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Indicators of Obesity and Serum Levels of Triglycerides in the First Trimester of Pregnancy as the Predictors of Gestational Diabetes Mellitus among Urmia Women

Azar Pazhohan,[1,*] Monireh Rezaee Moradali,[1] Nahideh Pazhohan,[2] and Ali Sadeghyanifar[3]

[1]Department of Midwifery, Urmia Branch, Islamic Azad University, Urmia, IR Iran
[2]Tabriz University of Medical Sciences, Tabriz, IR Iran
[3]Urmia University of Medical Sciences, Urmia, IR Iran

[*]*Corresponding author*: Azar Pazhohan, Department of Midwifery, Urmia Branch, Islamic Azad University, Urmia, IR Iran. Tel: +98-9104001990, E-mail: azarpaghohan@gmail.com

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Abstract

Background: Obesity is a major risk factor of gestational diabetes mellitus (GDM), therefore, we aimed to determine which indicators of obesity can be used as predictors of GDM and also to study the association of maternal serum levels of triglycerides (TG) in early pregnancy to expression of GDM.

Methods: A total of 436 primigravida women, who attended public health centers in 6 - 10 weeks of gestation, were prospectively followed until 24 - 28 weeks of gestation to control the expression of GDM. The indicators of abdominal obesity and the serum concentration of TG were measured at 6-10 weeks of gestation. All participants underwent a 75 g oral glucose tolerance test (OGTT) as a routine test at 24 - 28 weeks.

Results: The incidence of GDM among our participants was 9.6%. The serum concentration of TG in 16.5% of them was more than 199 mg\dL. The majority of participants (62.8%) had a body mass index (BMI) more than its normal range. Waist circumference (WC) in the majority (84.4%) was 80 - 95.9 cm. The mean (SD) waist to height ratio (WHtR) and waist to hip ratio (WHR) were 0.58 (0.05) and 0.84 (0.06), respectively. WC, WHtR, WHR, BMI, and the serum levels of TG in early pregnancy are associated with the expression of GDM.

Conclusions: Abdominal obesity and serum levels of TG can be used as early predictors of GDM. Strategies consisted of monitoring of TG levels in women planning for pregnancy as well as training obese and overweight women to modify their lifestyle in the means of decreasing the body fat mass can help to partially prevent GDM.

Keywords: Serum Triglycerides, Obesity, Gestational Diabetes Mellitus

1. Background

Gestational diabetes mellitus is defined as impaired glucose tolerance, which onset or is first diagnosed after mid-pregnancy. About 7% of all pregnancies are affected by GDM (1).

Several diagnostic standards and screening approaches have been developed to diagnose GDM, which influence its prevalence rate among different populations (2). Its prevalence in the US and European countries is 3% - 7% and 2% - 6%, respectively (3-5). A higher incidence rate was reported in Asian, Indian, and African women (6-8).

Gestational diabetes has several adverse effects on pregnancy outcomes. GDM is related to primary caesarean delivery, trauma to reproductive tract, and bleeding after delivery due to a hypotonic uterus in mothers (9). In addition, macrosomia is a more common complication of GDM, which is associated with increased rate of birth trauma, hypocalcemia, hypoglycemia, and hyperbilirubinemia in infants. In the future, the risk of diabetes and obesity in the children of mothers with GDM as well as the possibility of metabolic syndrome in those mothers will be vigorously increased (1).

The prevalence of GDM in many countries is increasing (10). Considering different ethnic groups in the US, the rate of GDM has doubled from 1994 to 2002 (11). Obviously, the undesirable effects of GDM are also increasing. Due to the increased prevalence of obesity (12), an increase in the proportion of elderly population (13), as well as a reduction in physical activity due to the modern lifestyle (14), the prevalence of GDM will continue to rise worldwide. It was estimated that the incidence of GDM in Iran be in a wide range from 1.3% to 11.9% in different provinces and the highest prevalence has been reported in the West Azarbijan province located in northwest Iran (15).

The findings of some studies revealed that there is a strong relationship between hypertriglyceridemia and the risk of Type 2 diabetes (16-18), however, the studies on its relationship with GDM is so restricted, especially in Middle Eastern mothers. This study aimed to clarify the association of serum levels of triglycerides during the 1st trimester with the risk of developing GDM. Also, the other aim of this study was to describe which indicators of obesity are associated with GDM expression in a population with a higher rate of GDM in Iran. It is understandable that identification of modifiable risk factors of GDM will help to prevent its expression.

2. Methods

This prospective descriptive study was carried out at 6 public health centers connected to the health ministry. First the city was divided into 6 regions based on the distribution of population and then 1 health center was randomly selected from each region. All of the facilities were in Urmia, which is the capital of West Azerbaijan province and is located in northwest Iran. According to family records, all primigravida women with a singleton pregnancy at the first trimester of pregnancy were invited to participate in the study. Women with Type 1 or Type 2 diabetes prior to pregnancy, FBS $\geq$ 126 mg/dL in the first trimester of current pregnancy, as well as women older than 35 years were excluded. The gestational age was calculated based on LMP, therefore, the women who did not know the exact date of their LMP were also excluded. Finally, from 482 eligible women, 436 women who continued their pregnancy beyond 24 - 28 weeks of gestation were accepted to participate in the study. The sample size was calculated based on the following formula: $n = z^2 \times P \times q/d^2$; z: alpha risk expressed in z-score; p: expected prevalence; q: 1 - p; d: design effect.

BMI, WC, WHtR, WHR, and the fasting serum levels of triglycerides (TG) were determined at 6 - 10 weeks of gestation. The WC was measured at the mid-distance between the iliac crest and last rib margin while the woman was in a standing position, after normal expiration. The hip circumference was measured at its most prominent part.

All participated women were followed-up until the 24th - 28th week of pregnancy by monthly visits. We used the IADPSG criteria for diagnose of GDM. Therefore, fasting plasma glucose equal or more than 92 mg/dL or 1 and 2 hours after 75 g oral glucose load equal or more than 180 and 153 mg/dL, respectively, at 24 to 28 weeks of gestation, were considered as GDM.

All analyses were performed with SPSS for Windows 16.0 (SPSS Inc, Chicago, IL). Descriptive statistics were used for categorizing the sample by variables and calculating the means and standard deviations (SDs). For analysis of factors associated to the expression of GDM, participants were divided into 2 groups. One group consisted of women who experienced GDM and the other consisted of those who did not. The analysis employed multiple logistic regression analysis, and the odds ratio (OR) of each item and its 95% confidence interval (CI) were computed controlling for age. Age was thought to influence the likelihood of GDM during pregnancy.

The study was approved by Urmia Islamic Azad University Research Ethical Committee (IR.IAU.URMI.REC.1396.07). After being informed that their participation was voluntary and they could withdraw at any stage of the study, the participants gave their verbal consent.

3. Results

This study was conducted in a 10-month period from October 2014 to July 2015. Among the participants, 19.3% were aged under 20 years, 7.8% were 31 - 35 years old and the majority (about 73%) were 21 - 30 years old, with a mean (SD) age of 24.1 (6.3) years. The serum concentration of total triglyceride in 55.5% of women was less than 150 mg\dL while in 16.5% of them was more than 199 mg\dL. The mean concentration of total triglyceride was 172 (19.3) mg\dL. The majority of participants (62.8%) had a BMI more than its normal range with a mean (SD) BMI of 27.3 (3.4) Kg\m^2. A total of 11% of participants had a WC equal to or more than 96 cm. WC in the majority of them (84.4%) was 80 - 95.9 cm, with a mean (SD) WC of 88.2 (14.2) cm. WHtR, in about 87% of women, was 0.51 - 0.61, with a mean (SD) WHtR of 0.58 (0.05). The mean WHR was 0.84 (0.06). WHR in 52 women (11.9%) was equal or more than 0.90. GDM was diagnosed in 42 women (9.6%).

Table 1 presents associations between participant characteristics and GDM. Age, BMI, WC, WHtR, WHR, and serum concentration of TG, in 6-10 weeks of gestation were significantly associated with expression of GDM. Results of logistic regression analysis controlling for age also are shown in Table 1.

GDM in women who were 31 - 35 years old (OR1.93; 95% CI, 1.84 - 2.03) were more likely than younger women. In addition, women who had a BMI more than 29 Kg\m^2 were more likely to have GDM than those who had a lower BMI (OR 1.86; 95% CI, 1.72 - 1.96). BMI in 23.8% of women who experienced GDM was more than 29 Kg\m^2, while the major-

Table 1. Associations of Participants' Characteristics with GDM (N = 436)[a]

Items	Whole Participants	GDM			
	N = 436	Yes (n = 42)	No (n = 394)	Odds Ratio[b]	95% CI
Age, y					
< 20	84 (19.3)	6 (14.3)	78 (19.8)	1.00	
21 - 25	202 (46.3)	18 (42.8)	184 (46.7)	0.87	0.45 - 1.67
26 - 30	116 (26.6)	12 (28.6)	104 (26.4)	1.09	0.58 - 1.39
31 - 35	34 (7.8)	7 (14.3)	27 (6.8)	1.93	1.84 - 2.03[c]
BMI, kg/m^2					
< 19.8	26 (6.0)	1 (2.4)	25 (6.3)	1.00	
19.8 - 26	136 (31.2)	8 (19.0)	128 (32.5)	0.89	0.49 - 1.57
26 - 29	218 (50.0)	23 (54.8)	195 (49.5)	1.13	0.68 - 1.39
> 29	56 (12.8)	10 (23.8)	46 (11.7)	1.86	1.72 - 1.97[c]
TG levels, mg/dL					
< 150	242 (55.5)	0 (0.0)	242 (61.4)	1.00	
150 - 199	122 (28.0)	10 (23.8)	112 (28.4)	0.93	0.51 - 1.59
200 - 499	64 (14.7)	27 (64.3)	37 (9.4)	2.97	2.08 - 3.58[d]
≥ 500	8 (1.8)	5 (11.9)	3 (0.8)	3.24	2.72 - 3.95[d]
WC, cm					
≤ 79.9	20 (4.6)	0 (0.0)	20 (5.1)	1.00	
80 - 86.9	175 (40.1)	12 (28.6)	168 (41.4)	0.91	0.52 - 1.43
87 - 95.9	193 (44.3)	21 (50.0)	172 (43.6)	1.58	1.45 - 1.78[c]
≥ 96	48 (11.0)	9 (21.4)	39 (9.9)	1.94	1.72 - 2.25[d]
WHtR					
≤ 0.50	14 (3.2)	0 (0.0)	14 (3.6)	1.00	
0.51 - 0.55	168 (38.5)	10 (23.8)	158 (40.1)	0.88	0.52 - 1.08
0.56 - 0.61	210 (48.2)	23 (54.8)	187 (47.5)	1.76	1.43-2.14[c]
≥ 0.62	44 (10.1)	9 (21.4)	35 (8.9)	2.02	1.79-2.65[c]
WHR					
≤ 0.78	20 (4.6)	1 (2.4)	19 (4.8)	1.00	
0.79 - 0.83	166 (38.1)	13 (31.0)	153 (38.9)	0.89	0.59 - 1.41
0.84 - 0.89	198 (45.4)	19 (45.2)	179 (45.4)	1.25	0.51 - 1.48
≥ 0.90	52 (11.9)	9 (21.4)	43 (10.9)	1.97	1.43 - 2.28[c]

Abbreviation: BMI, body mass index; CI, confidence interval; TG, serum levels of triglycerides; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.
[a]Values are expressed as No. (%).
[b]Results of multiple logistic regression analysis controlling for age are shown.
[c]$P < 0.05$.
[d]$P < 0.01$.

ity of them (78.6%) had a BMI more than 26 Kg\m^2. There was no association between other different BMI groups in expression of GDM.

None of the women with serum concentration of triglyceride less than 150 mg\dL were affected by GDM while more than 3-quarters of women (76.2%) who were diagnosed with GDM had a serum concentration of triglyceride more than 200 mg\dL. Of the 8 women who had triglyceride more than 500 mg\dL, 5 women were diagnosed with GDM. Women who their triglyceride levels was higher than 200 mg\dL were more likely to have GDM than others (OR 2.97; 95% CI, 2.08 - 3.58 and OR 3.24; 95% CI, 2.72

- 3.95 for groups with serum concentration of triglyceride 200 - 499 and $\geq$ 500 mg\dL, respectively). A total of 12 women (28.6%) who were diagnosed with GDM had a waist circumference less than 87 cm and the WC in the rest of them (n = 30, 71.4%) was equal or more than 87 cm. WC of over 87 cm increased the likelihood of GDM (OR 1.58; 95% CI, 1.45 - 1.78 and OR 1.94; 95% CI, 1.72 - 2.25 for groups with WC 87 - 95.9 and $\geq$ 96 cm, respectively).

In addition, WHtR was associated with GDM; therefore, the women who had a WHtR more than 0.55 were more likely to affect with GDM (OR 1.76; 95% CI, 1.43 - 2.14 and OR 2.02; 95% CI, 1.76 - 2.65 for groups with WHtR 0.56 - 0.61 and $\geq$ 62, respectively).

Only the women with WHR equal to or more than 0.90 had a higher chance of being affected with GDM (OR 1.97; 95% CI, 1.43 - 2.28).

4. Discussion

Although gestational diabetes is one of the well-known complications of pregnancy, its exact prevalence is unknown in Iran. In a review study on epidemiology of GDM in Iran, the prevalence of GDM was reported to be almost 4% in Tehran. In other parts of country, its incidence varied between 1.3% - 11.9% (15). It seems, these differences arise from using the various methods for screening of GDM, different diagnostic criteria or the existence of different ethnic groups living in Iran, which make the comparison of prevalence of GDM in different parts of country difficult. In this study, 9.6% of participants had been affected by GDM. It is obvious that this number does not represent the true prevalence of GDM due to the fact that older and multiparous women were excluded from the study.

For years, the relationship between BMI and GDM has been proven. Having a BMI equal to or more than 30 kg/m^2 is a major risk factor of GDM, therefore, all women with a BMI $\geq$ 30 kg/m^2 in the first trimester of pregnancy, a diagnostic test (OGTT, using 75 g) at 24 - 28 weeks was recommended by national institute for health and clinical excellence (NICE) (19). This study confirmed that women with BMI > 29 kg/m^2 in early pregnancy have a higher chance of being affected by GDM in the 2nd trimester of pregnancy.

Although, obese women are more exposed to Type 2 diabetes, most researchers have believed that abdominal obesity have a greater role in this regard. On the other hand, BMI cannot differentiate being overweight caused by increased in fat from that caused by increased in muscle mass (20). In a study on Asian white women, it was shown that diabetes had a stronger relationship with WC (as a marker of central obesity) and WHR than BMI (21), which had been found by Ford et al. (22) previously. In a study in Iran, the WHtR was a better predictor of diabetes than BMI (23). Although studies on the predictors of GDM is not as wide as diabetes, some researchers suggested that the risk factors of GDM and diabetes mellitus are the same and their prevalence are also similar (24). Visceral adiposity, independently to BMI, is associated with an increase in insulin resistance (25) and the risk of GDM (26). Martin et al. measured the visceral and subcutaneous fat depth using the ultrasound machine at 11 - 14 weeks of gestation and studied their differences in having a positive GCT (50 g glucose challenge test) at 24 - 28 weeks. According to their findings, visceral adiposity was accompanied with a higher risk of GDM (26). Ultrasound facilities and sonographer are not available in public mother's health care centers in Iran; therefore, we used WC, WHtR, and WHR as abdominal obesity indices.

In the present study, logistic regression analysis revealed that WC, WHtR, WHR, and serum concentration of triglycerides before 10 weeks of gestation, independent of age, were predictors of GDM. Brisson and colleagues studied the association of WC and hypertriglyceridemia in the first trimester of pregnancy with GDM in 144 pregnant mothers. They concluded that women with WC greater than 85 cm accompanied by hypertriglyceridemia, known as "hypertriglyceridemic waist phenotype", are more likely to be diagnosed with GDM (27). Lipids metabolism in mothers alters during pregnancy and the serum concentration of triglycerides begins to arise after 10 weeks of pregnancy (28), thus, its serum levels before 10 weeks can be considered as its concentration before pregnancy. According to our results, the serum levels of TG more than 200 mg in mothers planning for pregnancy can be a valid predictor of GDM. Although the maternal serum triglycerides do not apparently transfer via placenta, its higher levels have detrimental effects on insulin resistance, especially in women with GDM, which can result macrosomia in infants. It is shown that women with GDM in combination with hypertriglyceridemia have a higher chance to deliver an LGA newborn than others (29). Therefore, it seems that hypertriglyceridemia can not only have a possible role in mechanism of GDM but can also be a predictor of some complications such a macrosomia, independent of maternal fasting plasma glucose levels (29). Seemingly, screening of hypertriglyceridemia and early intervention to modify serum levels of TG, especially before pregnancy, can be a new research field in early and effective prevention of GDM. Increasing the prevalence of obesity and Type 2 diabetes (30, 31) worldwide is a warning sign of rising in the frequency of GDM in future. In a period of 3 years, from 1999 to 2002, the prevalence of obesity among Iranian women increased 6% while the incidence of abdominal obesity increased 2 times among 20 - 29 year old women in the same time (32). Currently, 53% of Iranian women are overweight or obese (33). All of these accompanied with unfavorable lifestyle routines will lead to increasing in prevalence of GDM in next years among Iranian mothers; thus, there is a crucial need to develop some accessible and inexpensive approaches to early prediction of GDM and prevention of its complications.

We used the criteria of the IADPSG as a diagnostic tool for GDM due to its wide use around the world. It is worth noting that, according to the guideline of prenatal care, these criteria are used to diagnose GDM in public health care centers in Iran. Although age and parity are risk factors of GDM and the history of previous pregnancies provides valuable information about the likelihood of GDM in current pregnancy, for controlling the confounding variables, multiparous and older women were excluded from the study. All biochemical analyses were done in the same referral laboratory, however, due to the study plan, the measurement of other parameters including BMI, WC, WHtR, and WHR, by the same midwife, was impossibl; thus, we had to use 6 trained midwives in 6 health centers. The other limitation of this study was the racial homogeneity of the participants. On the other hand, the prevalence of GDM in Urmia is higher than the other parts of the country (15), which may limit the generalization of our findings. However, we think it cannot be a major concern due to the fact that other studies have shown the effects of abdominal obesity and hypertriglyceridemia on impaired glucose tolerance on different population (27).

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