Assessment of Serum Galectin-3 Levels in Patients with Gestational Diabetes Mellitus

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Abstract

Objective: *This study was aimed to compare serum galectin-3 (Gal-3) levels in gestational diabetes mellitus (GDM) and healthy pregnant women and to evaluate the relationship between insulin resistance parameters and serum Gal-3 levels.* **Materials and Methods:** Fifty-nine pregnant women who were screened for GDM with oral glucose tolerance tests (OGTT) at the 24th–28th gestational weeks were included in the study. According to the results of OGTT, 34 pregnant women were included in the GDM group and 25 pregnant women were included in the control group. **Results:** Serum Gal-3 value was found to be similar in the GDM and control group ($P < 0.471$). However, there was a significant positive association between Gal-3 and fasting insulin (r = 0.509, $P < 0.001$) and homeostasis model assessment of insulin resistance (HOMA-IR) (r = 0.479, $P < 0.001$) in the whole pregnancies, and between Gal-3 levels and fasting insulin (r = 0.608, $P < 0.001$), HOMA-IR (r = 0.609, $P < 0.001$), and OGTT 60 min glucose (r = 0.444, $P = 0.016$) in the GDM patients. **Conclusions:** There was no difference in the last trimester serum Gal-3 levels between GDM and healthy pregnant women. However, a significant positive correlation was determined between Gal-3 and fasting insulin, HOMA-IR, and OGTT 60 min glucose values in the GDM group, and fasting insulin and HOMA-IR values in whole pregnancies. The results of our study support previous data reporting the relationship between Gal-3 and GDM through insulin resistance.

Keywords: Galectin-3, gestational diabetes mellitus, subclinical inflammation

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance of varying degrees that begins during pregnancy or is first recognized during pregnancy.[1] The pathophysiological mechanism responsible for the development of GDM is not clearly understood, but two main mechanisms are thought to cause GDM: insulin resistance and chronic subclinical inflammation.[2]

Previous studies have shown that proinflammatory cytokine levels such as tumor necrosis factor-alpha, interleukin-1β (IL-1β), and IL-6 increase in patients with GDM during and after pregnancy.[3] In our recent study, we have shown that secreted frizzled-related protein 4 and prorenin increase in patients with GDM.[4] It is thought that these cytokines cause insulin resistance and glucose metabolism disorders by disrupting the insulin signaling system.

Galectin-3 (Gal-3) is a member of the soluble beta-galactoside-binding lectin family and plays a key role in the regulation of different pathological processes, for instance, cancer, inflammation, and metabolic disorders.[5-8] Our recent study and other studies have shown that Gal-3 levels increase with impaired glucose homeostasis in obese and diabetic individuals.[9,10]

There are few studies investigating the relationship between GDM and Gal-3. In these studies, it is seen that there is

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no similarity between the groups in important parameters such as antidiabetic drug use, gestational week, and body mass index (BMI). This study aimed to compare serum Gal-3 levels in GDM and healthy pregnant women, who did not receive any diet or antidiabetic drug therapy, had similar BMI values, and had similar age and gestational age, and to evaluate the relationship between insulin resistance parameters and serum Gal-3 levels.

Materials and Methods

This was a cross-sectional study carried out at the Endocrinology Department of Selcuk University Hospital. All participating women were selected randomly from admitted to our Endocrinology and Obstetrics Department for oral glucose tolerance tests (OGTT) between the 24th and 28th weeks after gestation between January 2019 and June 2020. The criteria for exclusion were pregestational diabetes and prediabetes, previous gestational diabetes or polyhydramnios, eclampsia, preeclampsia, history of hypertension before pregnancy, pregnancy-induced hypertension, chronic inflammatory disease, acute or chronic infection, malignancy, morbid obesity, familial hyperlipidemia, metabolic syndrome, being on medication, smoking, and fetal and placental anomalies.

Procedure

All pregnant women included in the study underwent 75 g OGTT between 24 and 28 weeks of gestation, and any of the plasma glucose values equal to or higher than the following according to American Diabetes Association criteria showed a positive OGTT: fasting = 92 mg/dL, 1-h = 180 mg/dL, and 2-h = 153 mg/dL.[11]

Thirty-four pregnant women with GDM and 25 healthy pregnant women were included in our study. Before the pregnant women included in the study received any diet therapy or treatment with subcutaneous or oral antidiabetic agents, blood samples were taken while screening for GDM. Age, gestational age, height, weight and BMI, gestational weight gain, family history of diabetes, systolic and diastolic blood pressure, waist and hip circumference, and waist–hip ratio (WHR) were noted for all participants. BMI was calculated as body weight divided by square height. WHR was calculated as waist circumference divided by hip circumference.

Blood sampling and assay

Samples were obtained after overnight fasting and at the time of OGTT for the serum analysis. Lipid parameters (triglyceride, high-density lipoprotein [HDL], and total cholesterol), fasting blood glucose (FBG), aspartate aminotransferase, alanine aminotransferase, and C-reactive protein (CRP) levels were measured with the ARCHITECT c16000 clinical chemistry analyzer. Fasting insulin and thyroid-stimulating hormone (TSH) levels were measured by a Cobas e601 autoanalyzer (Roche Diagnostics, Germany). Low-density lipoprotein (LDL) cholesterol levels were determined according to the commonly used formula previously reported by Friedewald *et al.*[12] The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated according to the following formula: HOMA-IR = fasting insulin (μU/mL) × fasting glucose (mg/dL)/405.[13] The homeostasis model assessment of insulin secretion (HOMA-β) was calculated according to the following formula: HOMA-β = 360 × fasting insulin (μU/mL)/fasting glucose (mg/dL)−63.[14]

Gal-3 assay

Samples taken for Gal-3 measurement were centrifuged and stored at −70°C until testing. Levels of Gal-3 were measured using a solid phase enzyme-linked immunosorbent assay (catalog no.: SK00199-01, AVISCERA BIOSCIENCE, INC., Santa Clara, CA, USA). This test had a high sensitivity (minimum detectable dose: 10 pg/mL), and no significant crossreactivity or interference was observed. All determinations were made in duplicate. The calibration and standardization of the test were performed in accordance with the manufacturer's protocol. All tests were performed in our clinical laboratory, and the inter- and intra-assay coefficients of variation were controlled between 8% and 4%, respectively.

Statistical analysis

Statistical analyses were performed by R version 3.6.0 (The R Foundation for Statistical Computing, Vienna, Austria; https://www.rproject.org). Shapiro-Wilk's test of normality and Q-Q plots were used to evaluate the data distribution. Levene's test was used to control the homogeneity of the variables. Numerical variables were given as mean ± standard deviation or median (interquartile range) as appropriate. Categorical variables were given as number (n) and percentage (%). Firstly, we evaluated the effect of galectin-3 levels, demographical characteristics of the patients, and laboratory findings on GDM. For this purpose, we conducted the independent samples *t*-test, two-proportion *Z*-test, Mann–Whitney *U* test, and Welch's *t*-test. Then, we performed the Pearson and Spearman's rho correlation analysis in univariate analysis to examine the relationship between galectin-3 levels and age, gestational age, BMI, WHR, gestational weight gain, FBG, OGTT 60 and 120 min glucose, fasting insulin, HOMA-IR, HOMA-*β*, and CRP. In multiple analyses, we carried out the multiple linear regression analysis to identify the factors affecting the Gal-3 levels. Significant variables at $P < 0.25$ in univariate analysis were included into multiple models, and stepwise elimination method was performed. Also, the relationship between Gal-3 levels and the variables found to be significant in the multiple regression analysis was analyzed according to the study groups using Pearson correlation analysis via scatter plot. *P* value less than 0.05 was considered as statistically significant.

Results

A total of 59 patients between the ages of 21 and 39 with a mean age of 29.45 ± 4.63 were included in the study. The mean gestational age was 26.37 ± 2.05 (range: 24–33) of the patients. According to the results of the OGTT screening performed between 24 and 28 gestational weeks, 34 pregnant women were included in the GDM group and 25 pregnant women were included in the control group.

The demographical characteristics and laboratory findings of the study groups were given in Table 1. The age distribution, gestational age, height, weight, BMI, waist and hip circumference, WHR, systolic and diastolic blood pressure, gestational weight gain, and family history of diabetes of the patients were similar in both groups ($P > 0.05$).

There were no significant differences in Gal-3 levels between the two groups. The mean Gal-3 level of the GDM group was 5.77 ± 1.77 mg/dL, and the mean Gal-3 level of the control group was 6.18 ± 2.38 ($P = 0.471$) [Table 1] [Figure 1(a)]. There was no significant difference between the groups with regard to total cholesterol, HDL, LDL, TSH, CRP, and hemoglobin levels ($P > 0.05$).

The triglyceride, FBG, OGTT 60 and 120 min glucose levels, fasting insulin, and HOMA-IR levels were higher in the GDM patients compared with the controls [Table 1]. On the other hand, HOMA-β levels were lower in the GDM patients than the controls [Table 1].

A Pearson and Spearman's rho correlation was run to determine the relationship between Gal-3 levels and some demographical and laboratory parameters both in all patients and in patients with GDM. There was a positive correlation between Gal-3 levels and insulin (Pearson's r = 0.509, $P < 0.001$) and HOMA-IR levels (Pearson's r = 0.479, $P < 0.001$), which were statistically significant [Table 2]. However, age, gestational age, BMI, WHR, and gestational weight gain of the patients and also FBG, HOMA-β, and CRP levels were not statistically relationship with Gal-3 levels (all P value > 0.05). Moreover, there was a significantly and positive relationship between Gal-3 levels and OGTT 60 min glucose (Spearman's rho = 0.444, $P = 0.016$), insulin (Pearson's r = 0.608, $P < 0.001$), and HOMA-IR (Pearson's r = 0.609, $P < 0.001$) in the GDM patients [Table 2].

Multiple regression analysis was conducted to predict galectin-3 levels from gestational age, insulin, HOMA-IR, and HOMA-β. Only insulin level from these variables statistically significantly predicted galectin-3 level (F = 10.493, $P = 0.008$, R2 = 0.488) [Table 2]. Although there was a significantly positive relationship between Gal-3 levels and insulin in the GDM patients (r = 0.608, $P < 0.001$), this relationship was not statistically significant in the controls (r = 0.282, $P = 0.228$) [Figure 1(b)].

Table 1: The comparisons of the demographical characteristics and laboratory findings of the patients according to the study groups

Parameters	Control ($n = 25$)	GDM ($n = 34$)	P value
Age (years)	27.95 ± 4.59	30.48 ± 4.44	0.059[1]
Family history (%)	8 (32.0)	16 (47.0)	0.12[2]
Gestational age (weeks)	26.04 ± 2.18	26.61 ± 2.64	0.404[1]
Height (m)	1.62 ± 0.05	1.61 ± 0.05	0.378[1]
Weight (kg)	70.76 ± 8.42	74.03 ± 6.17	0.115[1]
BMI (kg/m^2)	26.88 ± 2.79	27.85 ± 2.95	0.090[1]
Waist circumference (cm)	94.88 ± 9.88	102.65 ± 9.63	0.056[1]
Hip circumference (cm)	106.5 ± 10.85	111.58 ± 8.09	0.162[1]
WHR	0.92 (0.86–0.93)	0.94 (0.91–0.96)	0.174[3]
Gestational weight gain (kg)	5.02 ± 3.36	6.58 ± 4.10	0.134[1]
SBP (mmHg)	105.4 ± 12.2	108.7 ± 13.1	0.12
DBP (mmHg)	65.4 ± 8.2	67.6 ± 9.3	0.80
Total cholesterol (mg/dL)	231.97 ± 44.73	242.55 ± 43.61	0.369[1]
Triglyceride (mg/dL)	184.42 ± 70.58	234.15 ± 72.94	0.013[1]
HDL (mg/dL)	60.96 ± 10.49	61.32 ± 12.95	0.909[1]
LDL (mg/dL)	132 (107.2–156)	129 (116–146.4)	0.906[3]
TSH (µU/mL)	1.63 ± 0.85	1.78 ± 0.84	0.556[1]
CRP (mg/L)	3.49 (2.05–9.12)	5.14 (3.52–9.41)	0.435[3]
FBG (mg/dL)	76 (75–81)	95 (88.75–104)	<0.001[3]
OGTT 60 min (mg/dL)	161 (160–163)	191 (182–225)	0.004[3]
OGTT 120 min (mg/dL)	132 (125–146)	169 (158–195)	0.024[3]
Hemoglobin (g/dL)	11.98 ± 0.90	12.16 ± 0.78	0.425[1]
Insulin (mIU/mL)	7.07 ± 1.72	8.63 ± 2.91	0.026[4]
HOMA-IR	1.36 ± 0.43	2.04 ± 0.73	<0.001[4]
HOMA-β	173.76 (127.94–218.78)	90.22 (65.98–139.72)	<0.001[3]
Galectin-3 (ng/mL)	5.77 ± 1.77	6.18 ± 2.38	0.471[1]

BMI = body mass index, CRP = C-reactive protein, DBP = diastolic blood pressure, FBG = fasting blood glucose, GDM = gestational diabetes mellitus, HDL = high-density lipoprotein, Hg = hemoglobin, HOMA-IR = homeostatic model assessment for insulin resistance, HOMA-β = homeostatic model assessment of β-cell function, LDL = low-density lipoprotein, OGTT = oral glucose tolerance test, SBP = systolic blood pressure, TSH = thyroid-stimulating hormone, WHR = waist–hip ratio

Data were presented as mean ± standard deviation or median (interquartile range: 25th percentile–75th percentile) and also were given a mean difference of the groups (95% confidence interval)

[1]Independent samples t-test

[2]Two proportion Z-test

[3]Mann–Whitney U test

[4]Welch's t-test

Discussion

Although there are many studies assessing the relationship between Gal-3 and type 2 diabetes and its complications, there are few studies assessing serum Gal-3 levels in the patients with GDM, and the results obtained in these studies are not consistent with each other.[15-18]

In their study conducted with two different patient groups, Talmor-Barkan *et al.*[15] compared the third trimester serum Gal-3 levels of the pregnant women

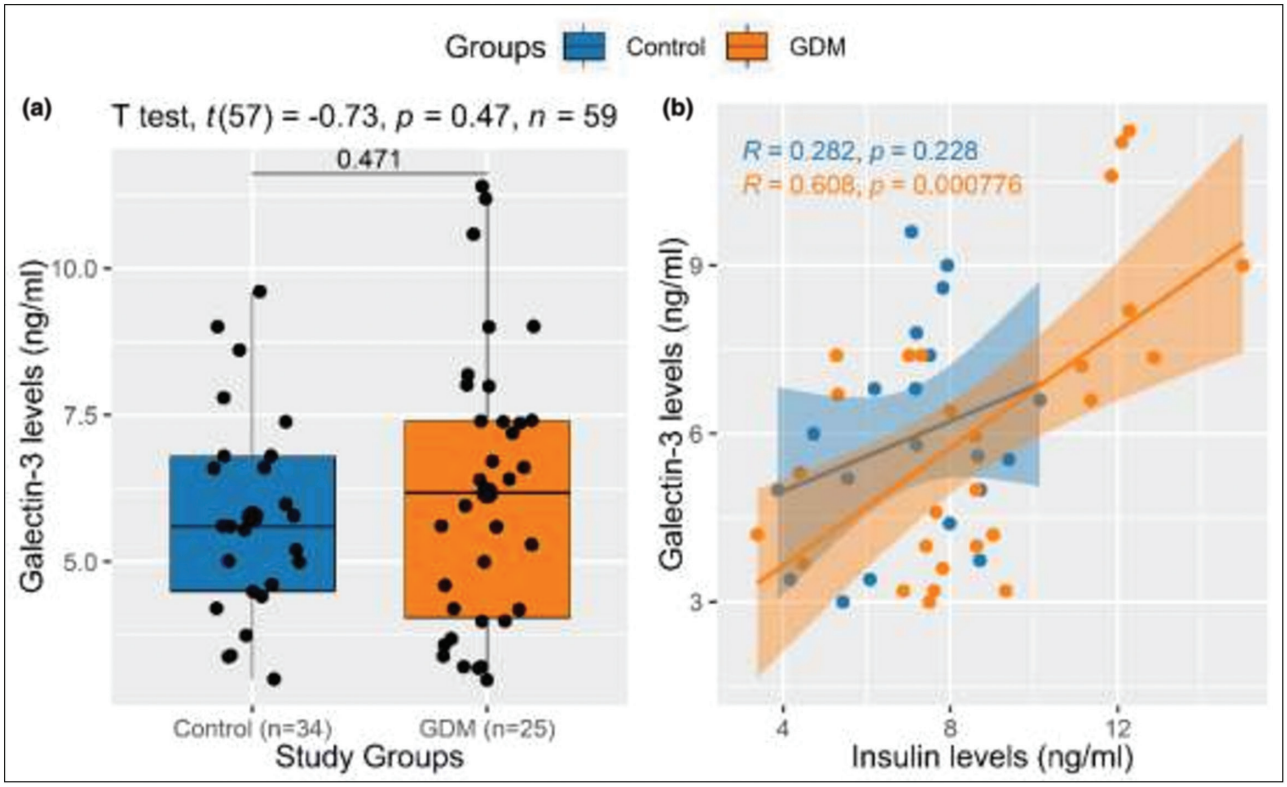

Figure 1: Comparison of the galectin-3 levels in patients with gestational diabetes mellitus and controls. (a) A box plot showing the galectin-3 levels between the study groups ($P = 0.471$). The difference between the two groups was compared using independent samples *t*-test. (b) A scatter plot showing the relationship of galectin-3 level and insulin level in patients with gestational diabetes mellitus (Pearson's r = 0.608, $P < 0.001$) and controls (Pearson's r = 0.282, $P = 228$). Relationship between the galectin-3 level and insulin level was determined using Pearson correlation analysis

with GDM and normal pregnant women in the first group and demonstrated that the Gal-3 level was significantly higher in patients with GDM. In the second group, the patients whose serum Gal-3 level was measured in the first trimester and who developed and did not develop GDM during their follow-up were compared, and the Gal-3 level was found to be significantly higher in the patients who developed GDM. The authors suggested that Gal-3 might be a predictor for the development of GDM and that the Gal-3 level could be used in a risk classification system to assess the risk of developing GDM. It is noteworthy in terms of the potential of affecting the results that both BMI and gestational diabetes history were significantly higher in both groups of patients with GDM assessed in this study.

Zhang *et al.*[16] demonstrated that serum Gal-3 and progesterone levels measured in the third trimester were significantly higher in GDM patients compared with normal pregnant women. They also demonstrated that Gal-3 level was in a strong relationship with both progesterone and insulin resistance parameters (fasting glucose, fasting insulin, HOMA-IR) and drew attention to the possible interaction of progesterone and Gal-3 through insulin resistance.

Freitag *et al.*[17] reported in their study with the patient groups followed in different centers that serum Gal-3 levels measured in the first, second, and third trimesters were stable and reached a significant level in the second and third trimesters in normal pregnant women compared with nonpregnant women. They also reported that there was no difference, in another patient group, in the first and second trimester serum Gal-3 levels in the patients diagnosed with GDM during follow-up and in normal pregnant women, while a significant decrease was observed in serum Gal-3 levels in the GDM patients in the third trimester. In addition, the authors, who assessed trophoblastic functions with exogenous Gal-3 stimulation in trophoblastic cell culture, combined the results of trophoblastic cell culture and serum result and stated that there may be a relationship between GDM and the lack of increase in serum Gal-3 level in the late gestational period.

In another recent study, Heusler *et al.*[18] made a comparison in terms of Gal-3 level and Gal-3 mRNA expression in maternal and umbilical cord blood and placental tissue samples of pregnant women with GDM and normal pregnant women at the time of delivery. There was no difference in serum Gal-3 levels measured at the time of delivery in the pregnant women with GDM and

Table 2: The univariate and multiple analysis result determining the relationship between galectin-3 and some parameters

	All patients (univariate)		GDM patients	
	Corr. coef. (95% CI)	*P* value	Corr. coef. (95% CI)	*P* value
Demographical characteristics				
Age (years)	0.165 (−0.122 to 0.426)	0.258[1]	0.120 (−0.258 to 0.466)	0.536[1]
Gestational age (weeks)	0.182 (−0.090 to 0.429)	0.188[1]	0.193 (−0.173 to 0.513)	0.297[1]
BMI	0.113 (−0.168 to 0.377)	0.429[1]	0.002 (−0.358 to 0.362)	0.990[1]
WHR	0.105 (−0.250 to 0.440)	0.555[2]	0.245 (−0.170 to 0.590)	0.228[2]
Gestational weight gain	0.066 (−0.198 to 0.321)	0.628[1]	0.232 (−0.121 to 0.533)	0.194[1]
Laboratory findings				
Fasting blood glucose	0.090 (−0.180 to 0.350)	0.503[2]	–0.010 (−0.360 to 0.340)	0.956[2]
OGTT 60 min	0.455 (0.130 to 0.690)	0.007[2]	0.444 (0.080 to 0.70)	0.016[2]
OGTT 120 min	0.360 (0.010 to 0.630)	0.036[2]	0.363 (−0.020 to 0.650)	0.053[2]
Insulin	0.509 (0.259 to 0.694)	<0.001[1]	0.608 (0.296 to 0.802)	<0.001[1]
HOMA-IR	0.479 (0.219 to 0.675)	<0.001[1]	0.609 (0.298 to 0.803)	<0.001[1]
HOMA-β	0.209 (−0.100 to 0.480)	0.169[2]	0.313 (−0.090 to 0.630)	0.111[2]
CRP	0.158 (−0.250 to 0.520)	0.432[2]	0.087 (−0.360 to 0.500)	0.702[2]

BMI = body mass index, β = standardized regression coefficient, Corr. coef. (95% CI) = correlation coefficient (95% confidence interval), CRP = C-reactive protein, GDM = gestational diabetes mellitus, HOMA-IR = homeostatic model assessment for insulin resistance, HOMA-β = homeostatic model assessment of β-cell function, OGTT = oral glucose tolerance test, WHR = waist–hip ratio

Regression equations: galectin-3 (ng/mL) = 0.999 + 0.580 × insulin level (ng/mL)

Model statistics: $F = 10.493$, $P = 0.008$, $R^2 = 0.488$, Durbin–Watson = 1.877, $P = 0.830$, $\beta = 0.699$

Data were presented as correlation or regression coefficient (95% confidence intervals)

[1]Pearson correlation coefficient analysis

[2]Spearman's rho correlation coefficient analysis

normal pregnant women, but a significant increase was observed in Gal-3 mRNA expression level in maternal blood and placental tissue samples in the patients with GDM. In addition, Gal-3 mRNA expression was found to be significantly decreased in the umbilical cord blood of the mothers with GDM compared to maternal blood and placental tissue samples. In this study, GDM patients were taking insulin, metformin, or glyburide at different doses. According to these results, the authors suggested that there may be a relationship between the development of GDM and placental intracellular changes and that the placenta may have a protective role for fetus against the potential negative effects of Gal-3.

These different results in serum Gal-3 levels in studies may have stemmed from the fact that the cohorts were of different sizes and characteristics, serum measurements were made at different gestational weeks, there were differences such as GDM, high HbA1c, and macrosomia and polyhydramnios history, and BMI value in the patients included in the study, and there were differences due to measurement in terms of GDM treatment provided and measurements made with different enzyme-linked immunosorbent assay kits. The fact that these conditions were not mentioned in some of the studies makes it difficult to interpret the results of the study.

In our study, the serum Gal-3 level measured during routine GDM screening, in the 24th–28th gestational weeks in pregnant women who did not use insulin or oral antidiabetic drugs, did not have a history of GDM and high A1c levels before or prediabetes and did not differ in terms of age, gestational age, family history of diabetes, BMI, and WHR, and was found to be similar in the pregnant women with GDM and normal pregnant women. However, a significant and strong correlation was determined between Gal-3 and fasting insulin, HOMA-IR, and OGTT 60 min glucose values in the GDM group and fasting insulin and HOMA-IR values in whole pregnancies. Unlike HOMA-IR, there was no significant correlation between Gal-3 and HOMA-β, suggesting that the possible contribution of Gal-3 in the pathogenesis of GDM may be related to insulin resistance rather than impaired insulin secretion.

The major limitations of our study are cross-sectional study, making a single measurement during pregnancy and having a limited number of subjects.

Conclusions

In conclusion, our study has important limitations such as being a cross-sectional study, making a single measurement during pregnancy, and having a limited number of subjects. For this reason, we know that it would not be appropriate to establish a causal connection between the data of our study and the relationship between serum Gal-3 and GDM, but we think that the significant positive correlation between serum Gal-3 levels and insulin resistance parameters demonstrated in our study provides important data on the relationship of Gal-3 with GDM through insulin resistance.

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Conflicts of interest

There are no conflicts of interest.

Ethical approval and patient consent

The study design was approved by the Ethical Committee and Institutional Review Board of the Selcuk University, Faculty of Medicine, where the study was conducted (decision number: 2013/287). Written informed consent was obtained from all participants.

References

1. Mohan V, Bodkin D, Bhavadharini B. Gestational diabetes mellitus: The silent epidemic. J Diabetol 2021;12:1-2.
2. Lauenborg J, Hansen T, Jensen DM, Vestergaard H, Mølsted-Pedersen L, Hornnes P, *et al*. Increasing incidence of diabetes after gestational diabetes: A long-term follow-up in a Danish population. Diabetes Care 2004;27:1194-9.
3. Lekva T, Norwitz ER, Aukrust P, Ueland T. Impact of systemic inflammation on the progression of gestational diabetes mellitus. Curr Diab Rep 2016;16:26.
4. Baldane S, Ipekci SH, Kebapcilar AG, Abusoglu A, Beyhekim H, Ilhan TT, *et al*. Prorenin and secreted frizzled-related protein 4 levels in women with gestational diabetes mellitus. Bratisl Lek Listy 2018;119:450-3.
5. Newlaczyl AU, Yu LG. Galectin-3—A jack-of-all-trades in cancer. Cancer Lett 2011;313:123-8.
6. Dumic J, Dabelic S, Flögel M. Galectin-3: An open-ended story. Biochim Biophys Acta 2006;1760:616-35.
7. Pugliese G, Iacobini C, Pesce CM, Menini S. Galectin-3: An emerging all-out player in metabolic disorders and their complications. Glycobiology 2015;25:136-50.
8. Pugliese G, Iacobini C, Ricci C, Blasetti Fantauzzi C, Menini S. Galectin-3 in diabetic patients. Clin Chem Lab Med 2014;52:1413-23.
9. Atalar MN, Abuşoğlu S, Ünlü A, Tok O, İpekçi SH, Baldane S, *et al*. Assessment of serum galectin-3, methylated arginine and hs-CRP levels in type 2 diabetes and prediabetes. Life Sci 2019;231:116577.
10. Menini S, Iacobini C, Blasetti Fantauzzi C, Pesce CM, Pugliese G. Role of galectin-3 in obesity and impaired glucose homeostasis. Oxid Med Cell Longev 2016;2016:9618092.
11. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2021;44:7-14.
12. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
13. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-9.
14. Monzillo LU, Hamdy O. Evaluation of insulin sensitivity in clinical practice and in research settings. Nutr Rev 2003;61:397-412.
15. Talmor-Barkan Y, Chezar-Azerrad C, Kruchin B, Leshem-Lev D, Levi A, Hadar E, *et al*. Elevated galectin-3 in women with gestational diabetes mellitus, a new surrogate for cardiovascular disease in women. PLoS One 2020;15:e0234732.
16. Zhang Z, Kang X, Guo Y, Zhang J, Xie J, Shao S, *et al*. Association of circulating galectin-3 with gestational diabetes mellitus, progesterone, and insulin resistance. J Diabetes 2021;13:54-62.
17. Freitag N, Tirado-González I, Barrientos G, Cohen M, Daher S, Goldman-Wohl D, *et al*. The Chimera-type galectin-3 is a positive modulator of trophoblast functions with dysregulated expression in gestational diabetes mellitus. Am J Reprod Immunol 2020;84:e13311.
18. Heusler I, Biron-Shental T, Farladansky-Gershnabel S, Pasternak Y, Kidron D, Vulih-Shuitsman I, *et al*. Enhanced expression of galectin-3 in gestational diabetes. Nutr Metab Cardiovasc Dis 2021;31:1791-7.