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ORIGINAL ARTICLE

Serum Irisin Levels in Normal Pregnant and Gestational Diabetic Rat Model

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a pregnancy complication characterized by insulin resistance. Irisin is a myokine that has been associated to obesity and inflammation. The data on irisin levels in pregnancy and GDM is still debatable. This study aimed to assess serum irisin levels and explore its association with some metabolic and inflammatory parameters in normal pregnant and GDM rats.

Methods: Forty-five female albino rats were randomly divided into 3 groups (n=15 animals). The rats of both normal pregnant and GDM-induced groups were fed a normal diet and a Fatty-sucrose diet respectively for five weeks before pregnancy induction. The later injected with streptozotocin on the 7th day of gestation. Body mass index (BMI), serum irisin, triglycerides, total cholesterol, low-density lipoprotein-cholesterol (LDL-c), and high-density lipoproteins-cholesterol (HDL-c), c-reactive protein (CRP), glucose, insulin levels and calculated homeostatic model assessment of insulin resistance index (HOMA-IR) were estimated.

Results: The irisin levels in normal pregnant rats increased significantly more than in controls, whereas it was significantly lower in GDM rats. In GDM rats, BMI, CRP, glucose, and lipid indices, all were significantly raised and negatively linked with irisin. In GDM rats, HDL-C levels were decreased significantly and positively associated with irisin.

Conclusions: Late pregnancy is associated with high serum irisin levels that were lower in GDM rats compared to normal pregnant rats and negatively correlated with insulin resistance, lipid, and inflammatory parameters.

Keywords: Gestational diabetes mellitus; Irsin; Pregnancy; Rats; Insulin resistance

INTRODUCTION

Gestational diabetes mellitus (GDM) is a severe prenatal complication which appears during pregnancy and is defined as glucose intolerance. It is generally disappeared after delivery. The pathogenesis of GDM is primarily caused by insulin resistance and insufficient insulin compensation [1]. Women who are diabetic during pregnancy have a higher chance of developing Type 2 Diabetes Mellitus (T2DM) and heart disease later in life [2]. Irisin is a novel myokine, adipokine, and neurokine [3,4]. It is made up of 112 amino acids and processed from the product of fibronectin type III domain containing protein 5 (FNDC5) due to the activation of Peroxisome- Proliferator-Activated -Receptor- γ (PPARγ) Coactivator-1α (PGC-1α) [3,4]. Irisin is transcribed from the FNDC5 gene, after its transference to the outer cell membrane; it is proteolytically cleaved on the extracellular surface of the muscle cells and released into plasma [3].

Previous research had found that patients with type 2 diabetes have significantly lower circulating irisin levels than people without diabetes [5,6], also there is a negative relationship between circulating irisin, obesity, and insulin resistance. FNDC5 in skeletal muscle and serum irisin levels are closely linked to body weight loss and improved insulin sensitivity [5,6,7]. Irisin operates primarily on white adipose tissue and enhances energy consumption, which can help to alleviate insulin resistance caused by a high-fat diet [7,8]. Irisin is a protein that is expressed in the human placenta and ovary and plays a role in

reproductive function as well as pregnancy-related metabolic alterations [9]. Human studies on the level of irisin in GDM are inconsistent, and their findings are confusing.

Many studies have found that women with GDM have lower irisin levels than healthy pregnant women [10,11,12,13,14], whereas others have found no difference [15,16]. Irisin levels, on the other hand, were elevated in GDM patients [17]. Similarly, in GDM, the link between irisin and energy metabolism indicators is still a disconcordant [12,13,17].

As a result, the goal of this work was to measure serum irisin levels in late pregnancy and to see how experimentally induced gestational diabetes affects irisin levels in albino rats. In addition, to see if there was a link between irisin level and certain metabolic and inflammatory parameters in both normal and GDM-induced.

METHODS

Forty-five virgin female albino rats of a local strain aged 6-9 weeks and weighing 100-130 g, in addition to ten adult males (For fertilization) were used in this experiment. They were obtained from the animal house of the Faculty of Veterinary Medicine, Zagazig University. Rats were housed in steel wire cages (5 per cage) measuring 50× 60×60 cm, at the animal house of the Faculty of Medicine, Zagazig University. They were kept at a suitable temperature, had a regular light/dark cycle, were fed ordinary chow, and had free access to water. The experimental procedure was approved by the Zagazig University Faculty of Medicine's Local Medical Ethics Committee (Institutional Review Board, IRB). All animal experiments comply with the ARRIVE guidelines and should be carried out in accordance with the U.K. Animals.

The rats were divided into three equal groups (n=12 each) after one week of acclimation [18]. Group I (Control) rats were fed a standard diet (25.8% protein, 62.8% carbohydrates, and 11.4% fat) [19] and were given citrate buffer as a vehicle intraperitoneally (I.P). Group II (normal pregnant) rats were fed a standard diet for five weeks prior to induction of pregnancy, after which they were injected I.P with a vehicle on the seventh day of pregnancy [19, 20]. Group III (GDM-induced) rats were fed a Fatty-sucrose diet (FSD) (25% sucrose, 40% beef tallow, and 20% casein protein- FSD was prepared in the Department of Nutrition, Faculty of Veterinary Medicine, Zagazig University) for five weeks prior to induction of pregnancy, then given a single I.P dose of streptozotocin (STZ) (25 mg/kg) on the seventh day of gestation [19,20].

Induction of pregnancy: After one week of acclimation, in order to induce pregnancy, animals were examined for estrous cycles for two consecutive weeks. [21]. Female rats that were found to be in estrus phase were paired with male rats. Females were segregated after mating until the time of investigation to ensure correct conception timing. A vaginal smear was taken in the next morning. The presence of a copulation plug or spermatozoa in the vaginal canal verified copulation. The presence of sperms indicates that the pregnancy had begun (first day) [22].

Induction of experimental GDM: Rats were time mated overnight with males after five weeks of FSD-feeding, and the presence of sperms in the vaginal smear checked in the morning was considered the first day of pregnancy [22].

After overnight fasting at the 7^{th} day of gestation, FSD-feeding rats were injected I.P. with a low dose of STZ (25 mg/kg) (Sigma–Aldrich, USA) which dissolved in 0.1 mol/L sodium citrate (PH 4.5) [20]. The blood glucose level for each rat was measured using a One Touch Glucometer (blood was drawn from the tail vein) [23]. After 6 hours of STZ injection, the rats were administered a 10% glucose solution orally for the next 48 hours. The same diet was given to all of the rats.

BMI (body mass index): The rats were fasted overnight, placed in a sealed plastic container, and weighed at the end of the study. A metal ruler was used to measure the rat's length from nose to anus. The body mass index (BMI) was calculated as body mass (g) divided by length (cm2); this index can be used as an indicator of obesity, with a cutoff value of >0.68 g/cm^2 [24].

Blood sampling: Blood samples were taken from virgin and pregnant rats (on day 21 of pregnancy) that had been fasted overnight and sedated with diethyl ether. Blood was drawn from the retro-orbital venous plexus and placed in clean plastic centrifuge tubes to clot. Blood was centrifuged at 3000 rpm for 15 minutes to remove the serum, which was kept at -20 ºC until used.

Serum analysis: Irisin levels were measured using rat enzyme-linked immunoassay kits (Uscn Life Science USA), as described by Tan et al. [25]. Estimation of total cholesterol (TC) values was done using total cholesterol kits (BioSource Europe S.A). according to Tietz [26]. Estimation of High-density lipoproteins (HDL-c) levels was done by using HDL-cholesterol kits (BioSource Europe S.A), according to Nauk et al. [27].

Low-density lipoproteins (LDL-c) were calculated according to Friedewald et al. [28], LDL=TC-HDL-TG/5. Total triglycerides (TG) levels were measured using triglycerides ESPAS SL kits A (Elttech S.A., Lyon, France) according to Naito [29].

C reactive proteins (CRP) levels were measured according to Ridker et al. [30] using CRP Kits (MonobindInc Lake Forest, Ca 92630, USA). Insulin levels were measured according to Temple et al. [31] using KAP1251-INS-EASIA (Enzyme Amplified Sensitivity Immunoassay) kits (BioSource Europe S.A., Belgium). Glucose levels were measured according to Tietz [26] using glucose enzymatic (GOD-PAP)-liquizyme rat Kits (Biotechnology, Egypt).

Calculation of homeostatic model assessment of insulin resistance index (HOMA-IR): was done according to the formula described by Matthews et al. [32] as HOMA- IR = fasting serum glucose (mg/dl) x fasting serum insulin (µIU/ml) /405.

Statistical analysis: The Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, United States version 20) was used for statistical analysis. The results were given as mean and standard deviation (SD). To compare the means of each two different groups, the One-way analysis of variance (ANOVA) was used, followed by the student-least significant difference (LSD) post hoc test. Pearson's correlation analysis was used to look for possible relationships between serum irisin levels and all other variables. P values less than 0.05 were statistically significant in all statistical tests.

RESULTS

Compared to control rats, normal pregnant rats had a significant increase in mean values of BMI (P<0.001), serum levels of irisin (P<0.001), insulin (P<0.01), CRP (P<0.01), TC (P<0.001), TG (P<0.001), LDL-c (P<0.001) and HOMA-R (P<0.05) (Table 1). However, mean values of serum levels of HDL-c were significantly decreased (P<0.05) in normal pregnant rats in comparison to controls, while serum glucose levels between both groups did not have a significant difference (P>0.05). Additionally, in the GDM-induced group, rats exhibited a significant increase in mean values of BMI (P<0.001), HOMA-R (P<0.001), serum glucose (P<0.001), TC (P<0.001), TG (P<0.001), LDL-c (P<0.001) and CRP (P<0.001) as compared to both control and normal pregnant groups. Also, they showed a significant reduction in mean values of serum irisin and insulin in relation to normal pregnant rats but a significant increase compared to controls (P<0.01, P<0.001 respectively) while the levels of HDL-C levels were significantly lower in relation to both groups (P<0.001).

Regarding Table 2 and Figures (1-9), the normal pregnant group displayed a positive correlation between the serum irisin levels and BMI (r= 0.719, P<0.01), serum glucose (r=0.734, P<0.01), insulin levels (r=0.561, P<0.05), HOMA-IR (r=0.708, P<0.01), serum TC (r=0.659, P<0.01), TG (r=0.666, P<0.01), LDL-c (r=0.524, P<0.05), CRP levels (r=0.848, P<0.001), HDL-c (r=0.659, P<0.001) However, in GDM rats, serum irisin levels were negatively correlated to BMI (r= -0.778, P<0.01), HOMA-IR (r=-0.782, P<0.01), serum glucose (r=-0.782, P<0.01), TC (r=-0.771, P<0.01), TG (r=-0.579, P<0.05), LDL-c (r=-0.559, P<0.05) and CRP (r=0.652, P<0.01) levels and they have positively correlated to serum HDL-c levels (r=-0.676, P<0.01).

Table 1: Statistical analysis of serum levels of all parameters in the three studied groups.

Parameters	Control	Normal Pregnant	GDM
BMI (g/cm2)	0.50 ± .01	0.64 ± 0.01 [a]	0.74 ±0 .02 [a, b]
Glucose (mg/dL)	83.67± 7.15	84.47± 6.99	179± 17.34 [a, b]
Insulin(uIU/mL)	6.53± 1.36	13.67 ± 2.38 [a]	8.20±1.26 [a, b]
HOMA-IR	1.38± 0.35	2.85± 0.68 [a]	3.51±0.79 [a, b]
TC (mg/dL)	110.93 ±5.15	147.20 ± 8.03 [a]	206.13 ± 7.58 [a, b]
LDL-cholesterol (mg/dL)	41.21± 7.45	56.40± 7.82 [a]	130.29± 7.04 [a, b]
TG (mg/dL)	72.40 ± 9.72	131.94 ± 23.65 [a]	234.87 ± 38.04 [a, b]
HDL-C(mg/dL)	57.07 ± 8.48	64.40 ± 8.54 [a]	28.87 ± 5.05 [a, b]
CRP (Ug/Ml)	0.62±0.15	1.43± 0.07 [a]	3.07± 0.08 [a, b]
Irisin (ng/ml)	7.6 ± 1.58	12.39 ± 1.74 [a]	9.96 ± 1.46 [a, b]

a = p-value of significance versus control.
b = p-value of significance versus normal pregnant group.

Table 2: Pearson's correlation analysis between serum irisin and all parameters in normal pregnant and GDM-induced groups.

	Normal Pregnant		GDM	
	r	P value	r	P value
BMI (gm/Cm^2)	0.719	0.003**	-0.778	0.001**
Glucose (mg/dL)	0.734	0.002**	-0.782	0.001**
Insulin (mIU/mL)	0.561	0.03*	-0.555	0.032*
HOMA-IR	0.708	0.003**	-0.779	0.001**
TC (mg/dL)	0.659	0.008**	-0.771	0.001**
LDL-c (mg/dL)	0.524	0.045*	-0.559	0.030*
TG (mg/dL)	0.666	0.007**	-0.579	0.024*
HDL-c(mg/dL)	0.659	0.008**	0.676	0.006**
CRP (Ug/Ml)	0.688	<0.005***	-0.708	0.003**

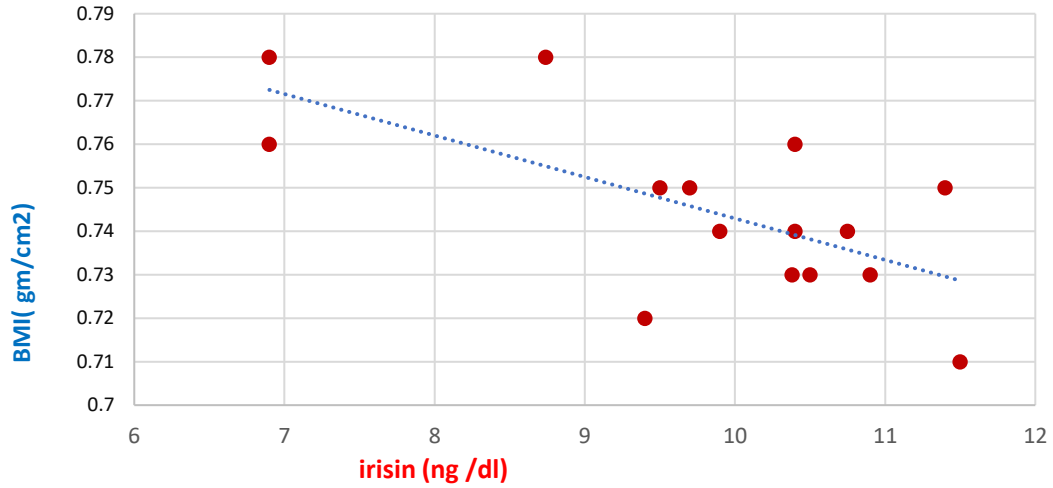

Figure (1): Pearson's correlation analysis between irisin and BMI in GDM rats.

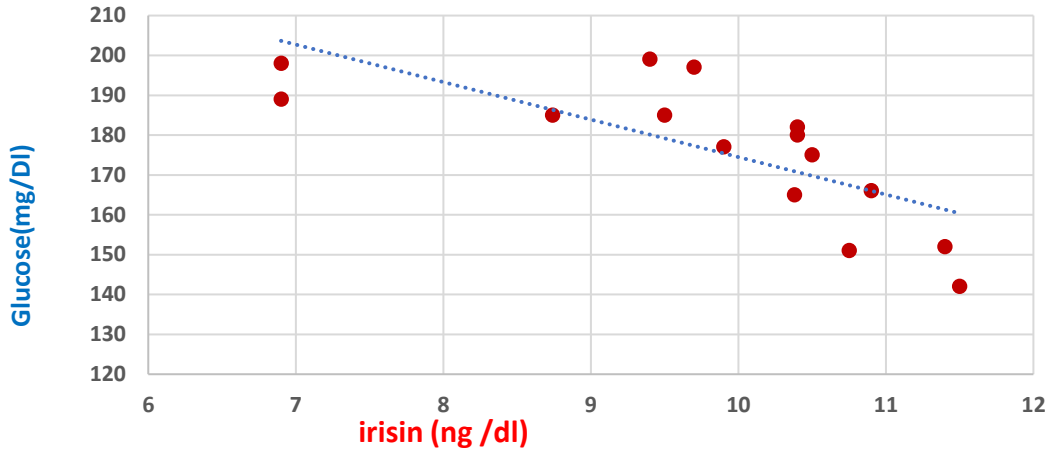

Figure (2): Pearson's correlation analysis between irisin and glucose in GDM rats.

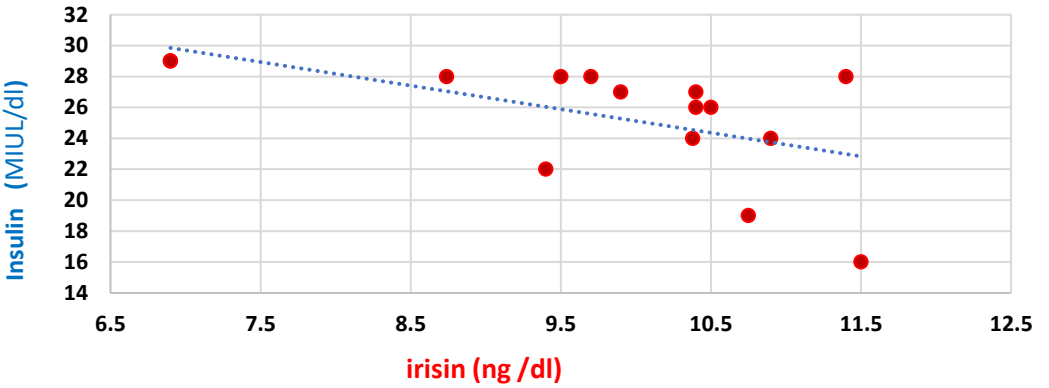

Figure (3): Pearson's correlation analysis between irisin and insulin in GDM rats.

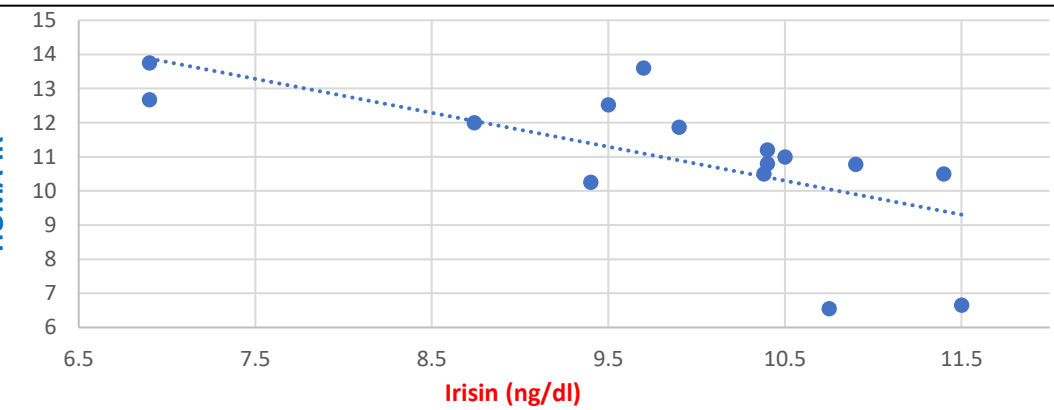

Figure (4): Pearson's correlation analysis between irisin and HOMA-IR in GDM rats

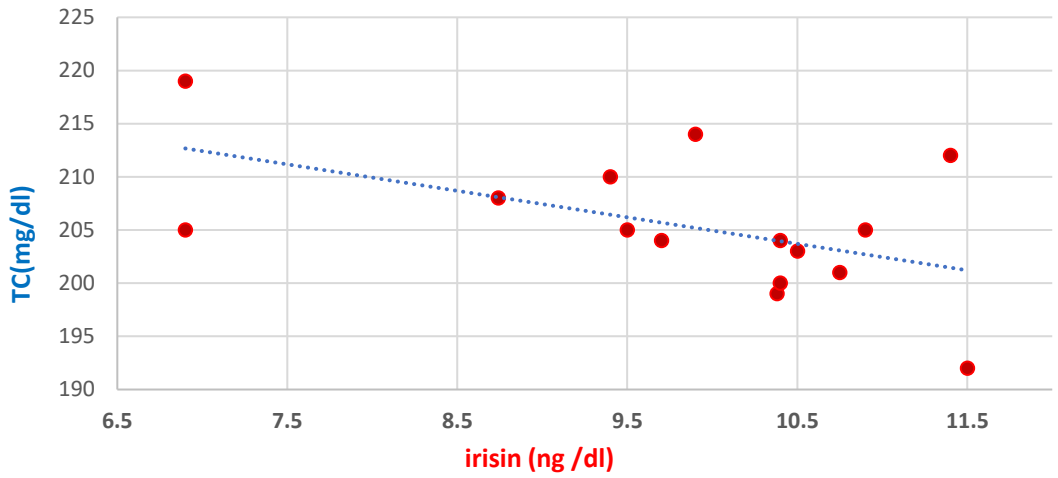

Figure (5): Pearson's correlation analysis between irisin and TC in GDM rats.

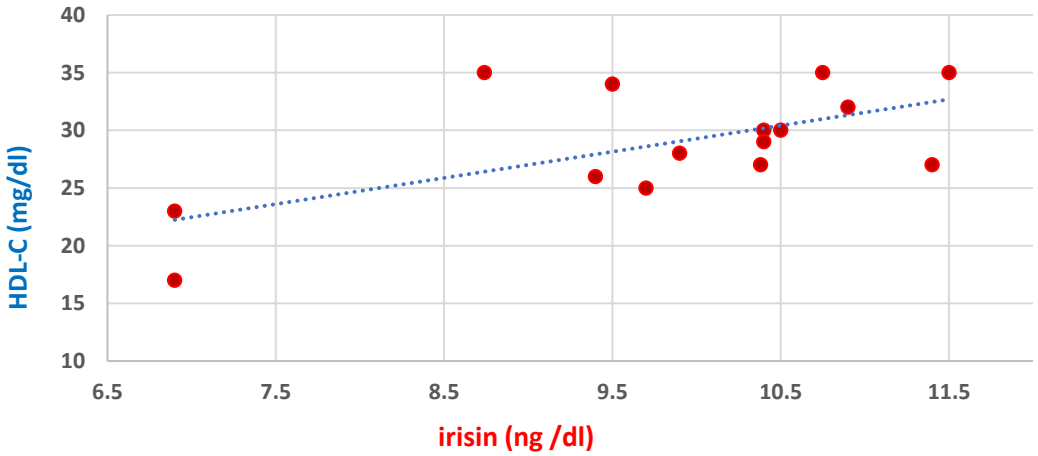

Figure (6): Pearson's correlation analysis between irisin and HDL-C in GDM rats.

DISCUSSION

The current study found that serum irisin levels in normal pregnant rats were considerably higher than in controls, but that this increase was significantly smaller in rats with GDM. In line with these findings, Ebert et al. [15] discovered that pregnant women have higher irisin concentrations than non-pregnant women, but no significant variations in irisin levels during and after pregnancy [16]. Garces et al. [9] proved that as the pregnancy progressed, serum levels of irisin and placental expression of its precursor raised, and irisin levels were positively linked with gestational age during pregnancy, compared to non-pregnant women. In normal pregnant women, an increase in irisin levels may occur to offset the insulin resistance that is frequent during pregnancy and to diminish the adverse metabolic and vascular implications of this condition [9].

Furthermore, as the pregnancy proceeds, the maternal BMI rises. BMI helps to maintain the balance of energy storage and expenditure by increasing circulating irisin levels [15]. The lower irisin level in GDM in late pregnancy could be attributed to the negative feedback of the initial rise in irisin's in early pregnancy, which negatively hampered its secretion from adipose tissues [4]. In addition, once diabetes develops, a compensatory

over-secretion of irisin will evolve into a secretion failure from the skeletal muscles and adipose tissues [33]. In addition, GDM is commonly accompanied by inflammation, which could be the main cause that explains why circulating irisin concentrations are low [34]. According to these findings, in comparison with normal pregnant, many studies have found that maternal serum irisin levels are significantly lower in women with GDM [10,11,13,35]

Ural et al. [14] and Erol et al. [36] both came to the conclusion that serum irisin levels might be used as a new marker for GDM and that decreasing irisin levels could be indicative of GDM. Other researchers, on the other hand, have no evidence that irisin can be used as a predictive risk marker for developing GDM in later pregnancy [35]. Newly, Cui et al. [37] discovered in a meta-analysis that low irisin levels in pregnant women with GDM may lead to increased blood glucose and poor insulin sensitivity. In contrast, Piya et al. [16] found that obese pregnant and GDM pregnant women had higher irisin levels than non-obese pregnant women. Ebert et al. [15] and Celik [38], on the other hand, observed no change significant difference between pregnant women with and without GDM.

In the current study, GDM rats had significantly more weight as a result of FSD intake, higher glucose levels, and insulin resistance (HOMA-IR) with lower insulin levels than healthy pregnant rats. Likewise, they revealed a rise in CRP levels and lipid profile (TC, TG, LDL-c), with a significant drop in HDL-C values. These results were concordant with those of Abdul Aziz et al. [19] and Liang et al. [39]. In GDM rats, placental hormone production, STZ, which led to partial pancreatic beta cell injury, and a fatty diet intake altered glucose tolerance and provoked insulin resistance [20, 19,40]. As a result of hormonal changes linked with pregnancy, glucose and lipid metabolism may be affected [30].

As a result, when compared to healthy controls in this experiment, normal pregnant rats displayed a profile of insulin resistance and dyslipidemia in the form of higher TC, LDL- cholesterol, and TG, as well as lower levels of HDL- cholesterol. Phuse [41] explained the changes in lipid metabolism in this study, he proposed that TC, TG, and LDL-cholesterol increased in the third trimester, whereas HDL-cholesterol dropped, compared to the first and second trimesters. Elevated TG levels and alterations in (HDL-c and LDL-c) metabolism are attributed to enhance hepatic lipase action caused by increased estradiol, which leads to increased hepatic TG synthesis and decreased lipoprotein lipase activity, resulting in decreased adipose tissue catabolism [42]. GDM is frequently characterized by hyperlipidemia [43].

Increased serum TC and TG may be due to FSD and increased dietary cholesterol and triglyceride absorption from the small intestine, as well as reduced T.G. uptake in peripheral tissues due to insulin-dependent Lipoprotein Lipase dysfunction, increased hepatic secretion of triglyceride-enriched Very Low-Density Lipoprotein, or activation of hepatic 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, which is a rate-limiting enzyme involved in cholesterol synthesis [44].

In the normal pregnant group, irisin had a significant positive correlation with BMI, TC, TG, LDL-C, glucose, HOMA-IR, insulin, and CRP, but the correlation was significantly negative in the gestational diabetic group. In both groups, however, irisin was strongly positively linked with HDL-C. Garcés et al. [9], Piya et al. [16], and Ebert et al. [15] are in agreement with us. They found that serum irisin was positively linked with BMI, fasting glucose, insulin, and HOMA-IR in healthy pregnant women. Yuskel et al. [12] and Ural et al. [14] found that irisin levels were adversely linked with BMI and insulin resistance in GDM women. Kulhan et al. [35] recently discovered that serum irisin levels in GDM women were negatively correlated with BMI but positively correlated with insulin resistance. Unexpectedly, none of the BMI or glucose parameters were linked to serum irisin levels, according to Al-Ghazali et al. [10]. These contradictory results of the former studies could be explained by changes in gestational age, sampling time, and screening criteria used for GDM. The irisin-encoding gene FNDC5 expression in adipose and muscular tissue is reduced in obese and diabetic patients [7]. In obesity, the physiological irisin was unable to maintain the balance between energy storage and expenditure, resulting in adipose tissue hypertrophy and an increase of fat storage [45]. In contrast to the current study, serum irisin in pregnant diabetic women was strongly positively linked with BMI [45], fasting insulin, and HOMA-IR [14]. However, there was no association between circulating irisin and BMI in GDM women [11,14,15].

In GDM, Zhao et al. [13] demonstrated a positive correlation between serum irisin and HDL-C. Furthermore, Choi et al. [5] concluded that serum

irisin levels were significantly negatively linked with triglycerides levels in diabetes individuals. In pregnant diabetic women, however, there was no link between serum irisin and total cholesterol, triglycerides, HDL-C and LDL-C [11,16], or CRP [15].

CONCLUSIONS

Late pregnancy is linked with an increase in blood irisin levels; however, irisin levels in GDM-induced rats were lower than in normal pregnant rats and were negatively correlated with glucose, lipid, and inflammatory markers. Irisin may play a critical role in the development of GDM and could be a promising marker for GDM diagnosis in the future, thus additional research is needed.

REFERENCES

1. Wendland EM, Torloni MR, Falavigna M, Trujillo J, Dode MA, Campos MA, et al. Gestational diabetes and pregnancy outcomes--a systematic review of the World Health Organization (WHO) and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria. BMC Pregnancy Childbirth 2012; 12 (23): 1-13.
2. Lee H, Jang HC, Park HK, Metzger BE, Cho NH. Prevalence of type 2 diabetes among women with a previous history of gestational diabetes mellitus. Diabetes Res. Clin. Pract. 2008; 81 (1): 124-9.
3. Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, et al. PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature 2012; 481 (7382): 463–8.
4. Roca-Rivada A, Castelao C, Senin LL, Landrove MO, Baltar J, Belén Crujeiras A, et al. FNDC5/irisin is not only a myokine but also an adipokine. PLOS ONE 2013; 8 (4): e60563.
5. Choi YK, Kim MK, Bae KH, Seo HA, Jeong JY, Lee WK, et al. Serum irisin levels in new-onset type 2 diabetes. Diabetes Res. Clin. Pract. 2013; 100 (1): 96–101.
6. Liu JJ, Wong MD, Toy WC, Tan CS, Liu S, Ng XW, et al. Lower circulating irisin is associated with type 2 diabetes mellitus. J. Diabetes Complicat. 2013; 27 (4): 365–9.
7. Moreno-Navarrete JM, Ortega F, Serrano M, Guerra E, Pardo G, Tinahones F, et al. Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. J. Clin. Endocrinol. Metab. 2013; 98 (4): E769–78.
8. Sesti G, Andreozzi F, Fiorentino TV, Mannino GC, Sciacqua A, Marini MA, et al. High circulating irisin levels are associated with insulin resistance and vascular atherosclerosis in a cohort of nondiabetic adult subjects. Acta Diabetol. 2014; 51 (5): 705–13.
9. Garcés MF, Peralta JJ, Ruiz-Linares CE, Lozano AR, Poveda NE, Torres-Sierra AL, et al. Irisin levels during pregnancy and changes associated with the development of preeclampsia. J Clin Endocrinol Metab 2014; 99 (6): 2113-9.
10. Al-Ghazali MJ, Ali, HA, Al-Rufaie, MM. Serum irisin levels as a potential marker for diagnosis of gestational diabetes mellitus. Acta Biomed 2020; 91 (1): 56–63.
11. Kuzmicki M, Telejko B, Lipinska D, Pliszka J, Szamatowicz M, Wilk J, et al. Serum irisin concentration in women with gestational diabetes. Gynecol. Endocrinol. 2014; 30 (9): 636-9.
12. Yuksel MA, Oncul M, Tuten A, Imamoglu M, Acikgoz AS, Kucur M, et al. Maternal serum and fetal cord blood irisin levels in gestational diabetes mellitus. Diabetes Res. Clin. Pract. 2014; 104 (1): 171–5.
13. Zhao L, Li J, Li ZL, Yang J, Li ML, Wang GL. Circulating irisin is lower in gestational diabetes mellitus. Endocr. J. 2015; 62 (10): 921-6.
14. Ural UM, Sahin SB, Tekin YB, Cüre MC, Sezgin H. Alteration of maternal serum irisin levels in gestational diabetes mellitus. Ginekol. Pol. 2016; 87 (5): 395–8.
15. Ebert T, Stepan H, Schrey S, Kralisch S, Hindricks J, Hopf L, et al. Serum levels of irisin in gestational diabetes mellitus during pregnancy and after delivery. Cytokine 2014; 65 (2): 153–8.
16. Piya MK, Harte AL, Sivakumar K, Tripathi G, Voyias PD, James S, et al. The identification of irisin in human cerebrospinal fluid: influence of adiposity, metabolic markers, and gestational diabetes. Am. J. Physiol. Endocrinol. Metab. 2014; 306 (5): E512–8.
17. Usluoğullari B, Usluogullari CA, Balkan F, Orkmez M. Role of serum levels of irisin and oxidative stress markers in pregnant women with and without gestational diabetes. Gynecol Endocrinol. 2017; 33 (5): 405-7.
18. Gui Y, Silha JV, Murphy LJ. Sexual dimorphism and regulation of resistin,

adiponectin, and leptin expression in the mouse. Obes. Res. 2004; 12 (9): 1481-91.
19. Abdul Aziz SH, John CM, Mohamed Yusof NI, Nordin M, Ramasamy R, Adam A, et al. Animal Model of Gestational Diabetes Mellitus with Pathophysiological Resemblance to the Human Condition Induced by Multiple Factors (Nutritional, Pharmacological, and Stress) in Rats. Biomed Res. Int. 2016; 2016: 9704607.
20. Abdel-Reheim ES, Abd-Elmoneim AA, Hosni AA. Fatty-sucrosed diet/minimal dose of streptozotocin treated rat: a novel model of gestational diabetes mellitus, metabolic and inflammatory insight. Journal of Diabetes & Metabolism 2014; 5 (9): P.430.
21. Marcondes FK, Bianchi FJ, Tanno AP. Determination of the estrous cycle phases of rats: some helpful considerations. Braz J Biol 2002; 62 (4): 609–14.
22. Klukovits A, Gáspár R, Sántha P, Jancsó G, Falkay G. Functional and histochemical characterization of a uterine adrenergic denervation process in pregnant rats. Biol Reprod 2002; 67 (3): 1013- 7.
23. Hoybergs YM, Meert TF. The effect of low-dose insulin on mechanical sensitivity and allodynia in type 1 diabetes neuropathy. Neurosci. Lett. 2007; 417 (2): 149-154.
24. Novelli EL, Diniz YS, Galhardi CM, Ebaid GM, Rodrigues HG, Mani F, et al. Anthropometrical parameters and markers of obesity in rats. Lab. Anim. 2007; 41 (1): 111-9.
25. Tan BK, Chen J, Farhatullah S, Adya R, Kaur J, Heutling D, et al. Insulin and metformin regulate circulating and adipose tissue chemerin. Diabetes 2009; 58 (9): 1971–7.
26. Tietz NW. Clinical guide to laboratory tests. Pbl. W.B. Saunders, Co., Philadelphia, 1995: 509-512.
27. Nauck M, März W, Jarausch J, Cobbaert C, Sägers A, Bernard D, et al. Multicenter evaluation of homogenous assay for HDL-Cholesterol without sample pretreatment. Clin Chem 1997; 43 (9): 1622-9.
28. 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 (6): 499-502.
29. Naito HK. Triglycerides in clinical chemistry: theory, analysis and correlation. Pbl. Kaplan LA and Pesce A.J., U.S.A., 1989; 997.
30. Ridker PM, Rifai N, Pfeffer MA, Sacks FM, Moye LA, Goldman S, et al. Inflammation, pravastatin and the risk of coronary events after myocardial infarction in patients with average cholesterol levels. Circulation 1998; 98 (9): 839- 44.
31. Temple R, Clark PM, Hales CN. Measurement of insulin secretion in type 2 diabetes: problems and pitfalls. Diabet. Med. 1992; 9 (6): 503-12.
32. 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 (7): 412-9.
33. Qiu S, Cai X, Yin H, Zügel M, Sun Z, Steinacker JM, et al. Association between circulating irisin and insulin resistance in non-diabetic adults: A meta-analysis. Metabolism 2016; 65 (6): 825-34.
34. Zhang M, Chen P, Chen S, Sun Q, Zeng QC, Chen JY, et al. The association of new inflammatory markers with type 2 diabetes mellitus and macrovascular complications: a preliminary study. Eur. Rev. Med. Pharmacol. Sci. 2014; 18 (11): 1567-72.
35. Kulhan NG, Kulhan M, Turkler C, Ata N, Kiremitli T, Kiremitli S. Could serum levels of irisin be used in gestational diabetes predicting? .Taiwan J Obstet Gynecol. 2019; 58 (3): 434–7
36. Erol O, Erkal N, Ellidağ HY, İsenlik BS, Aydın Ö, Derbent AU, et al. Irisin as an early marker for predicting gestational diabetes mellitus: a prospective study. J. Matern.-Fetal Neonatal Med. 2016; 29 (22): 3590-5.
37. Cui L, Qiao T, Xu F, Li Z, Chen T, Su H, et al. Circulating irisin levels of prenatal and postnatal patients with gestational diabetes mellitus: A systematic review and meta-analysis. Cytokine 2020; 126: 15492.
38. Celik N. Serum irisin levels are correlated with insulin resistance in women with gestational diabetes mellitus. Int J Med Biochem. 2020; 3 (2): 91-5.
39. Liang C, DeCourcy K, Prater MR. High-saturated-fat diet induces gestational diabetes and placental vasculopathy in C57BL/6 mice. Metab. Clin. Exp. 2010; 59 (7): 943–50.

40. Holemans K, Caluwaerts S, Poston L, Van Assche FA. Diet-induced obesity in the rat: a model for gestational diabetes mellitus. Am J Obstet Gynecol. 2004; 190 (3): 858–65.
41. Phuse SS. Effective study of lipid profile during pregnancy. Int J Appl Biotechnol and Biochem 2016; 2 (4): 381–6.
42. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J. Clin. Endocrinol. Metab. 2004; 89 (6): 2548–56.
43. Herrera E, Ortega-Senovilla H. Disturbances in lipid metabolism in diabetic pregnancy—are these the cause of the problem? Best Pract Res Clin Endocrinol Metab. 2010; 24 (4): 515–25.
44. Shah SS, Shah GB, Singh SD, Gohil PV, Chauhan K, Shah KA, et al. Effect of piperine in the regulation of obesity-induced dyslipidemia in high-fat diet rats. Indian J. Pharmacol. 2011; 43 (3): 296-9.
45. Chen JQ, Huang YY, Gusdon AM, Qu S. Irisin: a new molecular marker and target in metabolic disorder. Lipids Health Dis. 2015; 14: 1-6.

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SUPPLEMENTARY FILES

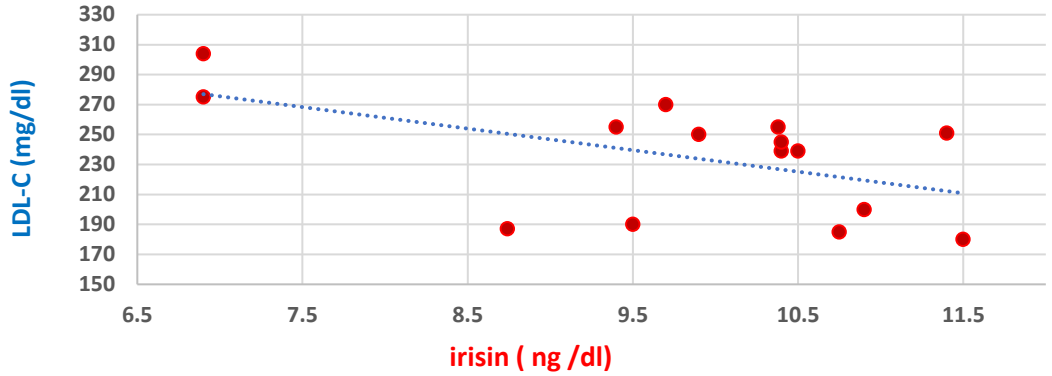

Figure (7): Pearson's correlation analysis between irisin and LDL-C in GDM rats

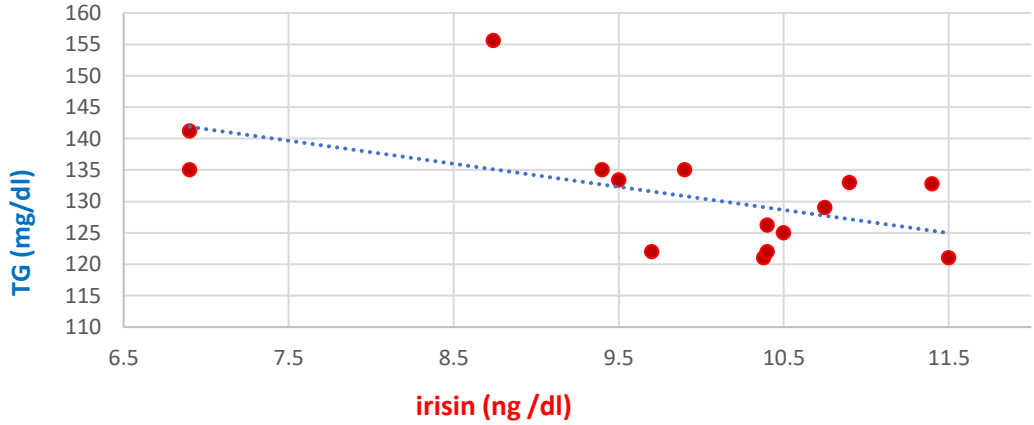

Figure (8): Pearson's correlation analysis between irisin and TG in GDM rats

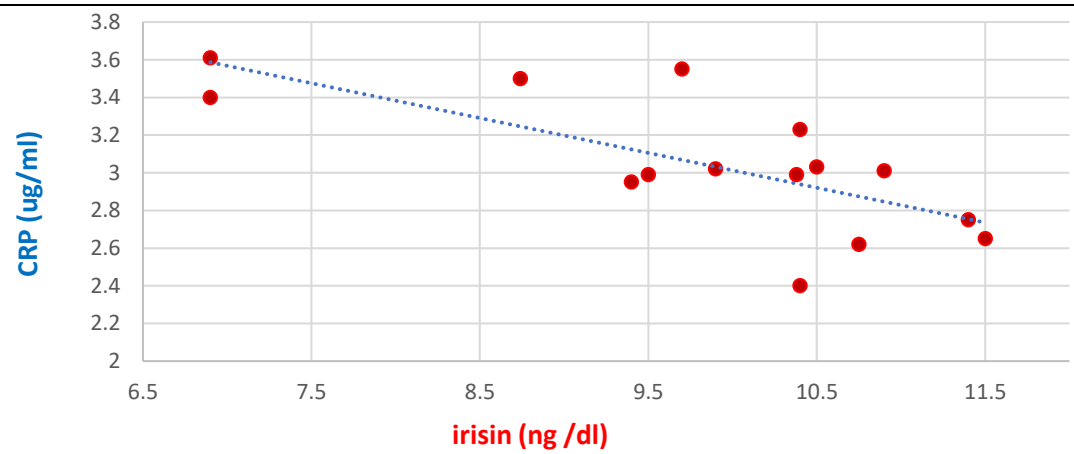

Figure (9): Pearson's correlation analysis between irisin and CRP in GDM rats.