



Association of Serum Vitamin D3 and Leptin Levels in Gestational Diabetes Mellitus in Baghdad

Aseel Hassan Qitan¹, Naghma Abdulsahib Hussein², Sara Ali Mutashar³

¹Biotechnology Research Center/ AL-Nahrain University, Iraq

²Baghdad Al-Karkh Health Directorate

³Medical College, Ibn Sina University of Medical and Pharmaceutical Sciences, Baghdad, Iraq.

ARTICLE INFO	ABSTRACT
Published Online: 18 April 2026	Background: White adipocytes secrete leptin, which regulates hunger and body weight. During pregnancy, leptin promotes glucose metabolism and fetal development by acting autocrinely and paracrinely in adipose tissue and the placenta. Methods: This case-control study from January 2024 through June 2025, researchers studied the leptin, body mass index (BMI), glucose, and lipid profiles of 30 pregnant women with gestational diabetes and 30 pregnant women without diabetes. Women were asked to provide blood samples at the beginning, middle, and end of their pregnancies. Ligand for peptidin-D3. Sixty pregnant women were included.. Results: There was no significant age difference between the groups. GDM patients had substantially higher fasting blood glucose and HbA1c levels than controls ($p < 0.001$). The GDM group had considerably lower serum vitamin D3 levels and significantly higher leptin levels ($p < 0.05$). Leptin had substantial positive relationships with RBS and HbA1c ($r = 0.769$ and 0.793 ; $p < 0.001$), while vitamin D3 had a negative connection with RBS, HbA1c, and leptin ($p < 0.001$). Conclusion: Gestational diabetes mellitus is associated with lower blood vitamin D3 and higher leptin levels, both of which are substantially connected with poor glycemic control. These findings point to a possible role for vitamin D deficiency and leptin dysregulation in the pathogenesis of GDM.
Corresponding Author: Aseel Hassan Qitan	
KEYWORDS: Leptin, Gestational diabetes, Vitamin D3, Glycated hemoglobin, Glycemic control.	

I. INTRODUCTION

Endocrine adipose tissue releases adipokines. Weight, adipokines, and pregnancy outcomes may be linked, but details are lacking (El Husseney et al., 2017). Adipokines concentration (Adiponectin and Leptin) is affected as diabetes progresses, given its effect on adipose tissue and its association with obesity (Raeef et al., 2025). Initially, leptin deemed the “missing link” between fat and reproduction (Friedman et al., 1998). Leptin affects weight and reproduction. This hormone is mostly produced by the placenta (Reitman et al., 2001). Pregnancy-diagnosed hyperglycemic GDM has no known cause. The prevalence of gestational diabetes is 3–8%. Age and obesity have raised childbirth above 20% in industrialized and developing nations in recent decades, making it a major public health issue. GDM is diverse, however overweight and obesity contribute for 50% (Powe et al., 2016). Since gestational diabetes symptoms disappear after birth, the placenta may be

to blame. Thus, placental overgrowth and other defects might cause GDM (Ericsson et al., 2007; Taricco et al., 2003).

GDM decreases placental and fetal nutrition due to insulin resistance, hyperinsulinemia, and hyperleptinemia. GDM is associated with elevated placental leptin and LEPR expressions, which may predict GDM in the first trimester (Iciek et al., 2013; Omazić et al., 2021). Hyperinsulinemia may alter placental leptin, a fetal homeostasis signal (Lepercq et al., 1998). Maternal hyperglycemia may alter cord blood leptin levels, raising GDM babies' obesity risk (Côté et al., 2016). High leptin levels in gestational diabetes mellitus (GDM) are linked to increased IL-6 and TNF α production, creating a chronic inflammatory environment that boosts leptin synthesis (Miehle et al., 2012).

Gestational diabetes mellitus (GDM) increases amniotic fluid volume and causes polyhydramnios, suggesting AQP9 expression may vary (Bednar et al., 2015). Normal amniotic fluid volume occurs when maternal

hyperglycemia is treated. Glycerol transporter AQP9 may provide the fetus. Gestational diabetes placentas had increased AQP9 mRNA and protein. High leptin plasma levels and AQP9 overexpression may increase glycerol transport to the fetus during gestational diabetes mellitus (GDM), satisfying the metabolic condition's energy needs. Even while any nutritional or lifestyle intervention that reduces weight lowers leptin in the general population, no leptin-targeted medication has been used to treat gestational diabetes (Vilariño-García et al., 2018).

This study aimed to evaluate serum resistin levels and to examine their relationship with vitamin D3, vitamin B12, and glycemic control in patients with type 2 diabetes mellitus compared with healthy individuals.

II. MATERIALS AND METHODS

A. Study design and patients

The protocol governing this research. (Thirty patients with gestational diabetes and thirty individuals in the pregnant as control group.) Fasting blood samples were collected to assess the circulating levels of fasting glucose (FBS), HbA1c, Leptin. The physical examinations of all participants were conducted by the same physician, and their blood pressure, height, and weight were documented.

B. Samples collection and preparations

Five millilitres of fasting blood samples were obtained from all participants. A portion of that (2 ml) was transferred to the EDTA vial. Half of this sample was subjected to centrifugation, and the plasma was utilized for the determination in accordance with the protocol provided by the kit manufacturer, while the entire blood sample was employed to measure HbA1c. The fasting sera separated from the clotted blood samples were also utilized for the assessment of FBS, and Leptin.

C. Determination of leptin

The serum leptin were performed by enzyme-linked immunosorbent assay (ELISA) kits from Biotek, ELx, USA. Automated washing of 96-well ELISA plates was performed by a microplate washer (BioTek™ 50TS, USA), and the absorbance was measured at 450 nm using an ELISA reader (BioTek 800TS). The measurements were conducted and results were recorded following the manufacturer's instructions.

D. Determination of biochemical parameters

The serum glucose was determined using an endpoint glucose oxidase method with an automated chemistry analyzer (RA-1000 Technicon, USA). HbA1c was determined using an automated analyzer base on chromatography method (Drew DS5, UK).

E. Statistical analysis

Data were expressed as Mean $\pm$ SD. Gestational DM of the different analytes were compared for the groups of male and female subjects using unpaired t-tests. All statistical analyses were generated by using SPSS (version 23.0). A

confidence level of $p < 0.05$ was considered statistically significant for all analyses.

III. RESULTS

A. Demographic characteristics of diabetic patients

The current study examined and contrasted various biochemical parameters between patients diagnosed with type 2 diabetes mellitus (case group) and healthy control subjects. The results are summarized in Tables 1 and 2.

There was no statistically significant difference in age between the case group (33.2 $\pm$ 2.52 years) and the control group (28.7 $\pm$ 2.1 years) ($P = 0.064$). The opposite, BMI exhibited significant difference between gestational diabetic patients (31.88 $\pm$ 5.14 kg/m²) and controls (26.40 $\pm$ 3.27 kg/m²) ($P = <0.0001$).

Table 1: comparison of age and BMI between Type2 diabetes patients and healthy controls

Parameters	Control group Mean $\pm$ SD	Case group Mean $\pm$ SD	P. value
Age	33.2 $\pm$ 2.52	28.7 $\pm$ 2.1	0.064
BMI	26.40 $\pm$ 3.27	31.88 $\pm$ 5.14	<0.0001

Note. Data were expressed as Mean $\pm$ SD; Statistical analyses were performed by t test (paired test) for multiple comparisons; ‡ t test significance (2-tailed).

B. Comparison of studied biomarkers between diabetic patients and controls

The gestational diabetes group had significantly higher fasting blood glucose (FBS) (194.2 $\pm$ 3.7 mg/dL) than the control group (93.96 $\pm$ 10.53 mg/dL) ($P 0.001$). Diabetic patients had significantly higher HbA1c levels (8.64 $\pm$ 1.36%) compared to controls (4.69 $\pm$ 0.62%), indicating poor glycemic control ($P 0.0001$).

Significantly higher leptin levels (18.62 $\pm$ 3.41 ng/mL) were seen in type 2 diabetes patients compared to the control group (8.82 $\pm$ 1.41 ng/mL) ($P 0.0001$).

Diabetics had considerably lower vitamin D3 levels (13.74 $\pm$ 3.58 ng/mL) compared to healthy persons (31.94 $\pm$ 6.82 ng/mL) ($P < 0.001$).

Table 2: Biochemical Parameters in Type 2 Diabetes Mellitus Compared to the Control Group.

Parameters	Control group Mean $\pm$ SD	Case group Mean $\pm$ SD	P. value
FBS	93.96 $\pm$ 10.53	194.2 $\pm$ 3.7	0.001
HbA1c	4.69 $\pm$ 0.62	8.64 $\pm$ 1.36	0.0001
Vitamin D	31.94 $\pm$ 6.82	13.74 $\pm$ 3.58	0.025
LEPTIN	18.62 $\pm$ 3.41	8.82 $\pm$ 1.41	0.0001

Abbreviations: RBS, Random Blood Sugar; HbA1c, Glycated hemoglobin. Note. Data were expressed as Mean $\pm$ SD; Statistical analyses were performed by t test (paired test)

for multiple comparisons; ‡ t test significance (2-tailed); p-value less than 5% is significant difference.

C. Correlation between resistin and other biochemical parameters

Pearson correlation analysis showed considerable positive relationships between glycaemic indices and serum leptin. Both RBS and HbA1c were favourably linked with leptin (r

$= 0.769$ and $r = 0.793$, respectively; $p < 0.001$). Conversely, vitamin D3 levels inversely correlated with RBS ($r = -0.719$), HbA1c ($r = -0.745$), and leptin ($r = -0.745$), demonstrating reduced glycaemic control was linked to lower vitamin D3 levels and increased leptin levels.

Table 3 illustrations gestational diabetes patients' Pearson correlation coefficients for biochemical markers.

Variables	Coefficient correlation	FBS	HbA1c	Leptin	Vit. D3
FBS	r	1			
	p				
HbA1c	r	0.809**	1		
	p	0.0001			
Leptin	r	0.769**	0.793**	1	
	p	0.0001	0.0001		
Vit. D3	r	-0.719**	-0.754**	-0.754**	1
	p	0.0001	0.0001	0.0001	

IV. DISCUSSION

In this investigation, both healthy pregnant women and patients with gestational diabetes mellitus were tested for glycemic indices, blood vitamin D3 levels, and leptin levels. Patients with GDM exhibited substantial hormonal and metabolic alterations, illuminating the intricate interplay of vitamin D status, adipokines, and glucose homeostasis.

The metabolic characteristics and diagnostic criteria for gestational diabetes mellitus are compatible with high levels of hemoglobin A1c and fasting blood sugar in the GDM group, confirming inadequate glycemic control (ElSayed et al., 2023). Decreased insulin sensitivity and pancreatic β -cell dysfunction are the causes of persistent hyperglycemia during pregnancy, as confirmed by these data.

The serum vitamin D3 levels of GDM patients were much lower than those of healthy pregnant controls, according to this research. During pregnancy, insulin secretion may decrease and insulin resistance may develop in patients with GDM who have vitamin D insufficiency (Palomer et al., 2008; Zhang et al., 2018). Vitamin D3 plays an important role in gestational diabetes, and this study found reduced amounts of it.

Reduced vitamin D status impairs glycemic control, as vitamin D3 levels inversely correlate with RBS and HbA1c. Vitamin D may influence glucose metabolism via insulin sensitivity and inflammatory pathways, as previous studies have discovered comparable inverse correlations (Pittas et al., 2007).

The serum leptin levels of GDM patients were significantly greater than those of healthy pregnant women. During pregnancy, the placenta and adipose tissue secrete leptin, which controls glucose and energy metabolism. Insulin resistance and metabolic dysregulation may be seen in GDM patients with elevated leptin levels (Hauguel-de Mouzon et al., 2006).

This study indicates that hyperleptinemia, a symptom of gestational diabetes, is linked to inadequate glycemic control because of the robust positive correlations between leptin levels, RBS, and HbA1c. Research has shown that gestational glucose intolerance and impaired insulin signaling are associated with elevated leptin levels (Fasshauer et al., 2015).

One possible association between vitamin D and adipokine secretion regulation is the strong inverse correlation between vitamin D3 and leptin levels shown in this research. Research has demonstrated that vitamin D can improve insulin sensitivity by decreasing inflammation in adipose tissue and leptin expression (Argano et al., 2023).

This provides more evidence that metabolic anomalies in gestational diabetes mellitus may be caused by a combination of vitamin D3 deficiency and elevated leptin levels. Improved metabolic regulation and prevention of GDM effects may result from monitoring and treating vitamin D insufficiency during pregnancy (Aghajafari et al., 2013).

V. CONCLUSION

Gestational diabetes mellitus is linked to lower blood vitamin D3 and higher leptin levels, both of which are strongly associated with poor glycemic control. These data indicate that vitamin D3 insufficiency and leptin dysregulation may play a role in the pathogenesis of GDM.

VI. ACKNOWLEDGMENTS

The author would like to express their appreciation to all supporter for supplying the materials and required things for this study.

REFERENCES

1. Aghajafari, F., Nagulesapillai, T., Ronksley, P. E., Tough, S. C., O'Beirne, M., & Rabi, D. M. (2013).

- Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and meta-analysis of observational studies. *Bmj*, 346, f1169. doi:10.1136/bmj.f1169
2. Argano, C., Mirarchi, L., Amodeo, S., Orlando, V., Torres, A., & Corrao, S. (2023). The Role of Vitamin D and Its Molecular Bases in Insulin Resistance, Diabetes, Metabolic Syndrome, and Cardiovascular Disease: State of the Art. *Int J Mol Sci*, 24(20). doi:10.3390/ijms242015485
3. Bednar, A. D., Beardall, M. K., Brace, R. A., & Cheung, C. Y. (2015). Differential expression and regional distribution of aquaporins in amnion of normal and gestational diabetic pregnancies. *Physiol Rep*, 3(3). doi:10.14814/phy2.12320
4. Côté, S., Gagné-Ouellet, V., Guay, S. P., Allard, C., Houde, A. A., Perron, P., . . . Bouchard, L. (2016). PPARGC1 α gene DNA methylation variations in human placenta mediate the link between maternal hyperglycemia and leptin levels in newborns. *Clin Epigenetics*, 8, 72. doi:10.1186/s13148-016-0239-9
5. El Husseny, M. W., Mamdouh, M., Shaban, S., Ibrahim Abushouk, A., Zaki, M. M., Ahmed, O. M., & Abdel-Daim, M. M. (2017). Adipokines: Potential Therapeutic Targets for Vascular Dysfunction in Type II Diabetes Mellitus and Obesity. *J Diabetes Res*, 2017, 8095926. doi:10.1155/2017/8095926
6. ElSayed, N. A., Aleppo, G., Aroda, V. R., Bannuru, R. R., Brown, F. M., Bruemmer, D., . . . on behalf of the American Diabetes, A. (2023). 2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes-2023. *Diabetes care*, 46(Suppl 1), S19-s40. doi:10.2337/dc23-S002
7. Ericsson, A., Säljö, K., Sjöstrand, E., Jansson, N., Prasad, P. D., Powell, T. L., & Jansson, T. (2007). Brief hyperglycaemia in the early pregnant rat increases fetal weight at term by stimulating placental growth and affecting placental nutrient transport. *J Physiol*, 581(Pt 3), 1323-1332. doi:10.1113/jphysiol.2007.131185
8. Fasshauer, M., & Blüher, M. (2015). Adipokines in health and disease. *Trends Pharmacol Sci*, 36(7), 461-470. doi:10.1016/j.tips.2015.04.014
9. Friedman, J. M., & Halaas, J. L. (1998). Leptin and the regulation of body weight in mammals. *Nature*, 395(6704), 763-770. doi:10.1038/27376
10. Hauguel-de Mouzon, S., Lepercq, J., & Catalano, P. (2006). The known and unknown of leptin in pregnancy. *Am J Obstet Gynecol*, 194(6), 1537-1545. doi:10.1016/j.ajog.2005.06.064
11. Iciek, R., Wender-Ozegowska, E., Zawiejska, A., Mikolajczak, P., Mrozikiewicz, P. M., Pietryga, M., & Brazert, J. (2013). Placental leptin and its receptor genes expression in pregnancies complicated by type 1 diabetes. *J Physiol Pharmacol*, 64(5), 579-585.
12. Lepercq, J., Cauzac, M., Lahlou, N., Timsit, J., Girard, J., Auwerx, J., & Hauguel-de Mouzon, S. (1998). Overexpression of placental leptin in diabetic pregnancy: a critical role for insulin. *Diabetes*, 47(5), 847-850. doi:10.2337/diabetes.47.5.847
13. Miehle, K., Stepan, H., & Fasshauer, M. (2012). Leptin, adiponectin and other adipokines in gestational diabetes mellitus and pre-eclampsia. *Clinical endocrinology*, 76(1), 2-11.
14. Omazić, J., Viljetić, B., Ivić, V., Kadivnik, M., Zibar, L., Müller, A., & Wagner, J. (2021). Early markers of gestational diabetes mellitus: what we know and which way forward? *Biochem Med (Zagreb)*, 31(3), 030502. doi:10.11613/bm.2021.030502
15. Palomer, X., González-Clemente, J. M., Blanco-Vaca, F., & Mauricio, D. (2008). Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. *Diabetes Obes Metab*, 10(3), 185-197. doi:10.1111/j.1463-1326.2007.00710.x
16. Pittas, A. G., Lau, J., Hu, F. B., & Dawson-Hughes, B. (2007). The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab*, 92(6), 2017-2029. doi:10.1210/jc.2007-0298
17. Powe, C. E., Allard, C., Battista, M. C., Doyon, M., Bouchard, L., Ecker, J. L., . . . Hivert, M. F. (2016). Heterogeneous Contribution of Insulin Sensitivity and Secretion Defects to Gestational Diabetes Mellitus. *Diabetes care*, 39(6), 1052-1055. doi:10.2337/dc15-2672
18. Raeef, A. A., Mohammed, M. H., & Abdullah, J. N. (2025). Assessment of the Influence of Adiponectin, Nesfatin-1, Insulin Resistance, and Various Biochemical Parameters in Samples of Iraqi Individuals Diagnosed with Type 2 Diabetes Mellitus and Pre-diabetes. *HAYATI Journal of Biosciences*, 32(4), 980-988. doi:10.4308/hjb.32.4.980-988
19. Reitman, M. L., Bi, S., Marcus-Samuels, B., & Gavrilova, O. (2001). Leptin and its role in pregnancy and fetal development--an overview. *Biochem Soc Trans*, 29(Pt 2), 68-72. doi:10.1042/0300-5127:0290068
20. Taricco, E., Radaelli, T., Nobile de Santis, M. S., & Cetin, I. (2003). Foetal and Placental Weights in Relation to Maternal Characteristics in Gestational Diabetes. *Placenta*, 24(4), 343-347. doi:<https://doi.org/10.1053/plac.2002.0913>
21. Vilariño-García, T., Pérez-Pérez, A., Dietrich, V., Guadix, P., Dueñas, J. L., Varone, C. L., . . .

Sánchez-Margalet, V. (2018). Leptin upregulates aquaporin 9 expression in human placenta in vitro. *Gynecol Endocrinol*, 34(2), 175-177.
doi:10.1080/09513590.2017.1380184

22. Zhang, Y., Gong, Y., Xue, H., Xiong, J., & Cheng, G. (2018). Vitamin D and gestational diabetes mellitus: a systematic review based on data free of Hawthorne effect. *Bjog*, 125(7), 784-793.
doi:10.1111/1471-0528.15060