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The serum leptin can be a predictable marker for gestational diabetes mellitus

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ABSTRACT

Background: This study assessed the serum leptin concentrations for development of gestational diabetes mellitus.**Materials and Methods:** This is a case-control study, included 120 participants (60: Gestational Diabetes Mellitus Cases and 60: Healthy Controls). We assessed BMI, FBS, HbA1c, Lipid Profile and serum leptin.**Results:** The serum leptin concentrations were significantly elevated in patients with gestational diabetes mellitus when compared to controls ($P=0.001^{**}$). There was a significant positive correlation between the serum leptin and BMI, FBS, HbA1c, Total Cholesterol and LDL ($P=0.001^{**}$).**Conclusion:** Based on study findings, significant elevated levels of serum leptin might be served as a marker for detection of gestational diabetes mellitus.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

Gestational Diabetes Mellitus (GDM) is one of the most prevalent conditions associated with pregnancy, and if untreated it can have a major negative impact on both the mother's and the child's health.^{1,2} It affects 3-8% of pregnancies and is defined by glucose intolerance identified during pregnancy due to obesity risk. Around thirteen to fourteen (13-14%) of pregnant women are getting converted to GDM and it is characterized insulin resistance and β -cell dysfunction.^{3,4} The etiology of GDM remains poorly understood. The most widely accepted explanation states that human placental lactogen, prolactin, glucocorticoids, and progesterone all of which are released by the placenta during pregnancy cause GDM by lowering insulin sensitivity and boosting anti-insulin hormones.⁵

Adipocytes produce adipocytokines like leptin that contribute to energy balance, metabolism of glucose and

insulin. According to certain research, leptin may also play a major role in controlling the body's overall glucose homeostasis. Leptin may therefore play a significant role in the onset and prognosis of GDM.⁶ According to certain research, there is a favorable relationship between plasma leptin concentrations and both direct and indirect markers of obesity. Leptin levels rise in expectant mothers who have altered maternal fat reserves and glucose metabolism. The concentration of leptin in mothers rises two to three times higher than in non-pregnant women, peaking at 28 weeks of gestation.^{7,8}

According to certain clinical research, that an increase of adipocyte leptin production in the context of rising insulin resistance and hyperinsulinemia in the second half of pregnancy may be the cause of rising maternal plasma leptin.⁹ Studies have demonstrated that leptin directly influences the body's sensitivity to insulin by controlling the skeletal muscle's ability to utilize insulin to metabolize glucose and by controlling the liver's gluconeogenesis.¹⁰⁻¹² According to certain research, leptin has an immediate

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inhibitory effect on insulin secretion. Vast epidemiological investigations have demonstrated a favorable correlation between men's and non-pregnant women's plasma leptin concentrations and insulin resistance.^{13,14} All things considered, the information at hand points to a complicated relationship between human glucose homeostasis and leptin.¹⁵ To the best of our knowledge, maternal leptin concentrations in women with GDM have only been investigated by two research teams, and the associated published results are inconsistent. However, it is unclear from the data at hand whether the changes in leptin concentrations are a cause or an effect of the inherent metabolic abnormalities associated with GDM. Hence, the present study aimed to evaluate the role of serum leptin in patients with gestational diabetes mellitus.

2. Materials and Methods

This case control study conducted at the Haveri Institute of Medical Sciences, Haveri, Karnataka between December 2022 to January 2024. A total sixty (n=60) patients diagnosed with gestational diabetes mellitus (GDM) and sixty (n=60) healthy volunteers were considered as controls.

2.1. Inclusion criteria

The study subjects age between 20 to 35 and diagnosed with gestational diabetes mellitus according to International Diabetic Federation (IDF) criteria.

2.2. Exclusion criteria

The subjects with other types of diabetes, Non-Diabetic Renal Disease, Urinary Tract Infections, Thyroid and liver disease, Macrovascular complications such as cardiovascular, cerebrovascular and peripheral vascular diseases and whoever is not willing to participate in the study were excluded. The study was conducted after approval of Institutional Ethics Committee (IEC) and also the study participants was recruited after informed consent form.

Seven (7) ml of overnight fasting blood sample was collected from all the subjects into two tubes: 2 ml transferred into a fluoride tube, 2 ml transferred into ethylene diamine tetra acetic acid and remaining 3 ml transferred into plain tube. The plasma and serum samples were separated by using centrifuge 3000 rpm for 10 mins and immediately transferred into properly labelled aliquots until analysis was done.

The fasting blood sugars (FBS) was estimated by using glucose oxidase peroxidase method, triglycerides (TGL), total cholesterol (TC), was analyzed by enzymatic method, high density lipoprotein was determined by using selective inhibitory method, very low-density lipoproteins and low-density lipoproteins were calculated by friedewald's formula. The serum leptin concentrations were determined

by enzyme linked immunosorbent assay.

2.3. Statistical analysis

For continuous data, the presentation of characteristics was represented mean and standard deviation (SD). The comparison between the groups by using analysis of variance (ANOVA). The Pearson's correlation analysis was used to correlate between the variables and the scatter plots was constructed between the variables. The microsoft excel spread sheets and SPSS windows version 20.0. The P-value is < 0.05 considered statistically significant.

3. Results

Table 1 shows the comparison of study variables between the cases and controls. The age and BMI showed a statistically significant between cases and controls (P=0.001**). There is a significantly increased levels of FBS, HbA1c, total cholesterol and LDL in cases when compared to controls (P=0.001**). The significant increase levels of serum Leptin in cases is observed when compared to controls (P=0.001**). Additionally, TGL, HDL and VLDL are not showing significant values between cases and controls.

Table 2 shows the correlation of serum leptin with study variables. The serum Leptin was positively correlated with BMI, FBS, HbA1C, TC and LDL. There is no significant correlation between Leptin and TGL, HDL, VLDL.

Figure 1 shows the comparison of serum Leptin between controls and gestational diabetes mellitus. The serum Leptin is significantly elevated in patients with gestational diabetes mellitus when compared with healthy controls

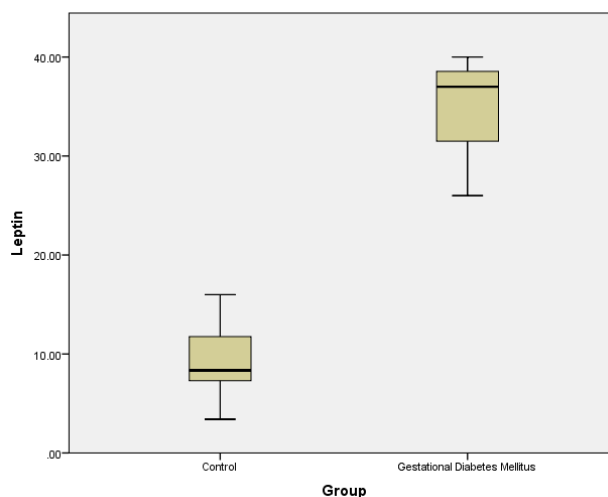


Figure 1: Comparison of serum Leptin between controls and gestational diabetes mellitus

Figure 2 shows the scatter plot between Leptin and BMI. The scatter plot reveals a significant positive correlation

Table 1: Comparison of study variables between the cases and controls

Parameters	Controls		Cases		P-Values
Age	25.45	± 2.53	30.77	± 2.35	0.001**
BMI	22.75	± 2.00	35.09	± 2.57	0.001**
FBS	98.12	± 8.52	169.65	± 73.13	0.001**
HbA1c	4.25	± 0.50	8.68	± 0.40	0.001**
TGL	186.30	± 39.28	194.18	± 59.61	0.394
TC	150.53	± 26.11	223.98	± 126.73	0.001**
HDL	37.98	± 10.89	38.25	± 8.71	0.882
VLDL	37.26	± 7.86	38.84	± 11.92	0.394
LDL	75.29	± 29.84	146.90	± 126.96	0.001**
Serum Leptin	9.68	± 3.74	35.10	± 4.35	0.001**

Table 2: Correlation of serum leptin with other study variables

Parameter	R	Leptin	P
BMI	0.888		0.001**
FBS	0.531		0.001**
HbA1c	0.940		0.001**
TGL	0.073		0.427
TC	0.354		0.001**
HDL	0.989		0.989
VLDL	0.073		0.427
LDL	0.345		0.001**

between Leptin and BMI.

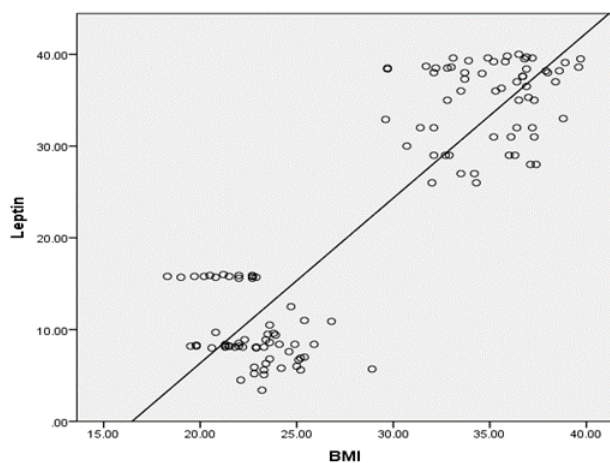
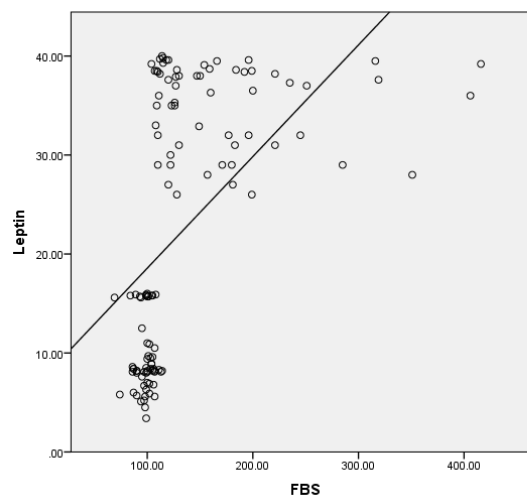
**Figure 2:** Scatter plot between Leptin and BMI

Figure 3 shows the scatter plot between Leptin and FBS. The scatter plot reveals the significant positive correlation between the Leptin and FBS.

Figure 4 shows scatter plot between Leptin and HbA1c. There is a relevant significant positive correlation between Leptin and HbA1c.

**Figure 3:** Scatter plot between leptinand fasting blood sugar

4. Discussion

The current study illustrated how maternal circulating leptin changes during gestational diabetes mellitus. Several studies have reported varying patterns of leptin variation with increasing gestational age in a typical pregnancy.^{16,17} The results of this investigation support the hypothesis that GDM and the mother's circulating leptin profile are related. An adaptive reaction to insulin resistance and the

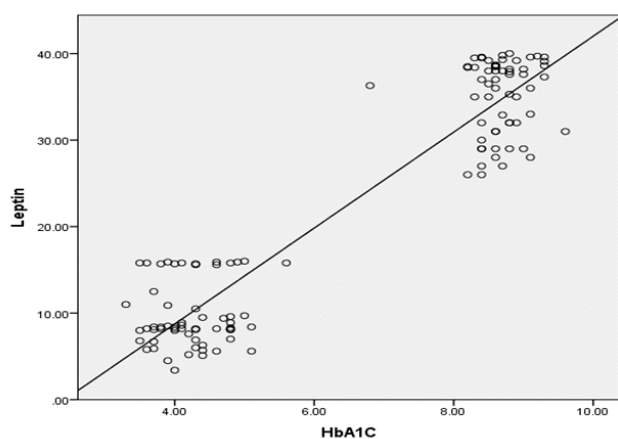


Figure 4: Scatter plot between Leptin and HbA1c

inflammatory response linked to GDM could account for the variation in

circulating leptin concentration observed in early gestation between women with and without GDM.^{18,19} By directly regulating the insulin receptor or indirectly through central neuronal pathways, leptin may enhance insulin sensitivity and it can also directly promote the absorption of glucose and the synthesis of glycogen in skeletal muscle.²⁰

It was also believed that the upregulation of the leptin gene and protein production constituted a sort of defense mechanism against the imbalance of pro-inflammatory cytokines that occurs in many abnormal pregnancies, including GDM.²¹ Another case control study also reported significantly elevated levels of leptin was observed in patients with GDM when compared to controls.²² Previous studies also found significant higher levels of leptin was positively correlated with glucose levels during pregnancy.^{23,24} Additionally, present study also supports previous studies, because we also observed significant elevated levels of serum leptin and its levels were significant positively correlated with fasting blood sugars and HbA1c.²⁵ Additionally, we also found BMI, total cholesterol and LDL was shown significant and this level was positively correlated with serum leptin. Hence, the present study findings, significant elevated levels of serum leptin might be served as a marker for detection of gestational diabetes mellitus.

5. Conclusion

Based on the present study findings, we concluded that significant elevated levels of serum leptin might be served as a marker for detection of gestational diabetes mellitus.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

- Ye W, Luo C, Huang J, Li C, Liu Z, Liu F. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. *BMJ*. 2022;377:e067946.
- Metzger BE, Buchanan TA, Coustan DR, Leiva AD, Dungan DB, Hadden DR, et al. Summary and recommendations of the fifth international workshop-conference on gestational diabetes mellitus. *Diabetes Care*. 2007;30:251–60.
- Gao XL, Yang HX, Zhao Y. Variations of tumor necrosis factor-alpha, leptin and adiponectin in mid-trimester of gestational diabetes mellitus. *Chin Med J (Engl)*. 2008;121(8):701–5.
- Picó C, Palou M, Pomar CA, Rodríguez AM, Palou A. Leptin as a key regulator of the adipose organ. *Rev Endocr Metab Disord*. 2022;23(1):13–30.
- Pérez-Pérez A, Sánchez-Jiménez F, Maymó J, Dueñas JL, Varone C, Sánchez-Margalet V. Role of leptin in female reproduction. *Clin Chem Lab Med*. 2015;53(1):15–28.
- Ceddia RB, Koistinen HA, Zierath JR, Sweeney G. Analysis of paradoxical observations on the association between leptin and insulin resistance. *FASEB J*. 2002;16(10):1163–76.
- Al-Dahhri N, Bartlett WA, Jones AF, Kumar S. Role of leptin in glucose metabolism in type 2 diabetes. *Diabetes Obes Metab*. 2002;4:147e55.
- Knegt VED, Hedley PL, Kanters JK, Thagaard IN, Krebs L, Christiansen M. The Role of Leptin in Fetal Growth during Pre-Eclampsia. *Int J Mol Sci*. 2021;22(9):4569.
- Obeidat RA, Abdo N, Sakee B, Alghazo S, Jbarah OF, Hazaimah EA, et al. Maternal and fetal serum leptin levels and their association with maternal and fetal variables and labor: A cross-sectional study. *Ann Med Surg (Lond)*. 2021;72:103050.
- Laivuori H, Kaaja R, Koistinen H, Karonen SL, Andersson S, Koivisto V. Leptin during and after preeclamptic or normal pregnancy: its relation to serum insulin and insulin sensitivity. *Metabolism*. 2000;49(2):259–63.
- Cohen B, Novick D, Rubinstein M. Modulation of insulin activities by leptin. *Science*. 1996;274(5290):1185–8.
- Song C, Lyu Y, Li C. Long-term risk of diabetes in women at varying durations after gestational diabetes: a systematic review and meta-analysis with more than 2 million women. *Obes Rev*. 2018;19(3):421–9.
- Peltokorpi A, Lisinen I, Viikari L, Kaaja R. Preconceptual leptin levels in gestational diabetes and hypertensive pregnancy. *Hypertens Pregnancy*. 2022;41(1):70–7.
- Lacroix M, Battista MC, Doyon M. Higher maternal leptin levels at second trimester are associated with subsequent greater gestational weight gain in late pregnancy. *BMC Pregnancy Childbirth*. 2016;16. doi:10.1186/s12884-016-0842-y.
- Pérez-Pérez A, Toro A, Vilariño-García T, Maymó J, Guadix P, Dueñas JL, et al. Leptin action in normal and pathological pregnancies. *J Cell Mol Med*. 2018;22(2):716–27.
- Kautzky-Willer A, Pacini G, Tura A, Biegelmayer C, Schneider B, Ludvik B. Increased plasma leptin in gestational diabetes. *Diabetologia*. 2001;44(2):164–72.
- Screening for Gestational Diabetes: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2021;326(6):531–8.
- Antuna-Puente B, Faraj M, Karelis AD, Garrel D, Prud'homme D, Rabasa-Lhoret R. HOMA or QUICKI: is it useful to test the reproducibility of formulas? *Diabetes Metab*. 2008;34(3):294–6.
- Vitoratus N, Salamalekis E, Kassanos D, Loghis C, Panayotopoulos N, Kouskouni E, et al. Maternal plasma leptin levels and their relation to insulin and glucose in gestational onset diabetes. *Gynecol Obstet Invest*. 2001;51(1):17–21.
- Qiu C, Williams MA, Vadachkoria S, Frederick IO, Luthy DA. Increased maternal plasma leptin in early pregnancy and risk of

- gestational diabetes mellitus. *Obstet Gynecol.* 2004;103(3):519–25.
21. Liu ZJ, Liu PQ, Ding Y, Wang AM, Zhang JJ, Zhao XF. Maternal plasma leptin levels and their relationship to insulin and glucose in pregnant women with gestational diabetes mellitus and gestational impaired glucose tolerance. *Zhonghua Fu Chan Ke Za Zhi.* 2003;38(5):261–3.
 22. Maghbooli Z, Hossein-Nezhad A, Rahmani M, Shafaei AR, Larijani B. Relationship between leptin concentration and insulin resistance. *Horm Metab Res.* 2007;39(12):903–7.
 23. Mohiti J, Afkhami M, Babaei A. Relation between leptin and insulin in patients with type II diabetes mellitus. *Int J Endocrinol Metab.* 2005;3:121–5.
 24. Lappas M, Yee K, Permezel M, Rice GE. Release and regulation of leptin, resistin and adiponectin from human placenta, fetal membrane, and maternal adipose tissue and skeletal muscle from normal and gestational diabetes mellitus complicated pregnancies. *J Endocrinol.* 2005;186:457–65.
 25. Soheilykhah S, Mojibian M, Rahimi-Saghand S, Rashidi M, Hadinedoushan H. Maternal serum leptin concentration in gestational

diabetes. *Taiwanese J Obstet Gynecol.* 2011;50(2):149–53.

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