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Research Article
Hypertriglyceridemia and Waist Phenotype as Markers in the Prediction of Gestational Diabetes in Iraqi Women

[1]Faris Anwer Rasheed, [2]Raghad Hasan Mshattat, [3]Ulfat Mohammad Alnakkash and [4]Saad Abdulrahman Hussain

[1]Consultant Obstetrician and Gynecologist, Al-Zuhur Private Hospital, Baghdad, Iraq
[2]Department of Obstetrics and Gynecology, Ibn Al-Baladi Maternity Hospital, Baghdad, Iraq
[3]Department of Obstetrics and Gynecology, Al-Elwyia Maternity Teaching Hospital, Baghdad, Iraq
[4]Department of Pharmacology and Toxicology, Faculty of Pharmacy, Al-Rafidain University College, Baghdad, 10052 Al-Mustansiriya St. 75, Baghdad, Iraq

Abstract

Background and Objective: Abdominal visceral adiposity in early pregnancy can be considered as an indicator of the risk of impaired glucose tolerance in later pregnancy. Accordingly, the "hypertriglyceridemic waist" phenotype can be utilized as a clinical marker of visceral obesity. The present study aimed to assess the association between the hypertriglyceridemic- waist phenotype in early pregnancy and glucose intolerance in later pregnancy. **Materials and Methods:** A case-control study was carried out at AL-Elweyia Maternity Teaching Hospital for one year from 1st of January, 2012 to the 1st of January, 2013. A 100 pregnant women were enrolled in this study. The women were allocated according to the waist girth equal to or greater than 85 cm and less than 85 cm. Plasma triglycerides and waist girth were measured at 11-14 weeks of gestation for all groups. Blood glucose was measured following a 75 g oral glucose tolerance test performed at 24-28 weeks of gestation. **Results:** A waist girth greater than 85 cm and a triglyceride level $\geq$ 1.7 mmol L^{-1} in the first trimester was associated with an increased risk of 2 h glucose $\geq$ 7.8 mmol L^{-1} following the 75 g oral glucose tolerance test (OR 7.75, $p = 0.0003$). This risk remains significant, even after the sample was controlled for maternal age and fasting glucose in the first trimester. **Conclusion:** Measurement of waist girth and plasma triglycerides levels (hyper-triglyceridemic-waist phenotype) during the early pregnancy may be useful as an early screening for the risk of gestational diabetes.

Key words: Waist girth, plasma triglyceride, gestational diabetes, hypertriglyceridemic-waist phenotype, first trimester

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Corresponding Author: Saad Abdulrahman Hussain, Department of Pharmacology and Toxicology, Faculty of Pharmacy, Al-Rafidain University College, Baghdad, 10052 Al-Mustansiriya St. 75, Baghdad, Iraq Tel: +9647901712624

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Gestational hyperglycemia increases the risk of the adverse outcomes of the pregnancy. Normally, pregnancy induces 50% decrease in the insulin sensitivity associated with 200-250% increase in insulin secretion for the aim of maintaining glucose homeostasis[1]. However, glucose metabolism may not be finely regulated during pregnancy in certain cases of low-insulin sensitivity that may lead to abnormal carbohydrate metabolism[2,3]. Moreover, the combination of pre-gestational obesity and gestational insulin resistance may predispose to greater maternal and perinatal adverse outcomes[4,5]. Plasma lipids were elevated normally under hormonal regulation during pregnancy and not considered atherogenic[6]. However, complicated pregnancy maybe associated with disturbed lipid profile that can be used to predict the risks of many complications including pre-eclampsia and gestational diabetes[7,8]. Accordingly, the relationship between elevated serum lipids and the risk of gestational proteinuric hypertension is highly suggestive of an expected role for the lipid profile evaluation as a diagnostic tool for pregnancy-associated complications[9]. It has been reported that the identification of increased waist circumference or elevated level of serum triglycerides before conception can be used as a predictor of subsequent gestational diabetes mellitus (GDM)[10].

Meanwhile, the prediction of the "hypertriglyceridemic waist" phenotype during the first trimester of pregnancy may represent an inexpensive and simply early test for gestational glucose intolerance[11]. In this regard, the hypertriglyceridemic waist can be considered as a clinical marker of visceral obesity, defined as the presence of abdominal obesity and elevated serum triglycerides level[12]. However, the use of this marker alone cannot adequately describe the expected outcomes. For the aim of providing local data, the present study was designed to assess the association between the hyper-triglyceridemic waist phenotype in early pregnancy and the risk of glucose intolerance in later pregnancy in Iraqi pregnant women.

MATERIALS AND METHODS

Patients' enrolment and clinical data: The present prospective study included a sample of 100 Iraqi women with a singleton pregnancy. They were recruited at the beginning of their routine obstetric follow-up at Al-Elweyia Maternity Teaching Hospital, Baghdad, Iraq. All the participants were sequentially recruited during their first visit, between 1st of January, 2012 to the 1st of January, 2013. They were between 11 and 14 weeks of gestation, according to the last normal menstrual period and the ultrasound examination performed on the same day of recruitment in the Department of Radiology and Sonography in the hospital. The inclusions criteria include: The age is up to 40 years, a single-tone viable pregnancy between 11 and 14 weeks of gestation and no previous history of DM and other carbohydrate metabolism disorders. The women older than 40 years of age, positive history of type 1 or 2 diabetes or other pathologies known to impact glucose metabolism before pregnancy were excluded and women with a positive history of smoking and alcohol or drug abuse during the current pregnancy were also expelled. The research protocol was approved by the local research ethics committee of the Iraqi Council of Medical Specialties (612-2012) in accordance with the Declaration of Helsinki. All participants were informed about the nature of the study and only those who agreed to participate and signed a written consent were included. All the clinical data of the participants were denominalized.

Clinical outcome measurements: The basic characteristics of the age, parity, past medical and drug history of each woman were recorded before clinical investigation. The waist girth was measured at 11-14 weeks of gestation according to the standardized procedures of Lohman *et al.*[13]. The measurements were carried out utilizing a tape at the mid-distance between the iliac crest and the last rib margin after normal expiration while the woman was in a standing position.

Biochemical outcome measurement: After 12 h fasting, blood samples were obtained from the antecubital vein in the first trimester of pregnancy (i.e., 11-14 weeks of gestation) and kept EDTA-containing tubes. Following 10 min centrifugation at 4000 rpm, the resulted plasma was utilized for measurement of glucose and total triglyceride concentrations in the plasma using ready-made kits for spectrophotometric procedures (Randox Co., UK). Moreover, the enrolled pregnant women were followed in the antenatal clinic and at 24-28 weeks of gestation oral glucose tolerance (OGT) test was performed. After 24 h fasting, baseline plasma glucose was estimated as mentioned previously and a 75 g glucose solution was administered orally, then, plasma glucose

concentrations were measured after 120 min. the concentration of ≥153 mg dL^{-1} (8.5 mmol L^{-1}) was considered as impaired glucose tolerance and ≥200 mg dL^{-1} (11 mmol L^{-1}) was considered as gestational diabetes mellitus (GDM).

Statistical analysis: The data were statistically analyzed using SPSS software, version 20 for windows. Data were presented as the Mean±Standard Deviation (SD) and median for continuous variables. For categorical variables, the data were presented as frequencies and proportions (%). Multivariate logistic regression models were used to calculate the relative odds of exhibiting a 2 h glucose level of ≥7.8 mmol L^{-1}. Additionally, Pearson's correlation test (for 2 normally distributed continuous variables) was used to assess the correlation of the age, BMI and FPG with the GTT levels. Spearman's correlation coefficient test was used to evaluate the correlation between parity, family history of DM with GTT. The p-values were set at <0.05 to consider significant difference.

RESULTS

Data in Table 1 showed the characteristics of the enrolled women. The mean age was 26.7±6.9 (range 14-39 years). The mean body mass index (BMI) of the participants was 28.76±3.6 kg m^{-2} (range 21.0-39.0 kg m^{-2}). The mean waist girth was 83.8±11.1 cm, ranging from 68-150 cm. Moreover, the mean serum triglycerides (TG) level was 1.7±0.36 mmol L^{-1}, the mean FPG was 4.3±0.9 mmol L^{-1} and the mean 2 h GTT was 7.3±0.7 mmol L^{-1}. Regarding the family history of DM, Table 1 showed that 25 participants (25%) had a positive family history of DM. Meanwhile, the distribution of parity revealed that 33% of participants were nulliparous, while 19% were Para 1, 14% Para 2, 18% Para 3,10% Para 4 and only 6% were Para 5 (Table 1). The Table 2 showed that the participants with waist girth >85 cm in association with TG level ≥1.7 mmol L^{-1} at 11-14 weeks were more likely to have FPG level of ≥7.8 mmol L^{-1} than other groups (OR 7.75, p = 0.0003) at the 24-28 weeks of pregnancy according to 2 h GTT results. Meanwhile, no significant risk was reported in the other groups based on the association of waist girth and TG levels. However, the estimated risk remained significant after adjustment for other variables like age, BMI, parity and FPG (OR 5.4, p = 0.0012). The results presented in Table 3 showed that the age, weight, FPG, parity and history of DM were not significantly correlated with the 2 h GTT levels (p>0.05). The results of Person's correlation between the BMI and the waist girth in all women, beyond the history of DM and the 2 h GTT value showed a highly significant (p<0.0001) positive correlation (r = 0.75) (Fig. 1). Moreover, when the BMI value was correlated with the FPG, plasma TG and 2 h GTT values, the best result of positive and significant correlation was obtained with plasma TG levels (r = 0.48 and p<0.0001) followed by GTT and FPG, respectively (Fig. 2).

DISCUSSION

The present study was performed for the aim of finding a predictive approach related to GDM in pregnant Iraqi women, using waist girth, BMI and plasma TG levels as independent

Table 1: Characteristics of the participants (n=100)

Characteristics		Values
Age (years)	Mean±SD	26.7±6.9
	Median (range)	27.5 (14-39)
BMI (kg m^{-2})	Mean±SD	28.76±3.6
	Median (range)	28.9 (21.0-39.0)
Waist girth (cm)	Mean±SD	83.8±11.1
	Median (range)	85 (68-150)
Serum triglycerides (mmol L^{-1})	Mean±SD	1.7±0.36
	Median (range)	1.69 (1.16-2.91)
FPG (mmol L^{-1})	Mean±SD	4.3±0.9
	Median (range)	4.1 (3.1-8.8)
GTT (mmol L^{-1}) (2 h)	Mean±SD	7.3±0.7
	Median (range)	7.3 (5.3-7.3)
Positive family history of DMn (%)	25 (25.0)	
Parity n (%)	P0	33 (33.0)
	P1	19 (19.0)
	P2	14 (14.0)
	P3	18 (18.0)
	P4	10 (10.0)
	P5	6 (6.0)

Table 2: Odd ratio and adjusted odds ratio for the association of waist girth with the triglycerides levels and glycemic control in pregnant women

Waist (cm)/TG (mmol L^{-1})	2 h FPG mmol L^{-1} 24-28 weeks					
11-14 weeks	≥7.8	<7.8	p-value	OR (95% CI)	Adjusted OR (95% CI)	p-value
≤85\< 1.7	6	31	1.0 (ref)	1.0	1.0 (ref)	1.0
≤85\≥1.7	6	15	0.48 (0.13-1.76)	0.44	1.6 (0.82-3.1)	0.18
>85\<1.7	2	15	1.45 (0.26-8.1)	0.98	2.8 (0.73-11.1)	0.31
>85\≥1.7	16	9	7.75 (2.84-21.1)	0.0003	5.4 (2.41-18.2)	0.0012
Total	30	70				

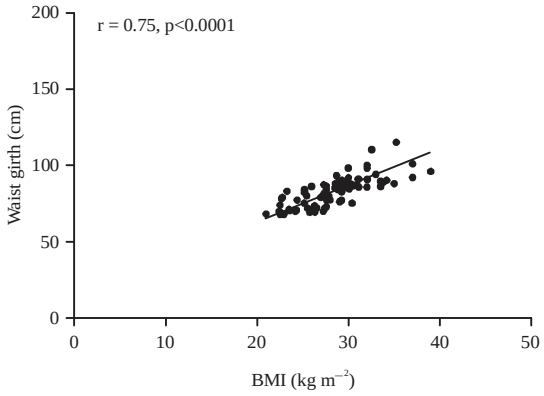

Fig. 1: Person correlation between the body mass index (BMI) and waist girth in pregnant women beyond the family history of DM, n = 100, r: Pearson's correlation coefficient

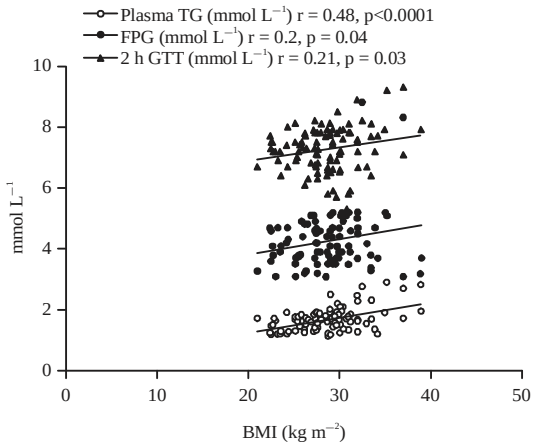

Fig. 2: Person correlation of the body mass index (BMI) with FPG, plasma TG and 2 h GTT in pregnant women beyond the family history of DM, n = 100, r: Pearson's correlation coefficient

Table 3: Correlation between age, weight, FPS, parity and history of DM with the GTT values

Variables	Correlation test	r-value	p-value
Age (Year)	Pearson's correlation	0.034	0.736
BMI (kg m^{-2})	Pearson's correlation	0.210	0.030
FPG (mmol L^{-1})	Pearson's correlation	0.173	0.085
Parity	Spearman's rho correlation	0.000	0.994
Positive history of DM	Spearman's rho correlation	0.172	0.088

variables during the first trimester of pregnancy. Currently, many studies of the early detection of GDM had been ongoing.

In response to the increasing prevalence of obesity and unfavorable lifestyle habits worldwide, gestational diabetes may be expected to become more frequent and epidemic in the next years[4]. This can be attributed to the "modern obesogenic environment" that associated with decreased physical activity and increased caloric intake especially with the excessive consumption of food rich in fat and sugar[14]. The relationship between body weight and mortality, CVD or DM has been investigated in numerous epidemiological studies for decades. When the BMI is used as an indicator of adiposity, there is a clear linear or curvilinear relationship between the relative weight and total mortality. Despite this epidemiological evidence, physicians are confused by the absence of metabolic abnormalities or of clinical signs of DM and/or CVD in some obese patients. Thus, obesity cannot be considered as a homogenous condition. In this regard, many data have provided evidence that the health hazards of obesity are more closely related to the localization of excess body fat rather than to an elevated body weight per se[15]. Such a critical role of abdominal obesity justifies the recommendations of many authorities to recognize that abdominal obesity is the most prevalent form of a cluster of atherogenic and diabetogenic metabolic abnormalities that has often been referred to as the metabolic syndrome[16]. Therefore, numerous organizations now recommend the estimation of waist circumference in addition to the BMI as an indicator of abdominal fat. The critical role of abdominal obesity in the development of metabolic syndrome also includes atherogenic dyslipidemia, insulin resistance state, a pro-inflammatory state, a prothrombotic state and elevated blood pressure[17]. Currently, many evidence revealed that the simultaneous presence of an elevated waist circumference and fasting triglyceride levels (hyper-triglyceridemic waist) may represent a relevant first-step approach to identify a subgroup of individuals at higher risk of being carriers of metabolic syndrome features. However, many biomarkers of insulin resistance and metabolic syndrome cannot be widely used in clinical practice, because of accessibility, cost and standardization problems, except for apolipoprotein B, which is now standardized. Accordingly, it was interested in developing a simple and inexpensive screening tool that could help general practitioners to identify pregnant women at risk of developing GDM due to the presence of abdominal obesity and metabolic syndrome features. In this regard, it have proposed that simultaneous presence of an increased waist circumference and elevated fasting TG concentrations (hyper-triglyceridemic waist) could be of value as a screening method to identify a subgroup of pregnant women likely to be at high risk of developing GDM[18].

A large-scale study reported that the age of the woman and her BMI played significant roles as risk factors in South Asian and black African women compared to white European

or black Caribbean women[19]. However, there was no correlation between the increased age of the pregnant women and GDM and for pre-pregnancy BMI, the incidence of GDM significantly increased as BMI increased from the Asian standard criterion. The rationale for simultaneous measurement of waist girth with fasting TG levels is based on the fact that not all pregnant women with elevated waist girth are viscerally obese and at high risk of GDM. Moreover, abdominal obesity can present in two phases: Isolated abdominal obesity with excess subcutaneous fat or abdominal obesity with metabolic complications. Meanwhile, the latter condition can be associated with an increased risk of T2DM and GDM closely related to excess visceral adipose tissue[20]. The precise estimation of visceral adiposity can be only be done with the aid of expensive imaging techniques, while measurement of waist girth may serve as a simple cost-effective surrogate marker of visceral adiposity. On the other hand, fasting TG levels have been reported to be positively correlated with visceral adiposity[21]. The results of the present study clearly showed that the hypertriglyceridemic-waist phenotype may be an early practical evaluation tool for GDM. Although some reports have mentioned that first-trimester fasting hyperglycemia could also be a significant predictor of GDM expression[22], the present study indicates that this feature was observed among women with a normal first-trimester fasting glucose level, this finding was in tune with the observation reported by Martin *et al.*[23], where visceral adiposity in early pregnancy was associated with the risk for gestational glucose intolerance[23]. However, measurement of visceral adiposity using ultrasonography is not always affordable especially at the beginning of pregnancy when follow-up takes place in primary care and general practice clinics. Consequently, although the data reported by Martin *et al.*[23] are promising for early GDM screening, they cannot be easily translated to the current clinical practice. Meanwhile, our results have the advantage of suggesting an alternative early screening tool for GDM, which is simple, readily accessible and cost-effective. Brisson *et al.*[11] reported that a waist girth greater than 85 cm in combination with a triglyceride level $\geq$1.7 mmol L^{-1} in the first trimester was associated with an increased risk of 2 h glucose $\geq$7.8 mmol L^{-1} following the 75 g oral glucose tolerance test, this risk remains significant even after controlling for maternal age, fasting glucose at first trimester and previous history of gestational diabetes[11]. Moreover, Yoon *et al.*[24] suggested that abdominal adiposity during pregnancy negatively impacts lipid levels and its evaluation with USG in early pregnancy may be a predictor of lipid profile disorders, however, it shows no association between abdominal adiposity and glucose intolerance, probably due to inadequate sample size[24]. Although the current study is not the first one in this field, the obtained result seems to be a good indicator of glucose intolerance among Iraqi pregnant women with negative history of GDM. Beyond the limitations of the study, the confidence in the obtained results may help to suggest that evaluation of hypertriglyceridemia and waist girth might one day be recommended at a first prenatal visit or possibly prior to conception for the early detection of high-risk women. However, this concept was still far from being implemented without further enough local and global data from more varied populations. The current results suggest that the evaluated markers might be an attractive tool in order to adopt early, accessible and cost-effective means to improve preventive strategies.

CONCLUSION

The results of this study indicated that measurement of plasma triglycerides and waist girth during the first trimester of pregnancy can be a valuable marker for predicting GDM during the second trimester. Accordingly, this information that can be easily obtained during the first trimester of pregnancy is expected to be increasingly utilized as a supplementary diagnostic criterion for predicting the risk of GDM during the second trimester of pregnancy in Iraqi women.

SIGNIFICANCE STATEMENT

The present study shed a light on the correlation between visceral adiposity, serum triglycerides and the impairment of 2 h GTT that can be beneficial for the prediction of the risk of gestational diabetes in later. The present data add further support to the previous global efforts and may help the researchers and clinicians to uncover the critical points of the role of visceral lipids derangements as etiology for many complications during pregnancy.

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