 yrs.	39	39%

	24 - 26 yrs.	20	20%
	27 - 28 yrs.	4	4%
Parity	Primi	78	78.0%
	Multi	22	22.0%
GDM	No	83	83.0%
	Yes	17	17.0%
BMI	Underweight	7	7.0%
	Normal weight	63	63.0%
	Overweight	30	30.0%
Family history of DM	No	77	77.0%
	Yes	23	23.0%

The data represented in Table 2 describes the clinical characteristics of study participants. patients' mean age was 21.45 ± 1.88 years. The mean Body Mass Index (BMI) was 23.26 ± 2.9 kg/m². Gestational age mean was 12.08 ± 0.81 weeks. Mean systolic blood pressure was 108.45 ± 6.84 mmHg, and mean diastolic blood pressure was 77.7 ± 6.94 mmHg. Mean pre-leptin level was 6.4 ± 1.38 ng/mL. Mean value for the Diabetes in Pregnancy Study Group India (DIPSI) test was 118.96 ± 23.85 mg/dL.

Table 2: Clinical Characteristics of Study Participants

	Mean	**Standard Deviation**
Age	21.45	1.88
BMI	23.26	2.9
GA	12.08	0.81
SBP	108.45	6.84
DBP	77.7	6.94
Pre leptin (ng/mL)	6.4	1.38
DIPSI	118.96	23.85

The data represented in table 3 describes the BMI and family History of Diabetes Mellitus among Patients with GDM. Among the patients, no underweight individuals developed GDM. Among normal weight individuals, 7.9% developed GDM. In the overweight group, 40.0% developed GDM. ($p<0.0001$). Among the 17 patients who were diagnosed as GDM, 12 patients were overweight (70%) which is statistically significant. Among individuals with no family history of DM, 7.8%

developed GDM. Among those with a family history of DM, 47.8% developed GDM. (p<0.0001). Among the 17 patients who were diagnosed as GDM, 11 (64.7%) patients had positive family history of DM which is statistically significant.

Table 3: BMI and family History of Diabetes Mellitus among Patients with GDM.

		GDM				P-value
		Yes		No		
		N	%	N	%	
BMI	Underweight (<18.5kg/m^2)	0	0.0%	7	100.0%	<0.0001
	Normal weight (18.5-22.9 kg/m^2)	5	7.9%	58	92.1%	
	Overweight (23.0-24.9 kg/m^2)	12	40.0%	18	60.0%	
Family history of DM	No	6	7.8%	71	92.2%	<0.0001
	Yes	11	47.8%	12	52.2%	

The data represented on table 4 describes the distribution of GDM Cases Based on Pre-Leptin Levels in Early Pregnancy. A higher portion of women with Pre-Leptin level >7.1 ng/mL developed GDM compared to those with lower leptin levels, suggesting serum leptin level in early pregnancy in early pregnancy as predictors of GDM.

Table 4: Distribution of GDM Cases Based on Pre-Leptin Levels in Early Pregnancy.

		GDM	
		Yes	No
Pre-Leptin (ng/mL)	>7.1	12	20
	<=7.1	5	63
Total		17	83

The data represented on table 5 and figure 1 describes the ROC Curve Analysis for Maternal Serum Leptin Levels as a Predictor of GDM. The ROC curve assessed maternal serum leptin levels in early pregnancy as predictors of GDM. A threshold of 7.1 ng/mL was identified as optimal, achieving an AUC of 0.847, indicating high predictive accuracy (p<0.0001). The test showed a sensitivity of 70.59%, correctly identifying 70.59% of women who developed GDM with leptin levels above 7.1 ng/Ml. Specificity was 75.90%, accurately identifying 75.90% of women without GDM with leptin levels below the cut-off. The positive predictive value (PPV) was 37.50%, indicating 37.50% of high-risk women (leptin > 7.1 ng/mL) developed GDM. The negative predictive value (NPV) was 92.65%, showing 92.65% of low-risk women (leptin < 7.1 ng/mL) did not develop GDM. Overall test accuracy was 75.00%, reflecting true results (both true positives and true negatives) in the population.

Table 5: ROC Curve Analysis for Maternal Serum Leptin Levels as a Predictor of GDM

Cut-off value	7.1
AUC	0.847
P value	<0.0001
Sensitivity	70.59%
Specificity	75.90%
PPV	37.50%
NPV	92.65%
Accuracy	75.00%

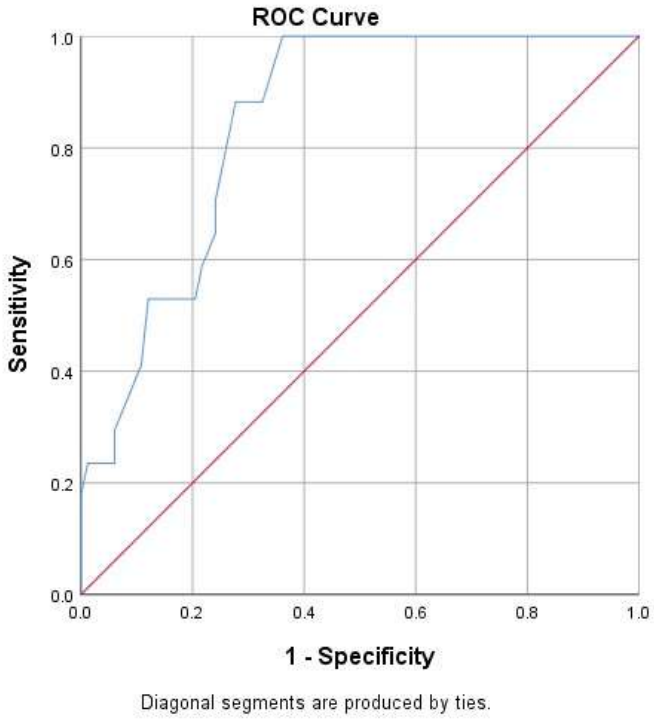

Figure 1: ROC Curve Analysis for Maternal Serum Leptin Levels as a Predictor of GDM.

4. DISCUSSION

GDM poses significant health concerns for mothers as well as newborns, such that early prediction and good control is a need of urgent imperative. Despite the extent to which GDM is now recognized, there still is no perfect biomarker for prediction in the early period. This research seeks to bridge the void in literature by examining the predictive value of first-trimester leptin level on the occurrence of GDM. The ongoing controversy regarding the most predictive biomarker indicates the need for continuing research to define the function of leptin in the augmentation of the care of GDM and patient outcome.

ROC curve analysis showed robust predictive power for leptin with an AUC of 0.847, which is highly accurate. Cut-point of 7.1 ng/mL serum leptin was highly predictive for GDM, with sensitivity 70.59% and specificity 75.90%. These values

suggest that leptin is a reliable early indicator of GDM and a practical tool for early diagnosis and intervention. The significant AUC indicates that leptin is a strong discriminator between those who will develop GDM which is also supported by Thagaard et al. with an AUC of 0.784 for leptin levels combined with maternal factors, and Florian et al. with an AUC of 0.775, sensitivity of 100%, specificity of 48.9 and (P<0.001). [10,11]

Our findings are consistent with those of some previous research studies describing leptin as a potential GDM biomarker. Qiu et al., for instance, found that elevated leptin levels in early pregnancy were associated with an increased risk of GDM there was a significant linear trend of increased risk of GDM with rising maternal plasma leptin levels. [9]

Similarly, Ye et al. noted that leptin was positively related to GDM in pregnant Chinese women.[12], which agrees with our findings. Similarly, Thagaard et al. also mentioned that higher levels of leptin during the first trimester were correlated with a higher rate of GDM [10]. In contrast, Kapustin et al. found that leptin levels were higher in women with GDM across all trimesters, correlating with various metabolic complications. [13] The alignment of our results with those of these studies suggests that leptin measurement could be integrated into routine prenatal screening protocols to identify women at risk of GDM early in pregnancy.

Our study had a PPV of 37.50% and NPV of 92.65%. The PPV may be lower owing to the multifactorial nature of GDM, and a high NPV underscores the utility of leptin in effectively identifying low-risk individuals. Göymen et al. similarly demonstrated significant findings in their study involving the 75 g oral glucose tolerance test (OGTT) group, where leptin exhibited sensitivity, specificity, and PPV values of 70%, 55%, and 60.8%, respectively.[14] These results underscore the importance of leptin as a valuable biomarker in screening protocols for GDM.

However, there have been some conflicting results in some studies. Mohana et al. reported that fasting leptin at 24-28 weeks of gestation is more closely associated with BMI but is not different between GDM and NGT and does not seem to be a good predictor for GDM.[15] However, there have been some conflicting results in some studies. Mohana et al. speculated fasting leptin at 24-28 weeks of gestation to be a stronger correlate with BMI but not significantly different between GDM and NGT and not found to be a good predictor for GDM.[15] Lifestyle determinants such as diet, exercise, and stress levels that can influence leptin levels also have to be investigated to ascertain their role in the prediction of GDM. By incorporating these variables into predictive models, we can develop more accurate and individualized screening regimens, optimizing early detection and treatment of GDM. [16,17]

Our study offers insights of leptin concentration distribution in women with and without GDM, exhibiting its potential for screening risk groups and allowing early intervention. Elevated leptin concentrations during pregnancy may warrant vigilant surveillance, dietary modification, and preventive strategies to avert the risk of GDM. Leptin also affects placental development, foetal growth, and energy balance, possibly indicating a metabolic derangement that could lead to GDM. Exploring the link between leptin and GDM can reveal new targets and treatments. [18-20]

5. CONCLUSION

Our study provides comprehensive evidence that maternal serum leptin levels during early pregnancy are a reliable predictor for gestational diabetes mellitus (GDM). The findings indicate that leptin can effectively identify women at risk of GDM and provide a valuable tool to detect and treat the condition early. This predictive value is supported by robust statistical tests and aligns with previous research, indicating the value of adding leptin to routine prenatal screening methods. The ability of leptin to identify correctly low-risk individuals allows for proper resource allocation and more targeted treatment. Adding more diverse demographic and clinical variables may enhance the validity and usefulness of leptin as a GDM biomarker.

Future research should aim to fine-tune predictive models with the addition of additional risk factors and concurrent use of leptin with other biomarkers to enhance early detection and management of GDM. By utilizing the predictive value of leptin, health workers can implement timely interventions with a subsequent improvement in maternal and foetal health outcomes.

6. LIMITATIONS

The limitations of this study included a smaller group of women which were not representative of a larger population. Narrow range of demographic population was included in the study. Population that differs in locality, socioeconomic status was not sampled. Confounding factors were present and high cost for testing of Serum Leptin levels were notable challenges

REFERENCES

[1] Chapman KR. Epidemiology and costs of chronic obstructive pulmonary disease. Eur Respir J [Internet]. 2006;27(1):188 207. Available http://dx.doi.org/10.1183/09031936.06.00024505
[2] Lassi ZS, Bhutta ZA. Risk factors and interventions related to maternal and pre-pregnancy obesity, pre-diabetes and diabetes for maternal, fetal and neonatal outcomes: a systematic review. Expert Rev Obstet Gynecol [Internet]. 2013;8(6):639 60. Available http://dx.doi.org/10.1586/17474108.2013.841453
[3] Dardeno TA, Chou SH, Moon H-S, Chamberland JP, Fiorenza CG, Mantzoros CS. Leptin in human physiology

and therapeutics. Front 2010;31(3):377–93. Neuroendocrinol Available http://dx.doi.org/10.1016/j.yfrne.2010.06.002
[4] Dardeno TA, Chou SH, Moon H-S, Chamberland JP, Fiorenza CG, Mantzoros CS. Leptin in human physiology and therapeutics. Front 2010;31(3):377–93. Neuroendocrinol Available http://dx.doi.org/10.1016/j.yfrne.2010.06.002
[5] Kautzky-Willer A, Pacini G, Tura A, Bieglmayer C, Schneider B, Ludvik B, et al. Increased plasma leptin in gestational diabetes. Diabetologia [Internet]. 82 2001;44(2):164–72. Available from: http://dx.doi.org/10.1007/s001250051595
[6] Hernandez TL, Friedman JE, Barbour LA. Insulin resistance in pregnancy: Implications for mother and offspring. In: Contemporary Endocrinology. Cham: Springer International Publishing; 2020. p. 67–94.
[7] Ryan DK, Haddow L, Ramaesh A, Kelly R, Johns EC, Denison FC, et al. Early screening and treatment of gestational diabetes in high-risk women improves maternal and neonatal outcomes: A retrospective clinical audit. Diabetes Res Clin Pract [Internet]. 2018;144:294–301. Available http://dx.doi.org/10.1016/j.diabres.2018.09.013
[8] Huhn EA, Rossi SW, Hoesli I, Göbl CS. Controversies in screening and diagnostic criteria for gestational diabetes in early and late pregnancy. Front Endocrinol (Lausanne) [Internet]. 2018;9. Available http://dx.doi.org/10.3389/fendo.2018.00696
[9] Qiu C, Williams MA, Vadachkoria S, Frederick IO, Luthy DA. Increased maternal plasma Leptin in early pregnancy and risk of gestational diabetes mellitus. Obstet
[10] Thagaard IN, Krebs L, Holm J-C, Lange T, Larsen T, Christiansen M. Adiponectin and leptin as first trimester markers for gestational diabetes mellitus: a cohort study. Clin Chem Lab Med 2017;55(11). http://dx.doi.org/10.1515/cclm 2017-0427
[11] Florian A, Cruciat G, Pop R, Staicu A, Daniel M, Florin S. Predictive role of altered leptin, adiponectin and 3 carboxy 4 methyl 5 propyl 2 furanpropanoic acid secretion in gestational diabetes mellitus. Exp Ther Med 2021;21(5).
[12] Ye Y, Wu P, Wang Y, Yang X, Ye Y, Yuan J, et al. Adiponectin, leptin, and leptin/adiponectin ratio with risk of gestational diabetes mellitus: A prospective nested case control study among Chinese women. Diabetes Res Clin Pract 2022;191(110039):110039. http://dx.doi.org/10.1016/j.diabres.2022.110039
[13] Kapustin RV, Chepanov SV, Babakov VN, Rogovskaya NY, Kopteeva EV, Alekseenkova EN, et al. Maternal serum leptin, adiponectin, resistin and monocyte chemoattractant protein-1 levels in different types of diabetes mellitus. Eur J Obstet Gynecol Reprod Biol 2020;254:284–91. http://dx.doi.org/10.1016/j.ejogrb.2020.09.050
[14] Göymen A, Öncül M, Güralp O, Fien C, Uluda¤ S, Gül DK, et al. Comparison of maternal serum adiponectin and Leptin measurements in screening and diagnosis of gestational diabetes mellitus Perinataldergi.com https://perinataldergi.com/Files/Archive/en-US/Articles/PD 1050.pdf
[15] Mohana CA, Paul S, Jahan S, Tofail T, Morshed MS, Saleh AA, et al. Serum Leptin correlates with obesity but does not differ between Gestational diabetes and normal glucose tolerance during 24-28 weeks of gestation. Mymensingh Med J. 2022;31(2):318–25.
[16] Gilbert L, Gross J, Lanzi S, Quansah DY, Puder J, Horsch A. How diet, physical activity and psychosocial well-being interact in women with gestational diabetes mellitus: an integrative review. BMC Pregnancy Childbirth 2019;19(1). http://dx.doi.org/10.1186/s12884-019-2185-y.
[17] Mohana CA, Paul S, Jahan S, Tofail T, Morshed MS, Saleh AA, et al. Serum Leptin correlates with obesity but does not differ between Gestational diabetes and normal glucose tolerance during 24-28 weeks of gestation. Mymensingh Med J. 2022;31(2):318–25.
[18] Sletner L, Moen AEF, Yajnik CS, Lekanova N, Sommer C, Birkeland KI, et al. Maternal glucose and LDL-cholesterol levels are related to placental Leptin gene methylation, and, together with nutritional factors, largely explain a higher methylation level among ethnic South Asians. Front Endocrinol (Lausanne) http://dx.doi.org/10.3389/fendo.2021.809916
[19] Lorenzo-Almorós A, Hang T, Peiró C, Soriano-Guillén L, Egido J, Tuñón J, et al. Predictive and diagnostic biomarkers for gestational diabetes and its associated metabolic and cardiovascular diseases. Cardiovasc Diabetol 2019;18(1). http://dx.doi.org/10.1186/s12933-019-0935-9
[20] Mack LR, Tomich PG. Gestational diabetes. Obstet Gynecol Clin North Am [Internet]. 2017;44(2):207–17. Available from: http://dx.doi.org/10.1016/j.ogc.2017.02.002.

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