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SERUM VASPIN LEVELS IN NORMAL PREGNANT AND GESTATIONAL DIABETIC ALBINO RAT MODEL

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a major pregnancy complication with increased blood glucose levels and insulin resistance. Vaspin is a visceral adipokine that is synthesized and secreted by abdominal fat tissue and one of the superfamily of serine protease inhibitors. Data proposed vaspin levels in normal pregnancy and GDM are still controversial.

Objective : To assess serum vaspin levels in both of late pregnancy and experimentally-induced GDM in relation to certain metabolic parameters in albino rats.

Material and methods: Thirty six virgin female albino rats of a local strain weighing 100-150 g were divided randomly into three equals groups. Group I (Control); virgin rats were fed normal diet. Group II (normal pregnant); rats were fed normal diet for five weeks before induction of pregnancy. Group III (experimentally-induced GDM); rats were fed fatty-sucrose diet (FSD) for five weeks before induction of pregnancy, then injected intraperitoneally with streptozotocin (25 mg/kg) on the 7^{th} day of gestation. In all groups, serum vaspin, body mass index (BMI), serum estradiol, progesterone, total triglycerides (TG), total cholesterol (TC), low density lipoproteins-cholesterol (LDL-c), high density lipoproteins-cholesterol (HDL-c), glucose, insulin levels and calculated homeostatic model assessment of insulin resistance index (HOMA-IR) were estimated.

Results: Normal pregnant rats showed a significant increase in BMI, serum vaspin, TG, TC, LDL-c, insulin levels and HOMA-IR compared to controls. Additionally, serum vaspin levels were significantly and positively correlated with BMI, serum glucose, TG levels and HOMA-IR. GDM-induced rats had significantly increased levels of serum vaspin, TC, TG, LDL-c, glucose, BMI and HOMA-IR, while decreased insulin and HDL-c levels compared to normal pregnant and control rats. Moreover, serum vaspin levels showed significant positive correlations with BMI, HOMA-IR, glucose, TG, TC levels, and an inverse correlation with HDL-c levels in GDM-induced group.

Conclusion: Serum vaspin levels increased in both of late pregnancy and experimentally-induced GDM, but more in the later possibly for compensating GDM-induced insulin resistance and dyslipidemia.

Key words: Gestational diabetes mellitus, vaspin, pregnancy, insulin resistance.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a major pregnancy complication with increased blood glucose levels and insulin resistance that affects mother and fetal health ***(Kalra et al., 2013)***. The pregnancy is accompanied by a gradual increase in insulin resistance until delivery which leads to an increase in insulin secretion in

order to maintain normal glucose tolerance. However, insulin sensitivity is restored to normal after delivery *(Miehle et al., 2012)*. As a long term complication, women with GDM have more risk for type 2 diabetes mellitus (T2DM) and cardiovascular diseases after pregnancy ***(Bao et al., 2015).*** The pathophysiological mechanisms for the insulin resistance with gestational diabetes are still unclear. Obesity is an important risk factor for the occurrence of GDM ***(Farren et al., 2015).***

Vaspin is a visceral adipokine that is synthesized and secreted by abdominal fat tissue. It is one of the superfamily of serine protease inhibitors ***(Hida et al., 2005).*** It has a biological role in inflammation, carbohydrate and lipid metabolism ***(Cura et al., 2014). Caminos et al. (2009)*** found that vaspin is present in rat and human placenta, where its expression increases gradually during pregnancy and reaching the maximal level at the end of gestation**.** In addition, it predominates in cytotrophoblasts and syncytiotrophoblasts during the first trimester, whereas its presence is limited to syncytiotrophoblasts in the third trimester ***(Caminos et al., 2009).*** However, ***Giomisi et al. (2011)*** reported that plasma vaspin levels decreased in pregnant women than non-pregnant.

The role of vaspin in GDM remains unclear. ***Stepan et al. (2010)*** found that vaspin serum levels did not change in women with GDM, preeclampsia and normal pregnancy. Conversely, ***Qian et al. (2014)*** reported high vaspin levels in serum and fatty tissue in GDM women than normal pregnancy. The present work aimed to assess serum vaspin levels in both of late pregnancy and experimentally-induced GDM in relation to certain metabolic parameters in albino rats.

MATERIAL AND METHODS

This study has been performed on a thirty six virgin females albino rats of a local strain weighing 100-150 g, 6-9 weeks old and 5 adult males for fertilization weighing 170- 200 g. They were obtained from the animal house from Faculty of Veterinary Medicine, Zagazig University. Rats were kept in steel wire cages (6/cage) measured 50c□x 60c□x 60cm, in the animal house in Faculty of Medicine, Zagazig University. They were fed standard chow, had free access to water, kept at comfortable temperature and were maintained on normal light/dark cycle. The rats were accommodated to animal house conditions for one week before the experiments went on ***(Gui et al., 2004).*** The experimental procedure was approved by the Physiology Department and by Local Medical Ethics Committee, Faculty of Medicine, Zagazig University (Institutional Review Board, IRB).

Animals were divided randomly into three groups: **Group I: Control group (**n=12 rats - virgin) were fed on normal diet (25.8% protein, 62.8% carbohydrates and 11.4% fat) and has been injected intraperitoneally (I.P) with citrate buffer as a vehicle. **Group II: Normal pregnant group (**n=12 rats) were fed on normal diet for five weeks before induction of pregnancy then has been injected I.P with a vehicle on the 7th day of gestation ***(Ahren and Scheurink, 1998 and Abdel-Reheim et al., 2014).*** **Group III: GDM-induced group** (n=18) rats were fed on

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 before induction of pregnancy. On the 7th day of gestation, rats received single dose of streptozotocin (STZ) ***(Abdel-Reheim et al., 2014)*.**

Induction of pregnancy: After one week of acclimation, animals were examined for estrous cycles for 2 consecutive weeks. Rats followed a 4-day pattern of estrous cycle, namely, estrous, metaestrous, diestrous, and proestrous. Every morning, vaginal smears were taken from rats by using a plastic pipette containing ~1-2 mL of normal saline by introducing the pipette tip into vagina of each rat and flushing the cells from the vaginal lining. One or two drops of vaginal secretion were placed onto a clean glass slide. Separate glass slides were used for each cage of animals. Unstained vaginal secretions were directly viewed under a light microscope at 40x magnification. Three types of cells were observed, which were round and nucleated epithelial cells, non-nucleated irregular cornified cells, and small round cells. These characteristics of cells were used for the identifying of estrous cycle phases ***(Marcondes et al., 2002)***. The female proved to be in estrus phase was paired with a mature male rat in a separate cage. After mating, females were isolated until the time of investigation to confirm accurate conception timing. In the next morning, a vaginal smear was obtained**.** Copulation was confirmed by the presence of a copulation plug or spermatozoa in the vagina. The presence of sperms indicated the first day of gestation ***(Klukovits et al., 2002)*.**

Induction of experimental GDM: After five weeks of dietary management, rats were time mated overnight with males and the presence of sperms in the vaginal smear tested in the morning was considered as the first day of pregnancy ***(Klukovits et al., 2002)*.** On the 7th day of gestation, FSD-fed rats were fasted for 16 hours and subsequently were injected I.P. with low dose of STZ (Sigma–Aldrich, U.S.A.) in a dose of 25 mg/kg dissolved in 0.1 mol/L sodium citrate (ph 4.5), and the rats were given 10% glucose solution orally after 6 hours of STZ injection for the next 48 hours ***(Abdel-Reheim et al., 2014)*.** The blood glucose level was measured (blood was sampled from the tail vein) in each rat with the One Touch Glucometer ***(Hoybergs and Meert, 2007)*.** The cases with blood glucose levels more than 190 mg/dl were selected for the experiment ***(Abdel-Reheim et al., 2014)*.**

Body mass index (BMI): At the end of experiments, rats weighed and BMI was calculated according to the equation: body weight (gm)/length^2 (nose to anus length) (cm^2) ***(Novelli et al., 2007)*.**

Blood sampling: Virgin and pregnant rats (at 21st day of pregnancy) were overnight fasted, anesthetized by diethyl ether and sacrificed. Blood was collected in clean plastic centrifuge tubes and left to clot. Serum was separated by centrifugation of blood at 3000 rpm for 15 minutes and stored frozen at -20 ?C until used.

Serum analysis was done for the following: **Vaspin levels** according to ***Plum et al. (2009)*** by using rat enzyme-linked immunoassay kits from (WKEA MED SUPPLIES CORP, 450 11th Ave, New York, USA), **total cholesterol (TC) levels** according to ***Tietz (1995)*** by using

total cholesterol kits (Bio Source, Europe S.A), **high density lipoproteins** (**HDL-c**) **levels** according to ***Nauk et al. (1997)*** by using kits for HDL-cholesterol (Bio Source, Europe S.A), **low density lipoproteins (LDL-c)** was calculated: LDL=TC-HDL-TG/5 **(*Friedewald et al., 1972)***, **total triglycerides (TG) levels** according to ***Naito (1989)*** using triglycerides ESPAS SL kits A (Elttech S.A., Lyon, France), **insulin levels** according to ***Temple et al. (1992)*** using KAP1251-INS-EASIA (Enzyme Amplified Sensitivity Immunoassay) kits (Bio Source Europe S.A., Belgium), **glucose levels** according to ***Tietz (1995)*** using glucose enzymatic (GOD-PAP)-liquizyme rat Kits (Biotechnology, Egypt), **estradiol (E2) and progesterone (PROG)** according to the method of ***Tietz (1995),*** using ELISA rat kits: BC-1029 and BC-1115, respectively, BioCheck Inc 323 Vintage Park Dr. Foster City, CA 94404**.** Calculation of **homeostatic model assessment of insulin resistance index (HOMA-IR)** based on serum insulin level (?IU/ml) and serum glucose level (mg/dl) according to the formula described by ***Matthews et al. (1985)*** as HOMA-IR = fasting serum glucose (mg/dl) x fasting serum insulin (?IU/ml)/405.

Statistical analysis: The results of this study were presented as mean ± standard deviation (SD). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 18 (SPSS Inc., Chicago, IL, United States). Repeated measures of analysis of variance (ANOVA) were applied followed by the Student-least significant deference (LSD), post hoc test to compare means of each two different groups. In addition, Pearson's correlation analysis was performed to screen potential relations between serum levels of vaspin and all measured parameters. P value < 0.05 was considered to be statistically significant.

RESULTS

Normal pregnant rats showed significant increases in the mean values ± SD of BMI, estradiol, progesterone, insulin, vaspin, TC, LDL-c, TG and HOMA-IR in comparison to those of control group. However, mean values of serum levels of HDL-c significantly decreased in pregnant rats in comparison to controls, while no significant difference was detected in serum glucose levels between both groups. In experimentally-induced GDM group, rats showed significant increases in the mean values ± SD of vaspin, BMI, HOMA-IR, serum glucose, TC, TG, and LDL-c as compared to both control and normal pregnant groups, while they showed significant decreases in mean values of serum insulin and HDL-C levels Vs. controls and pregnant rats. Moreover, serum estradiol and progesterone were significantly different when compared to control group. However, not differences as compared to normal pregnant group (Table 1).

Serum vaspin levels in normal pregnant group were positively correlated to BMI, serum glucose, HOMA-IR, and TG, while they showed non-significant correlations with serum HDL-c, estradiol and progesterone levels. Also, in GDM group, serum vaspin levels were positively correlated to BMI, HOMA-IR, serum glucose, TC, and TG. However, they were inversely correlated to serum HDL-c levels and in significantly correlated to serum estradiol or progesterone levels (Table 2 and Figures 1-6).

Table (1): Serum levels of all parameters in the three studied groups.

Groups / *Parameters*	*Control N=12*	*Normal pregnant N=12*	*GDM N=12*
Vaspin (ng/ml)	0.44±0.06	2.14±0.36 P<0.001[a]	3.36±0.43 P<0.001[a, b]
BMI (g/cm^2)	0.49±0.02	0.61±0.02 P<0.001[a]	0.71±.09 P<0.001[a,b]
Glucose (mg/dL)	83.36±6.72	84.89±6.42 NS[a]	253.68±32.8 p<0.001[a,b]
Insulin (?IU/mL)	10.8±0.9	14.57±1.1 P<0.001[a]	8.5±0.75 P<0.001[a,b]
HOMA-IR	2.18±0.2	3.04±0.3 P<0.05[a]	5.33±0.98 P<0.001[a,b]
TC (mg/dL)	108.97±2.3	128±5.1 P<0.001[a]	164.77±14.1 P<0.001[a,b]
LDL-c (mg/dL)	37.5±4.96	59.67±4.35 P<0.001[a]	101.4±3.98 P<0.001[a,b]
TG (mg/dL)	75.1±6.96	113.99±15.06 P<0.001[a]	168.37±18.33 P<0.001[a,b]
HDL-c (mg/dL)	57.2±4.28	51±2.5 P<0.01[a]	36.8±3.76 P<0.001[a,b]
Estradiol (pg/ml)	45.9±3.53	88.09±3.36 P<0.01[a]	88.5±3.8 P<0.001[a] , NS[b]
Progesterone (pg/ml)	19.28±1.6	60.39±4.3 P<0.001[a]	60.6±5.9 P<0.001, NS[b]

(a) = P value of significance versus control, (b) = P value of significance versus normal pregnant group, (NS) = non-significant.

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

Groups / **Parameters**	**Normal Pregnant**		**GDM**	
	R	**P value**	**r**	**P value**
BMI (g/cm^2)	0.873**	**0.001**	0.782**	**0.003**
Glucose (mg/dL)	0.753**	0.005	0.7*	0.01
Insulin (?IU/mL)	0.067	0.836	-0.38	0.249
HOMA-IR	0.871**	0.001	0.814**	0.001
TC (mg/dL)	0.302	0.33	0.693**	0.01
LDL-c (mg/dL)	0.457	0.135	0.25	0.43
TG (mg/dL)	0.897**	0.001	0.842**	0.001
HDL-c (mg/dL)	-0.319	0.218	-0.799**	0.002
Estradiol (pg/ml)	0.376	0.228	0.303	0.3
Progesterone (pg/ml)	-0.097	0.765	0.33	0.29

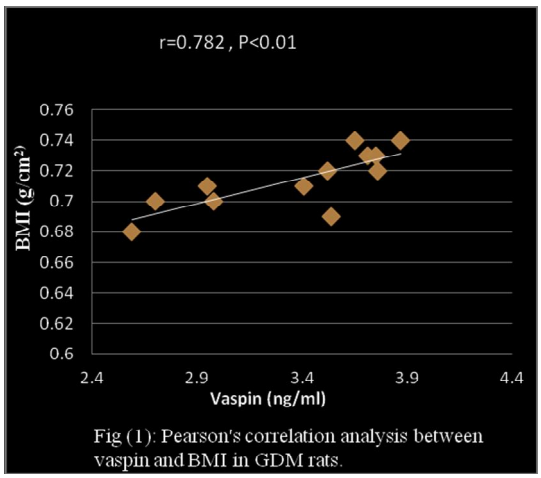

Fig (1): Pearson's correlation analysis between vaspin and BMI in GDM rats.

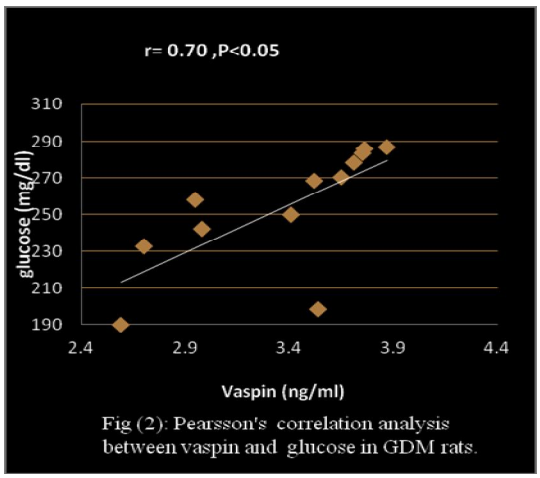

Fig (2): Pearsson's correlation analysis between vaspin and glucose in GDM rats.

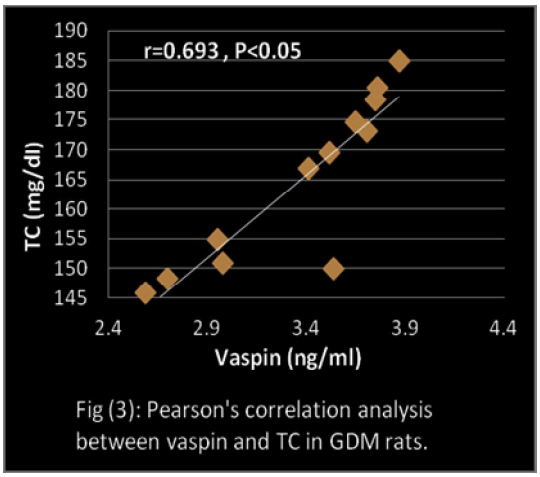

Fig (3): Pearson's correlation analysis between vaspin and TC in GDM rats.

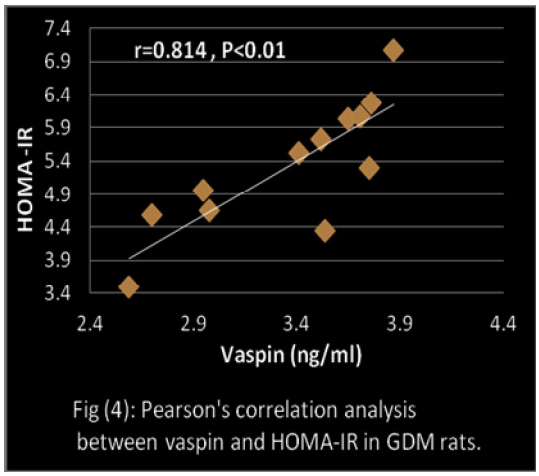

Fig (4): Pearson's correlation analysis between vaspin and HOMA-IR in GDM rats.

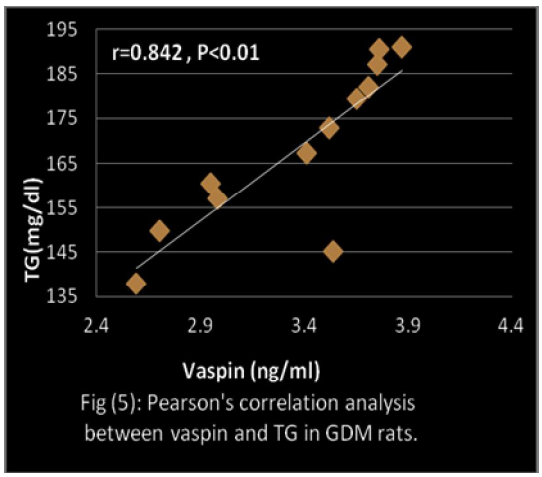

Fig (5): Pearson's correlation analysis between vaspin and TG in GDM rats.

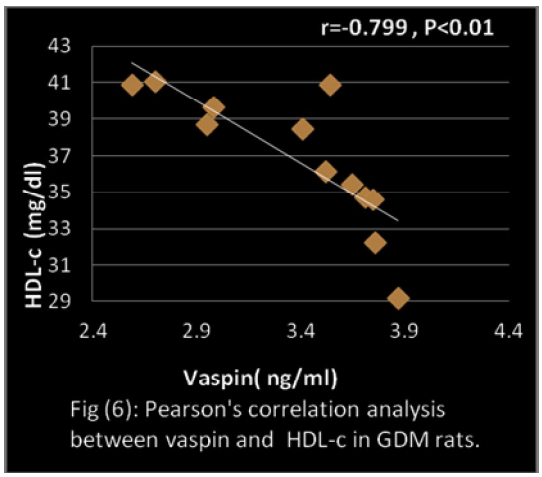

Fig (6): Pearson's correlation analysis between vaspin and HDL-c in GDM rats.

DISCUSSION

Vaspin is a specific visceral fat protease inhibitor with insulin-sensitizing effects, which may play a role in the regulation of energy metabolism ***(Buranapin et al., 2014)***. ***Yang et al. (2015)*** found that it might be involved in the occurrence of insulin resistance and GDM. Healthy pregnant rats in current study showed a profile of insulin resistance and dyslipidemia in the form of elevated TC, LDL-c and TG, while

decreased levels of HDL-c as compared to healthy control rats.

These results may be due to hormonal changes associated with pregnancy ***(Mankuta et al., 2010)*.** Placental growth hormone and placental lactogen hormone were reported to be involved in the state of insulin resistance, as they reduce phosphatidyl inisitol 3-kinase (PI3-kinase) activation which leads to depression in translocation of glucose transporter-4 (GLUT4) and the subsequent reduction in insulin-stimulated glucose uptake to skeletal muscle ***(Linda et al., 2007)*.**

Alterations in lipid metabolism in this study were supported by various human studies ***(Okojie et al., 2011 and Phuse, 2016)*** who proposed that TC, TG and LDL-c increased in third trimester, while HDL-c decreased when compared to first and second trimesters. Elevated TG levels and changes in HDL-c and LDL-c metabolism may be due to enhanced hepatic lipase action by increased estradiol, which leads to increased hepatic TG production and reduces lipoprotein lipase activity, causing decreased catabolism of adipose tissue ***(Fischer-Posovszky et al., 2007)*.** High TG concentrations are used for maternal metabolic requirements whereas sparing glucose for the fetus. Interestingly, HDL-c levels initially increase and then drop in the third trimester ***(Herrera and Ortega-Senovilla, 2014)***.

As gestational diabetes and obesity are currently common disorders happening during gestation, the present study attempted to develop an experimental GDM animal model in albino rat. GDM rats in this study exhibited a significant increase in body weight which can be attributed to consumption of FSD ***(Liang et al., 2010 and Abdel-Reheim et al., 2014),*** increased glucose levels and insulin resistance (HOMA-IR), in addition to decreased insulin levels than those of healthy pregnant rats. Also, they showed increased lipid profile parameters TC, TG and LDL-c, while decreased HDL-c levels. Insulin resistance in GDM rats may be caused by hormonal production of placenta and fatty diet intake and partly induced by STZ that leads to partial damage of pancreatic beta cell, insulin deficiency and hyperglycemia ***(Hariri and Thibault 2010, Abdel-Reheim et al., 2016 and Abdul Aziz et al., 2016)***.

A state of hyperlipidemia is commonly observed in GDM ***(Herrera and Ortega-Senovilla, 2010)***. Increased serum TC and TG may be due to elevated dietary cholesterol and triglycerides absorption from the small intestine next to the ingestion of FSD, reduced TG uptake in peripheral tissues as an outcome of dysfunction of insulin-dependent lipoprotein lipase, increased hepatic secretion of triglycerides enriched very low density lipoprotein, or through activation of hepatic 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductas which is a rate limiting enzyme involved in cholesterol synthesis ***(Shah et al., 2011)*.**

Results of the current study revealed that serum vaspin levels in healthy pregnant rats were significantly higher than virgin control rats. Also, its levels in GDM rats were significantly higher than those in healthy pregnant and virgin control rats. Consistent with these findings, ***Qian et al. (2014)*** found that vaspin levels were higher in GDM women

than non GDM control. Also, ***Jia et al. (2015)*** showed that serum vaspin levels were significantly higher in women with GDM than healthy pregnant and non-pregnant women.

As in the present study, rat models of GDM suffered from obesity and insulin resistance, it was expected to find increased vaspin levels in their serum because vaspin has been proposed to be an insulin-sensitizing adipocytokine and its production has been shown to rise possibly as a compensatory mechanism in insulin- resistant conditions and obese subjects ***(Gulcelik et al., 2009; Liu et al., 2014 and Jia et al., 2015)*.** However, other studies found that serum vaspin levels were not different between subjects with GDM and healthy pregnant controls in the 2nd or 3rd trimesters of pregnancy ***(Stepan et al., 2010 and Gkiomisi et al., 2013)***. Moreover, the current study disagreed with ***Giomisi et al. (2011) and Huo et al. (2015)*** who reported that subjects with GDM had lower Vaspin levels than healthy pregnant control. The discrepancy of the present results from previous studies may be attributed to species difference as previous studies were on human subjects or time point of blood sampling according to the stage of pregnancy.

The previous studies showed conflicting results regarding vaspin and biochemical parameters in GDM women. In the present study, vaspin levels were positively correlated with BMI, glucose, HOMA-IR, TC, TG in both GDM and normal pregnant rats while were negatively correlated with HDL-c in GDM rats only. The present findings were in line with those of ***Jia et al. (2015)*** who demonstrated that vaspin was positively correlated with HOMA- IR and TG in GDM but not in non GDM and healthy non pregnant women. Moreover, vaspin was found to be significantly correlated with LDL-c levels and negatively correlated with HDL-c levels in GDM but not in pregnant control women ***(Cheng et al., 2017)*.** In addition, ***Sommer et al. (2014)*** reported that vaspin was associated with weight gain, HOMA–IR, and TC in pregnant women with or without GDM, but not in non-pregnant women. Furthermore, vaspin levels were positively correlated with insulin, HOMA-IR and TG at the third trimester in the GDM women in the studies by ***Stepan et al. (2010)*** and ***Gkiomisi et al. (2013),*** but they did not find any correlation between vaspin and other parameters of lipid metabolism in pregnant women.

However, there were negative correlations between vaspin levels and TC, TG and LDL-c in the study by ***Giomisi et al. (2011)***, while no correlation was detected between vaspin levels and BMI, fasting blood glucose, HOMA-IR in the GDM women ***(Qian et al., 2014 and Huo et al., 2015)*.**

CONCLUSION

Late pregnancy was associated with rising of serum vaspin levels which correlated positively with insulin resistance and greatly increased in gestational diabetes mellitus possibly for compensating GDM-induced insulin resistance and dyslipidemia. Further studies are required to prove this hypothesis.

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خلفية البحث : يعد داء الحمل السكري من مضاعفات الحمل الأكثر حدوثا، ويصاحبه زيادة في مستوي السكر في الدم والمقاومة للإنسولين. والفاسبين هو أحد الأديبوكينات الحشوية التي يتم إفرازها من الأنسجة الدهنية في منطقة البطن، وهو واحد من مثبطات البروتين سيرين. وقد أوضحت الدراسات وجود تضارب حول العلاقة بين مستويات الفاسبين في الدم وكلا من الحمل الطبيعي و داء الحمل السكري.

الهدف من البحث : تقييم مستويات الفاسبين في كل من المرحلة الأخيرة من الحمل ونموذج الحمل السكري المحدث في الجرذان البيضاء، وكذلك العلاقة بين الفاسبين وبعض المعاملات الأيضية.

مواد وطرق البحث : تم تقسيم الجرذان الإناث البيضاء البكر والتي تزن 100-150 جم عشوائيا إلى ثلاث مجموعات (العدد = 12): المجموعة الأولى (الضابطة): الجرذان البكر غير الحوامل، وتم تغذيتها علي نظام غذائي عادي. المجموعة الثانية (الحمل الطبيعي): تم تغذية الجرذان على النظام الغذائي العادي لمدة خمسة أسابيع قبل إحداث الحمل. المجموعة الثالثة (الحمل السكري): تم تغذيتها على نظام غذائي دهنى مضاف إليه سكر السكروز لمدة خمسة أسابيع قبل إحداث الحمل، ثم حقنت بالحقن البريتونى بمادة ستربتوزوتوسين (25 مج / كجم من وزن الجسم) في اليوم السابع من الحمل. وتم بعد ذلك قياس كلا من مستوى الفاسبين، ومؤشر كتلة الجسم، ومستويات الإستراديول والبروجسترون، والدهون الثلاثية، والكوليسترول الكلي، والكوليسترول المنخفض الكثافة، والكوليسترول العالي الكثافة، والجلوكوز، والإنسولين، ومقاومة الإنسولين فى كل المجموعات.

النتائج : أظهرت الجرذان ذات الحمل الطبيعى زيادة ذات دلالة إحصائية في كل من مؤشر كتلة الجسم، ومستويات الفاسبين، والدهون الثلاثية، والكولسترول الكلي، والكولسترول المنخفض الكثافة، والأنسولين ومقاومة الإنسولين عن مثيلاتها في الجرذان الضابطة. علاوة على ذلك، فقد إرتبط هرمون الفاسبين بشكل إيجابي ذو دلالة إحصائية مع مؤشر كتلة الجسم، والجلوكوز، والدهون الثلاثية ومقاومة الإنسولين.

كذلك أظهرت الجرذان المصابة بسكر الحمل زيادة كبيرة ذات دلالة إحصائية في مستويات الفاسبين، ومؤشر كتلة الجسم، والدهون الثلاثية، والكولسترول الكلي، والكولسترول المنخفض الكثافة،

ومستويات الجلوكوز ومقاومة الإنسولين. في حين إنخفضت مستويات الإنسولين والكولسترول العالي الكثافة انخفاضا ذات دلالات إحصائية مقارنة بالمجموعتين السابقتين. بالإضافة إلى ذلك، فقد إرتبط الفاسبين إرتباطا إيجابيا ذو دلالة إحصائية مع مؤشر كتلة الجسم، والجلوكوز، ومقاومة الانسولين، والدهون الثلاثية، والكولسترول الكلي، فى حين ارتبط ارتباطا عكسيا ذا دلالة إحصائية مع مستويات الكولسترول المنخفض الكثافة .

الاستنتاج : هناك زيادة فى مستوبات الفاسبين في مجموعتى الحمل الطبيعى و الحمل السكري، ولكن الزيادة في المجموعة الأخيرة كانت أعلى الذي قد يرجع إلى تعويض ما يسببه سكر الحمل من مقاومة الإنسولين وإضطراب شحوم الدم .