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ORIGINAL ARTICLE

Association of plasma Omentin-1 and gestational diabetes mellitus in local population of Pakistan.

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ABSTRACT… Objective: To determine plasma omentin-1 levels in pregnant females suffering from gestational diabetes mellitus (GDM). **Study Design:** Case Control study. **Setting:** Outpatient Department of Obstetrics and Gynecology, Tertiary Care Hospital of Karachi, Pakistan. **Period:** June 2021 to December 2021. **Material & Methods:** Ninety-nine gestational diabetic and ninety-six healthy pregnant women were included in this study. A diagnostic criterion for gestational diabetes was oral glucose tolerance test between 24th to 28th weeks of pregnancy. ELISA was performed at KIBGE lab for estimation of plasma omentin-1 levels. Data was analyzed by SPSS software version 22. **Results:** Mean age of the patients was 30.8±6.4 years. GDM patients had increased body mass index (BMI) (36.0± 6.6vs 32.3 ±4.7; p=0.001), Fasting Blood Glucose (FBG) (110 ±14 vs 77± 9; p=0.001), however, plasma omentin-1levels (4.90±9.01vs 9.56±12.11; p=0.001) were found reduced in GDM as compared to nGDM females. Statistically significant negative correlation was found between plasma omentin-1 and (BMI) (p=0.02). Simple and multi variable regression analysis revealed the statistically significant association of plasma omentin-1 with GDM. **Conclusion:** Our study has concluded that reduced plasma omentin-1 levels may play a significant role in the development of GDM during pregnancy, so it might be a new possible biomarker for early GDM diagnosis.

Key word: Gestational Diabetes Mellitus, Omentin-1, Oral Glucose Tolerance Test.

INTRODUCTION

Pregnancy is a physiological state that frequently results in the development of metabolic problems.[1] To provide a constant source of glucose to the fetus while it is being developed, a physiological state of insulin resistance is created by the body while the mother is in pregnancy.[2] However, women still have normal glycemic levels throughout their pregnancy, even though insulin resistance is developed, this is due to the adequate β-cell function maintained in the body.[3] Unfortunately, this mechanism to maintain normal glycemic levels in the face of physiological insulin resistance fails and leads to what is termed as Gestational Diabetes mellitus (GDM). GDM is an associated metabolic condition with a prevalence of 16-18 % prevalence with increasing ubiquity.[4-5] It is defined as a type of Diabetes that is diagnosed during pregnancy (first or second trimester) and that is not a preexisting type I or type II diabetes mellitus.[5] Within the following ten years after child birth, up to half of women with GDM develop DM2.[6] If proper diagnosis and treatment is not carried out there are several threats that the baby as well as the mother can face which include premature birth and death of the baby during intrauterine life.[7] Even though the precise pathophysiology of GDM is unclear, however, a well-illustrated cause for it is considered to be a resistance of the body to insulin.[8] Insulin resistance is caused by a wide variety of diabeto-genic hormones secreted by the placenta, including placental lactogen, growth hormone, corticotrophin-releasing hormone, and progesterone. Females with GDM are unable to create enough supplemental insulin by pancreas to compensate such insulin sensitivity caused

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by diabeto-genic hormones.[9] Pregnancy-induced insulin resistance in GDM can be exacerbated by maternal age, obesity, high parity, a family history of GDM, inflammation, and autoimmune disease.[10]

Adipocytokines are proteohormones primarily secreted by adipose tissue, have been shown to play a part in the onset of metabolic conditions.[11] Several adipocytokines, including leptin, resistin and adiponectin, have already been extensively studied with GDM.[12]

Omentin-1 is a 313 amino acid adipokine created by fat tissues, ovaries, and the placenta and is considered to be a probable suspect for acting as a intermediary for insulin resistance in the body.[13] It may play a role in the development of GDM by enhancing chronic inflammation and developing insulin resistance.

Studies concerning omentin-1 and its relationship to GDM remain anecdotal and sparse. To bridge this vacuum we conducted a study to assess any association between GDM and omentin-1.

MATERIAL & METHODS

This case control study which was carried out from June 2021 to December 2021 was carried out at the Obstetrics and Gynecology outpatient department of tertiary care Hospital, Karachi.

The protocol was submitted, reviewed, and finally approved by the Al-Tibri Medical College and Hospital, Isra University, institute review board (IRB# ATMC/IERC/04(2021)). Prior to recruitment, all participants provided their informed consent. Over the period of six months 270 pregnant women were requested to take part in the study, only 195 females agreed to take part though. Through oral glucose tolerance test (OGTT), 99 women that were pregnant were confirmed to have GDM and these 99 women were to be enrolled in this study. As controls, ninety-six pregnant women with adequate OGTT were recruited. Any women with a history of hypertension, multiple births, congenital malformations, and already having diabetes mellitus were to be excluded. Consecutive non-probability sampling technique was used.

Between 24 and 28 weeks of pregnancy, OGTT test was done on all the women included in the study using 75g of glucose, in accordance with the guidelines by the American Diabetes Association (ADA).[5] 180 and 153mg/dl, were set as the upper normal limits for fasting glucose, after glucose ingestion at 1 and 2 hours.

5ml plasma specimen was taken from the participants of the study to carry out maternal blood analysis. It was then centrifuged and kept at - 80^{o}C. omentin-1 levels in the plasma were carried out using enzyme-linked immunoassay ELISA test. Omentim-1 ELISA kit (Cusabio Biotech Co), was used as stated by the manufactures guidelines. The determined inter-assay and intra-assay coefficients of variation (CV) were less than 10%, with the identification limit of the assay being 1.6ug/ml. Furthermore, measurements of triglyceride (TG), high-density lipoprotein (LDL), low-density lipoprotein (HDL), and total cholesterol (TC) were also done.

Continuous data and categorical variables were presented as mean ± SD or in percentage. Independent sample t-test and chi-square tests was done to compare the difference in means among study groups. Comparison of groups was done by one way ANOVA. Correlations between plasma concentrations of omentin-1 and other parameters were studied by Pearson's correlation analysis. Simple and multivariate logistic regression analyses was carried out to see which factors are independently associated with omentin-1 in GDM.

RESULTS

Table-I shows the clinical traits of the groups. In term of age, TG, HDL, LDL and TC between GDM and nGDM females, no differences were seen. However, GDM patients had increased BMI (36.0± 6.6vs 32.3 ±4.7; p=0.001), Fasting Blood glucose (FBG) (110 ±14 vs 77± 9; p=0.001), however, plasma omentin-1levels (4.90±9.01vs 9.56±12.11; p=0.001) were found reduced in GDM as compared to nGDM females.

Table-II Describes the mean omentin-1 levels in subgroups of GDM females. The majority of the women (74%) were between the ages of 26 and 30. Twenty-four women (24.2%) had a normal BMI, thirty-eight (38.3%) were overweight, and thirty-seven (37.3%) were obese. Omentin-1 concentration was found less in GDM group between 30-35 years (4.95±3.71 vs7.7±2.67, 8.1±3.28; p=0.001). GDM patients with BMI more than 30 were found with reduced omentin-1 (5.98±2.02 vs 6.37±2.88, 7.59±3.63) but not found statistically significant.

Table-III shows relationship of omentin-1 and study parameters in GDM patients. Omentin-1 was positively correlated with HDL-c, whereas negatively with BMI. It was not found statistically significant. Simple and multi variable regression analysis revealed the association of plasma omentin-1 with GDM.

DISCUSSION

The study has revealed that pregnant females with GDM were found with significant reduced plasma omentin-1 levels as compared to pregnant women without GDM. Furthermore, when compared in GDM sub-groups, females aged more than 30 years and with a greater BMI have lower omentin-1 levels.

In our study, females with GDM had a mean age of 25.810.4 years, however in a similar study conducted in India in 2016, the age of the participants with GDM was said to be 28.9+ 3.64 years.[15] Another study from China found that the average gestational age was 25.40+0.82 weeks, which agrees with our findings.[16]

Study Parameters	GDM Females (*n* = 99)	nGDM Females (*n* = 96)	P-Value
Age of Patient (in years)	25.9±7.5	22.7±8.4	0.89
Body Mass Index (kg/m^2)	36.1 ± 5.6	32.4 ± 4.5	0.001
FBG (mg/dl)	110 ± 14	77 ± 9	0.001
1-hour post-load Glucose (mg/dl)	180±29	130±30	0.001
2-hour post-load Glucose (mg/dl)	140±35	105±26	0.001
TG (mg/dl)	298±133	271±112	0.32
HDL (mg/dl)	61±12	59±15	0.12
LDL (mg/dl)	154±34	156±65	0.93
Omentin-1 (ug/ml)	8.84±9.01	15.56±12.11	0.001

Table-I. Clinical characteristics of study groups.

Variables	Groups	n=99(%)	Omentin-1 (ug/ml)	P-Value*
Age (Years)	20-25 26-30 30-35	16(16.2) 74(74.7) 9(9.1)	8.1±3.28 7.7±2.67 4.9±3.71	0.001
Gestational Age (Weeks)	24-25 >25	38(38.4) 61(61.6)	7.00±2.95 6.83±2.84	0.779
Body Mass Index (Kg/m^2)	Normal BMI (18-24.9) Overweight BMI (25-29.9) Obese BMI (>30)	24(24.2) 38(38.4) 37(37.4)	7.59±3.63 5.37±2.88 5.98±2.02	0.043
Parity	Nulliparous Primiparous Multiparous	23(23.2) 34(34.3) 42(42.4)	6.57±2.71 6.12±2.99 7.26±2.88	0.556

Table-II. Plasma omentin-1 levels in subgroups of GDM
*** p-value <0.05**

Previous literature has gone onto document Omentin-1 and its function concerning GDM: a research found reduced levels of Omentin-1 in GDM patients in contrast to control group.[17], whereas GDM concentrations were found to be lower in another cohort research.[18] Franz et al, in his study conducted on 192 women that were pregnant, with 92 of them having GDM gave conflicting data when he measured the plasma levels of Omentin-1 at 32 weeks of pregnancy and also at the time of delivery from the umbilical cord. Franz found no significant difference in the level of omentim-1 when comparing the GDM and non-GDM groups.[19]

The results of our study shows that concentration in plasma of Omentin-1 are negatively related to BMI, which is consistent with Pan et al, results, who demonstrated lower omentin-1 levels in GDM females with higher BMI.[20] However, Franz et al reported no significant relationship between BMI and plasma omentin-1 levels.[19]

Insulin and glucose have been demonstrated to suppress omentin-1 expression.[21] The alteration in sensitivity of insulin during period of pregnancy can be the considered likely cause that lowers the omentin-1 during the last trimester in women who have GDM, and also in those pregnant women who have normal blood glucose concentration.

Another relevant study carried out by Barker et al, went onto observed Body mass index, GDM, and omentin-1 concentration, and concluded in his study that omentin-1 is linked to fasting hyperglycemia and maternal BMI.[22] Abell et al. studied levels of Omentin-1 in 103 women who were pregnant (25 of whom went on to develop GDM) and found out that when contrasted with control groups, the plasma levels of Omentin-1 was reduced in pregnant women having GDM, as well as a unfavorable relationship in regards to OGTT 1 and 2 hour glucose concentration. It was also concluded that if a concentration of Omentin-1 was found to be less than 38.36ng/dl caused a 4 time increase in risk of GDM, and that the risk of GDM was OR 0.97 (95 %CI 0.94–0.99) for every 1 ng/mL decreased in omentin-1 levels. They concluded that omentin-1 in the first trimester may be able to predict GDM.[23]

The functions of omentin-1 in regards to pregnancy is still questionable, however, it has some connection with the up regulation of glucose concentration in the blood as it increased uptake of glucose in visceral and subcutaneous fat cells.[24] GLUT-4 expression was found to be reduced in obese pregnant women in previous investigations.[25]

The feto-placental vascular system can be compromised by the weight gain during maternal life, thus the reduced levels of omentin-1 levels seen in this study in accordance with maternal obesity can lead to significant negative consequences in the growth and development of the fetus.

CONCLUSION

At the end of our study, we can conclude that omentin-1 concentration in the plasma perhaps plays a vital part in the development of insulin resistance which ultimately causes GDM. Furthermore, omentim-1 plasma levels might act as a biological marker for early diagnosis and prevention of GDM. However, further large scale diagnostic studies are required in our population, to establish the sensitivity and specificity.

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