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Research Article

ASSOCIATION OF SERUM PREPTIN LEVELS WITH INSULIN RESISTANCE IN IRAQI WOMEN WITH GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Gestational Diabetes Mellitus (GDM) is one of the most common metabolic disorders of pregnancy. This disease is characterized by an abnormal glucose tolerance recognized for the first time during pregnancy due to a decreased insulin sensitivity combined with insufficient insulin secretion. To estimate preptin concentrations in pregnant with gestational diabetes mellitus comparison with healthy pregnant. A total of 45 pregnant were divided into pregnant women with gestational diabetes mellitus(n=30) and healthy pregnant (n=15)with gestational age-matched serum levels of biomarkers and cytokine were measured in second and third trimester using Oral Glucose Tolerance Test [OGTT]preptin and insulin levels were measured with ELISA. Metabolic parameters were measured by spectrophotometer methods. The correlation coefficients between serum preptin levels and age, BMI, insulin resistance, insulin sensitivity were also evaluated. Serum preptin levels were significantly high in Patients with gestational diabetes mellitus (446.33±81.34) compared with control healthy pregnant (157.26±36.50) (P <0.001). The correlation of Preptin levels in GDM pregnant was negatively with insulin resistance, age, BMI and fasting blood glucose but positively with fasting insulin levels and insulin sensitivity. In summary, serum preptin concentration were increased in GDM pregnant compared with normal pregnant. Serum preptin concentration is associated with glucose tolerance status, insulin resistance, insulin sensitivity, Beta-cells functions disrupted

Keywords: Preptin, Insulin resistance, Gestational Diabetes Mellitus

INTRODUCTION

Gestational diabetes mellitus [GDM] is one of the major problems and most common metabolic disorders of pregnant during pregnancy period. Its diagnostic via abnormal oral glucose tolerance recognized for the first time during pregnancy caused by a low of insulin sensitivity joined with insufficient insulin secretion[1]. The prevalence of GDM ranges from 3.8 to 12.5% according to the American Diabetes Association and World Health Organization criteria. Furthermore, women with GDM are at increased risk of type 2 diabetes, hypertension, and cardiovascular disease in future[2]. Until now, although the etiology of gestational diabetes mellitus is still unclear, it is thought to share similar pathophysiology with T2D, Contains deficient insulin secretion and insulin resistance due to fail of pancreatic β-cells[3, 4]. Insulin is secreted from the pancreatic β-cells postprandially, signaling the fed state and directly stimulating glucose removal into peripheral insulin target tissues in addition to repression hepatic glucose output[5]. Insulin resistance (IR) occurs to some degree in all pregnancies[6], and both IR and decreased insulin secretion are reported to be associated with gestational diabetes mellitus7. Which symbolizes a reduced physiological reaction of the peripheral tissues to the action of the normal concentration of insulin, and is a major finding in several metabolic disorders, including type 2 diabetes and metabolic syndrome[8]. Preptin is a recently isolated [34-amino acid peptide hormone] from secretory granules insulated from cultured b-cells, sideways with amylin and insulin, that is consecrated with insulin from the pancreatic β-cells[9, 10]. Yang and his group reported that preptin may be had a role in the pathogenesis of T2DM by enhance insulin secretion[11]. Preptin enhances glucose-stimulated insulin secretion on the other hand, its effects on gestational diabetes mellitus are unidentified[9, 11]. In addition, preptin was described physiologically to mediate insulin secretion related with glucose level[9,11]. The mechanisms that which PRD could be seen to exert such a mixture of effects are complex, PRD was found to promote (but not initiate) insulin secretion Further, those most (non-nutrient modulators) of insulin secretion effects on the changes in inositol triphosphate or cAMP levels. The elements which cause a targeted increase in the second phase of insulin secretion is found in the priming of β-cells, and maybe do not involve cAMP[12].

MATERIALS AND METHODS

The case-control study was directed at pregnant care center, AL-Najaf province, Iraq, between July 2017 and April 2018. Fifteen non-GDM healthy controls and 30 newly diagnosed GDM pregnant women. The GDM cases and healthy controls were matched for age and at the same gestational age (24-28 weeks). Information written approval obtained from all the topics. The women pregnant with Gestational Diabetes Mellitus recently diagnosed and not treated with oral hypoglycemic agents. Neither of the control nor patient topics were use any medication known to change glucose tolerance, there is no family history of T2DM and no clinical sign of any major disease, multiple pregnancy, pre-existing glucose intolerance, hypertension, preeclampsia, acute or chronic inflammation, and smokers. Urinary tract contaminations, urolithiasis, liver cirrhosis, congestive heart failure or other recognized major diseases were excepted. Blood glucose was tested using the glucose oxidase method. BMIs measured during OGTT screening in 25 weeks of gestational age using the following formula: weight (kg)/height (m^2). An overnight fasting venous blood sample was obtained from all

participants to assess lipid profile, preptin levels and other biochemical parameters on the day of OGTT screening. All samples were stored at room temperature for at least 30 min to allow the blood to clot, followed by centrifugation (3000 rpm) for 15 min to separate serum. Lipid profile (TG, Cholesterol, HDL-C) Serum were determined by colorimetric method for the quantitative *in vitro* diagnostic measurement using a kit (BIOLABO). Preptit and Insulin levels were determined by using Human ELISA Kit (Elabscience). Insulin resistance were assessed using the homeostasis model assessment (HOMA-IR: [fasting glucose (mmol/L) x fasting insulin (microU /L)/22.5]. HOMA-S% and HOMA-β% were obtained according to the HOMA-calculator (www.dtu.ox.ac.uk/homacalculator/).

STATISTICAL ANALYSIS

Statistical analysis was performed using two statistical software, the Statistical Package of Social Science (SPSS ver. 21) and Graphpad Prism ver.5. Continuous variables were expressed as mean ± standard deviation (SD). Significant differences were assessed using Paired t-test and independent t-test for variables with equal and unequal frequencies respectively. Bivariate correlations were assessed using standardized Pearson coefficients. The p values obtained of less than 0.05 and 0.01 were considered as statistically and highly statistically significant respectively.

RESULTS AND DISCUSSION

The anthropometric characteristics of all participants are shown in Table 1.

Table 1, represented the baseline characteristics of the two study groups, Control (n=15) and patients (n=30). Mother age of both groups were approximately have same values and no significant differences were obtained. BMI of patients in 2nd and 3rd trimester were lower (P<0.05 & P<0.01) than control subjects respectively.

Table (1) demonstrates measurements for patients and control. The first measurement was in 2nd Trimester (before GDM), while second measurement was in 3rd Trimester (after GDM), with the mean±SD of mother's age, Age of gestational and BMI parameters.

Table 1: Characteristics of the study participants

Parameters	Patients(n=30)	Control(n=15)	P value
Mother's age (Years)	28.93±3.67	29.87±3.44	0.416 NS
Age of gestational 2nd trimester (weeks)	20.67±1.56	20.38±1.08	0.249NS
Age of gestational 3rd trimester(weeks)	28.57±0.87	28.79±0.88	0.0689NS
BMI 2nd trimester	31.21±4.20	29.78±2.48	0.034*
BMI 3rd trimester	36.14±4.33	31.20±8.17	0.009**

Data represented as Mean ±SD**,** *=significant differences at (P≤ 0.05), **=significant differences at (P≤ 0.01). BMI: Body mass index.

Table 2: Comparisons of clinical parameters for the GDM group and healthy pregnant group during gestation periods (2nd and 3rd trimester).

Parameters	Gestation Period	GDM group(30) Mean±SD	Healthy pregnant(15) Mean±SD	P value
FBG(mg/dl) OGTT(mg/dl)	FBG(mg/dl) 2nd Trimester	102.17±17.23	94.13±8.70	0.098NS
	OGTT 1h	182.40±4.23	133.20±5.22	0.000**
	OGTT 2h	149.38±8.19	103.11±2.15	0.000**
	FBG(mg/dl) 3rd Trimester	150.83±16.98	99.60±7.52	0.000**
Insulin (mlU/ml)	2nd Trimester	13.46±0.78	6.27±1.43	0.000**
	3rd Trimester	16.78±2.46	6.08±1.22	0.000**
HOMA-IR	2nd Trimester	1.76±0.12	1.11±0.19	0.000**
	3rd Trimester	2.40±0.34	1.25±0.21	0.000**
HOMA-S%	2nd Trimester	57.13±4.09	128.90±38.14	0.000**
	3rd Trimester	42.60±8.29	81.83±14.38	0.000**
HOMA-β%	2nd Trimester	116.83±38.01	77.37±15.94	0.000**
	3rd Trimester	63.80±15.29	90.77±15.68	0.000**
T.G(mg/dl)	2nd Trimester	158.41±54.49	119.47±29.78	0.014*
	3rd Trimester	194.65±106.19	122.47±19.29	0.013*
Cholesterol(mg/dl)	2nd Trimester	191.78±9.89	161.90±13.49	0.000**
	3rd Trimester	182.17±11.73	160.23±9.92	0.000**
HDL-C(mg/dl)	2nd Trimester	40.00±10.38	48.73±2.96	0.003**
	3rd Trimester	36.67±6.93	45.40±3.13	0.000**
LDL-C(mg/dl)	2nd Trimester	119.98±63.40	154.33±53.78	0.072NS
	3rd Trimester	184.60±67.65	95.58±34.23	0.000**
LDL-C/HDL-C	2nd Trimester	3.21±1.81	3.16±1.09	0.900NS
	3rd Trimester	5.10±1.23	2.10±1.38	0.003**
TG/HDL-C	2nd Trimester	4.27±1.85	2.49±0.67	0.001**
	3rd Trimester	5.45±2.80	2.71±0.42	0.000**
TG/Cholesterol	2nd Trimester	0.81±0.30	0.43±0.19	0.308NS
	3rd Trimester	1.03±0.60	0.76±0.12	0.012*
Preptin (pg/ml)	2nd Trimester	226.39±34.20	178.13±34.37	0.000**
	3rd Trimester	446.33±81.34	157.26±36.50	0.000**

BMI: body mass index FBG: fasting blood glucose HOMA-IR: hemostasis model assessment-insulin resistance, HOMA-S%: hemostasis model assessment-sensitivity percentage. HOMA-β%: hemostasis model assessment-beta cell percentage. TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol. Vit D: vitamin D. Data represented as Mean ±SD: standard deviation, NS= non-significant differences at (P>0.05). *=significant differences at (P≤ 0.05), **=significant differences at (P≤ 0.01).

Table 4: The involvement of Preptin in directing for the clinical parameters in gestational diabetes mellitus

Parameters	r	P
Age (Years)	-0.12	0.051NS
BMI(kg/m^2)	-0.23	0.102NS
FBG (mg/dl)	-0.20	0.000**
OGTT/2h	0.66	0.021*
Insulin (miU/L)	0.03	0.000**
HOMA-IR	-0.16	0.000**
HOMA-S%	0.16	0.005**
HOMA-β%	0.16	0.007**
TG(mg/dl)	-0.17	0.003**
Cholesterol(mg/dl)	-0.12	0.040*
HDL-C(mg/dl)	0.02	0.008**
LDL-C	-0.15	0.100NS
LDL-C/HDL-C ratio	0.04	0.050*
TG/HDL-C ratio	0.23	0.007**
TG/Cholesterol ratio	0.07	0.006**

BMI: body mass index; FBG: fasting blood glucose HOMA-IR: hemostasis model assessment-insulin resistance, HOMA-S%: hemostasis model assessment-sensitivity percentage. HOMA-β%: hemostasis model assessment-beta cell percentage. TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol. Data represented as Mean ±SD: standard deviation, NS= non- significant differences at (P>0.05). *=significant differences at (P≤ 0.05), **=significant differences at (P≤ 0.01).

Table 5: Correlation between HOMA-IR and studied variables in 3rd trimesters of patients

Variables	r	P
Age(Years)	0.19	0.015*
BMI(kg/m^2)	0.30	0.008**
FBG (mg/dl)	0.10	0.000**
OGTT/2h	0.33	0.001**
HOMA-S%	-0.08	0.000**
HOMA-β%	-0.12	0.001**
TG(mg/dl)	0.05	0.003**
Cholesterol(mg/dl)	0.21	0.011*
HDL-C(mg/dl)	0.20	0.008**
LDL-C(mg/dl)	-0.13	0.050*
LDL-C/HDL-C	-0.12	0.056NS
TG/HDL-C	0.09	0.001**
TG/Cholesterol	0.10	0.006**

BMI: body mass index; FBG: fasting blood glucose HOMA-IR: hemostasis model assessment-insulin resistance, HOMA-S%: hemostasis model assessment-sensitivity percentage. HOMA-β%: hemostasis model assessment-beta cell percentage. TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol. Data represented as Mean ±SD: standard deviation, NS= non- significant differences at (P>0.05). *=significant differences at (P≤ 0.05), **=significant differences at (P≤ 0.01).

Table 6: Correlation between HOMA-S% and studied variables in 3rd trimesters of patients

Parameters	r	P
Age(Years)	-0.15	0.033*
BMI(kg/m^2)	-0.23	0.028*
FBG (mg/dl)	0.20	0.000**
OGTT/2h	0.16	0.002**
HOMA-β%	0.21	0.000**
TG(mg/dl)	0.30	0.000**
Cholesterol(mg/dl)	0.10	0.045*
HDL-C(mg/dl)	-0.23	0.036*
LDL-C(mg/dl)	0.11	0.101NS
LDL-C/HDL-C	-0.12	0.060NS
TG/HDL-C	-0.17	0.007**
TG/Cholesterol	0.12	0.003**

BMI: body mass index, , FBG: fasting blood glucose HOMA-IR: hemostasis model assessment-insulin resistance, HOMA-S%: hemostasis model assessment-sensitivity percentage. HOMA-β%: hemostasis model assessment-beta cell percentage. TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol. Data represented as Mean ±SD: standard deviation, NS= non- significant differences a**t** (P>0.05).*=significant differences at (P≤ 0.05), **=significant differences at (P≤ 0.01)

Table 7: Correlation between HOMA-β% and studied variables in 3rd trimesters of patients

Parameters	r	P
Age(Years)	-0.12	0.051NS
BMI(kg/m^2)	-0.23	0.102NS
FBG (mg/dl)	-0.20	0.000**
OGTT/2h	0.66	0.021*
TG(mg/dl)	-0.17	0.003*
Cholesterol(mg/dl)	-0.12	0.040*
HDL-C(mg/dl)	0.02	0.008*
LDL-C(mg/dl)	-0.15	0.100NS
LDL-C/HDL-C	0.04	0.050*
TG/HDL-C	0.23	0.007*
TG/Cholesterol	0.07	0.006*

BMI: body mass index, , FBG: fasting blood glucose HOMA-IR: hemostasis model assessment-insulin resistance, HOMA-S%: hemostasis model assessment-sensitivity percentage. HOMA-β%: hemostasis model assessment-beta cell percentage. TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol. Data represented as Mean ±SD: standard deviation, NS= non- significant differences at (P>0.05). *=significant differences at (P≤ 0.05), **=significant differences at (P≤ 0.01).

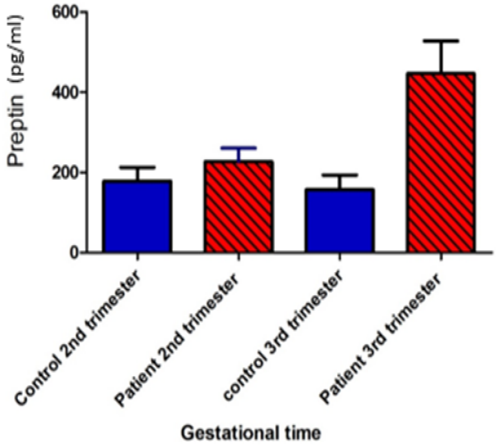

Figure 1: Preptin levels during 2nd and 3rd Trimester for gestational period

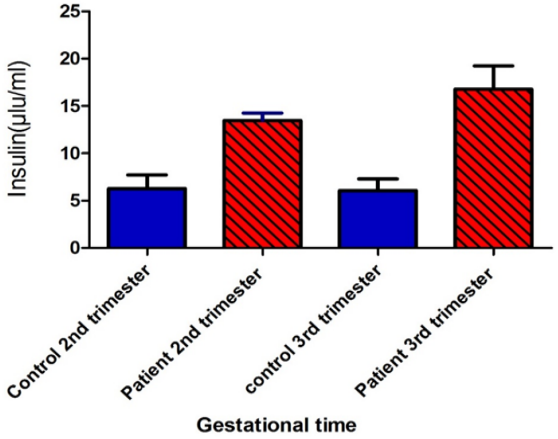

Figure 2: Insulin levels during2nd and 3rd Trimester for gestational period

It can be noticed from Table 1 that the mean values of age for both patients and control were 28.93±3.67 and 29.87±3.44 respectively with no significant differences. The mean values of gestational age in 2nd trimester for both patients and control were 25.67±1.56 and 25.38±1.08 respectively with no significant differences, while the mean values of gestational age in 3rd trimester for both patients and control were 28.57±0.87 and 28.79±0.88 respectively with no significant differences. BMI in 2nd trimester for patients and control was (31.21±4.20, 29.78±2.48 respectively) significant differences with P value (P<0.01). While BMI in 3rd trimester for patients and control was (36.14±4.33 and 31.20±8.17 respectively) significant differences with P value (P<0.01).

Table 2 summarized the comparison between clinical parameters for both GDM patients and healthy pregnant in the two periods of gestation (2nd and 3rd trimesters).All biochemical parameters showed significant differences between patient and control groups except FBG, LDL, LDL/HDL ratio and TG/Cholesterol in 2nd trimester which revealed no significant differences.

FBG level in 2nd Trimester for GDM group was (102.17±17.23mg/dl) which have no significant differences as compared with control (94.13±8.70mg/dl). While, FBG level in 3rd Trimester was (150.83±16.98mg/dl) was significantly increased (P <0.001) as compared with control group (99.60±7.52mg/dl). With OGTT (mg/dl) in 1h for patients and control was (182.40±4.23 and 133.20±5.22 respectively) significantly increased (P <0.001) while in 2h for patients and control was (149.38±8.19 and 103.11±2.15 respectively) significantly increased (P <0.001). Insulin level (mlU/ml) in 2nd and 3rd Trimester for GDM group (13.46±0.78and 16.78±2.46respectively) were significantly increased (p<0.001) compared with control (6.27±1.43 and 6.08±1.22respectively). HOMA-IR value in 2nd and 3rd for patients (1.76±0.12 and 2.40±0.34 respectively) were significantly increased (p<0.001) compared with healthy pregnant (1.114±0.197 and 1.25±0.21 respectively). HOMA-S% in 2nd and 3rd Trimester for patients were (57.13±4.09 and 42.60±8.29 respectively) were significantly increased (p<0.001) compared with healthy pregnant (128.90±38.14 and 81.83±14.38 respectively). HOMA-β% in 2nd and 3rd Trimester for patients were (116.83±38.01 and 63.80±15.29 respectively) significantly increased (p<0.001) compared with healthy pregnant (77.37±15.949 and 90.77±15.68 respectively). T.G (mg/dl) in 2nd and 3rd Trimester for patients were (158.41±54.49 and 194.65±106.19 respectively) were significantly increased (p<0.001) compared with control (119.47±29.78 and 122.47±19.29 respectively). Cholesterol (mg/dl) in 2nd and 3rd Trimester for patients were (191.78±9.89 and 182.17±11.73 respectively) were significantly increased (p<0.001) compared with control (161.90±13.49 and160.23±9.92 respectively). HDL-C (mg/dl) in 2nd and 3rd Trimester for patients were (40.00±10.38 and 36.67±6.93 respectively) were significantly decreased (p<0.001) compared with control (48.73±2.96 and 45.40±3.13 respectively). LDL-C in 2nd Trimester for patients was (119.98±63.40) which have no significant as compared with control (154.33±53.78) (P=0.072). LDL in 3rd Trimester was (184.60±67.65) was significantly decreased as compared with control (95.58±34.23) with (P value <0.001). Preptin (pg/ml) in 2nd and 3rd Trimester for patients were

(226.39±34.20) and control was (178.13±34.37), patients was (446.33±81.34), control was (157.26±36.50) respectively, were significantly increased (p<0.001).

Correlations between preptin and studied variables of patients during 3rd trimester (Table 4). Although most parameters showed positive correlation, except BMI, FBG, HOMA-IR, TG, Cholesterol, LDL-C, and showed negative correlation.

It can be noticed from Table (5) that the correlation and P value during 3rd trimester with HOMA-IR of each of:
Age is positive correlation (0.199) and significant with P value (P=0.015). BMI is positive correlation (0.301) and significant with P value (P=0.008). FBG (mg/dl) is positive correlation (0.102) and significant with p value (P=0.000**). OGTT is positive correlation (0.311) and significant with P value (P=0.001). HOMA-S% is negative correlation (-0.088) and significant with P value (P=0.000**). HOMA-β % is negative correlation (-0.127) and significant with P value (P=0.001*). TG (mg/dl) is positive correlation (0.051) significant with P value (P=0.003). Cholesterol (mg/dl) is positive correlation (0.212) and significant with P value (P=0.011). HDL-C (mg/dl) is positive correlation (0.207) significant with P value (P=0.008).LDL-C is negative correlation (-0.131) and no significant with p value (P=0. 050NS). LDL-C/HDL-C ratio is negative correlation (0.123) and no significant with p value (p=0.056NS). TG/HDL-C ratio is positive correlation (0.093) and significant with p value (p=0.001). TG/Cholesterol ratio is positive correlation (0.100) and significant with p value (p=0.006).

Correlations between HOMA-S% and studied variables of patients during 3rd trimester (Table 6). Although most parameters showed positive correlation, except Age, BMI, HDL-C and LDL-C/HDL-C showed negative correlation.

It can be noticed from Table (6) that the correlation and P value during 3rd trimester with HOMA-S% of each of **:**
Age is negative correlation (-0.153) and significant with P value (P=0.033). BMI is negative correlation (-0.231) and significant with P value (P=0.028). FBG (mg/dl) is positive correlation (0.201) and significant with p value (P=0.000**). OGTT is positive correlation (0.165) and significant with P value (P=0.002). HOMA-β % is positive correlation (0.218) and significant with P value (P=0.000*). TG (mg/dl) is positive correlation (0.309) significant with P value (P=0.000**). Cholesterol (mg/dl) is positive correlation (0.105) and significant with P value (P=0.045). HDL-C (mg/dl) is negative correlation (0.237) significant with P value (P=0.036). LDL-C is positive correlation (0.115) and no significant with p value (P=0. 101NS). LDL-C/HDL-C ratio is negative correlation (-0.129) and no significant with p value (p=0.060NS). TG/HDL-C ratio is negative correlation (-0.178) and significant with p value (p=0.007). TG/Cholesterol ratio is positive correlation (0.125) and no significant with p value (p=0.003).

Correlations between HOMA-β% and studied variables of patients during 3rd trimester (Table 7). Although most parameters showed positive correlation, except Age, BMI, FBG, TG, Cholesterol and LDL-C showed negative correlation.

It can be noticed from Table (7) that the correlation and P value during 3rd trimester with HOMA-β% of each of:
Age is positive correlation (0.008) and no significant with P value (P=0.968NS). BMI is positive correlation (0.003) and no significant with P value (P=0.989NS). FBG (mg/dl) is negative correlation (-0.061) and significant with p value (P=0.001). OGTT is positive correlation (0.712) and significant with P value (P=0.001). HOMA-IR is negative correlation (-0.984) and significant with p value (P=0.000**). HOMA-S% is negative correlation (-0.973) and significant with P value (P=0.000**). TG (mg/dl) is positive correlation (0.112) significant with P value (P=0.000). Cholesterol (mg/dl) is negative correlation (-0.248) and significant with P value (P=0.008). HDL-C (mg/dl) is positive correlation (0.016) significant with P value (P=0.003). LDL-C is negative correlation (-0.046) and no significant with p value (P=0. 808NS). LDL-C/HDL-C ratio is positive correlation (0.166) and no significant with p value (p=0.054NS). TG/HDL-C ratio is positive correlation (0.069) and significant with p value (p=0.003). TG/Cholesterol ratio is positive correlation (0.111) and no significant with p value (p=0.131NS).

The modern understanding of diabetes mellitus is that it is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both[13]. Although GDM speedily vanished directly after the pregnancy, there are no conclusive data about how gestational diabetes mellitus develops in the time of pregnancy[14]. Hence, the present research discover the possible effects of peptide hormone Preptin on the etiopathogenesis of gestational diabetes mellitus.

Preptin showed to regulate glucose-mediated insulin secretion in normoglycaemia and diabetic patients[15]. Preptin had a direct effect on the β-cell, enhancing the maximal glucose-stimulated secretion of insulin from cultured (bTC6-F7 cells). We found that higher Preptin concentrations were observed in GDM women compared with respective control. The up regulation of Preptin in the diabetic subjects either might be the result of the decreased Preptin metabolism or increased Preptin secretion. The high levels of preptin may redound insulin secretion. Also these results are in good agreement with those of Aslan *et al*. who found that plasma preptin in diabetic topics was higher than in a control group of normal persons[16]. In agreement to our findings, some previous research showed increased preptin concentration in diabetic topics associated with increase insulin resistance.

Preptin may have role in the pathogenesis of T2DM via enhance insulin secretion[9]. Preptin concentration were found to be high in patients with T2DM and glucose intolerance, comparative to the control group in a previous research[17]. These studies suggest that Preptin concentration increase in cases of (IR). In response to glucose, Preptin is described to be secreted together with insulin. GDM subjects suffer from clear insulin resistance with increased concentration of insulin, as we have found in our study[18]. And hence, we were able to notice increase concentration of Preptin in pregnant with GDM comparison with controls. If these research supported by more studies, then Preptin concentration may provide a novel method to identifying pregnant with GDM.

Changes in insulin levels in women with and without GDM with increasing gestational age can become resistant to insulin, showing (a physiological insulin resistance). All tissues during pregnancy show decreased sensitivity to insulin, and to maintain glucose Metabolism and to stabilize hyperinsulinism, especially pancreatic β-cell hyperfunction; insulin secretion can be increased to meet the needs of the body and to maintain normal blood glucose levels[19]. The current study showed a positive correlation between HOMA-IR and insulin levels in women with gestational diabetes mellitus, in addition to between Preptin level and age. This results is agreement with study in which Preptin has been found to be associated with glucose-mediated insulin secretion[9].

This is established by the positive correlation as we found between fasting insulin concentration and preptin concentration in patients with gestational diabetes mellitus[16]. Agreement with previous research, which reports on changes in insulin levels both in those with GDM and those with NGT following an OGTT at (24 – 28) weeks gestation, demonstrates that, although fasting insulin concentration in the gestational diabetes mellitus group were higher than those seen in the normal pregnancy group (19.1

±6.4 mU/L and 14.7 ±5.1 mU/L, respectively), the difference was not statistically significant[20]. Then insulin resistance (IR) is a (key feature) of metabolic disorder[21], it would be predicted that measurement of insulin level alone might be of value in the calculation of Insulin Sensitivity (IS). Hyperinsulinaemia in the presence of normoglycaemia has been found to be responsible for sign of IR[22].

Fasting insulin level appreciation are far wide used in clinical environments for providing mark of insulin resistance[23]. Development of IR and GDM showed positive significant correlation with baseline maternal BMI and development of GDM showed positive significant correlation with maternal age[24].

These findings go in hand with Shepherd *et al*.[25] who detected reduced risk of GDM with their proposed diet and exercise interventions for pregnant women versus women received no intervention. Also, Pan et al. [26] reported that women with GDM were older and had higher BMI than women free of GDM and Li et al.[27] found the levels of FBG, lipid profile and HOMA-IR score were significantly higher in GDM than in normal glucose tolerance women with a positive correlation between HOMA-IR and BMI and concluded that with the increases of FBG, the progression of IR is increased and pancreatic β-cell function progressively declines. Recently, Lindsay et al.[28] reported a high rate of late IR among pregnant women of moderately older age and high rate of obesity.

CONCLUSION

The results of our study showed that serum preptin levels were increase in GDM patients compared with normal pregnant. Serum preptin levels is related with glucose tolerance status, insulin resistance, insulin sensitivity, beta-cells functions disrupted

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