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GESTATIONAL DIABETES MELLITUS IN IRANIAN WOMEN: A RISING RATE

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Abstract

Context. Rising incidence of Gestational diabetes mellitus (GDM) has been reported in the recent years and it has become an important public health problem, mainly among women aged 35-39 years.

Objectives. Frequency of GDM in the females who are living in the northwest of Iran was evaluated.

Subjects and Methods. Two hundred and fifty pregnant women at 24-28th weeks of gestation were screened using 50 g oral glucose challenge test (OGCT), and the subjects with blood sugar levels equal or greater than 130 mg/dL were referred to diagnostic 100 g oral glucose tolerance test (OGTT). GDM was diagnosed according to Carpenter and Coustan criteria.

Results. Eighty six women (34.4%) with positive result of screening test were selected for subsequent OGTT with 100g oral glucose. GDM was diagnosed in twenty four women (9.6 %) with at least 2 abnormal values. Frequency of GDM in the older subjects or the subjects with high pre-pregnancy or 24-28th weeks' body mass index (BMI) were significantly higher than younger pregnant females or the subjects with low BMI.

Conclusion. Prevalence of GDM in the current study was 11.9%, which is higher than earlier reports and implicates that the prevalence of gestational diabetes mellitus has markedly been increasing in Iran and associated with maternal age and body mass index.

Key words: Gestation Diabetes Mellitus, Oral Glucose Challenge Test, Oral Glucose Tolerance Test, Prevalence, body mass index, maternal age.

INTRODUCTION

Pregnancy always comes with some anatomic and physiologic changes, and metabolic and hormonal adaptations are essential parts of it that occur in the function of the hypothalamus, pituitary, parathyroid, thyroid, and adrenal glands to support the growth and development of the fetus (1).

Placental hormones such as progesterone, placental lactogen, corticotropin-releasing hormone and growth hormone were proposed as factors which produce insulin resistance and increase insulin excretion (2).

Therefore pregnancy is a circumstance that may lead to diabetes and gestational diabetes mellitus (GDM) is the most prevalent metabolic abnormality during pregnancy (2-4).

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The effect of mono-and dizygotic gestation on the glucose tolerance has been reported by Sarac *et al.* (5).

It causes various maternal and infant outcomes such as macrosomia, laboring problems, polyhydramius, preeclampsia, and newborn metabolic disorders (hypoglycemia, hypercalcemia, hyperbilirubinemia) (6). So, early diagnosis and management of the disease could have a significant role in the controlling of its complications (7). Screening for GDM is an accepted concept, but in the case of methodology a worldwide agreement has not been achieved yet (8). There are several laboratory diagnostic tests for diagnosis of GDM. Oral glucose challenge test (OGCT), a tolerance test to 50 grams glucose, and oral glucose tolerance test (OGTT), a tolerance test to 75 or 100 grams glucose, were suggested as screening and diagnostic tests for GDM, respectively (9, 10). The incidence of GDM was reported between 1 to 14% of all pregnancies in various regions of the world (11-15) and its incidence in Iran was estimated about 4.5% of all pregnancies (16, 17), but it has indicated that the rate of GDM is increasing in different countries and it is going to become an important public health problem, mainly among women aged 35-39 years (18-21). So the current study was done as a preliminary study to compare the current rate of GDM in Urmia city, a northwest province in Iran with previously reported rate.

MATERIALS AND METHODS

Subjects

Two hundred and fifty pregnant women who referred to Urmia health center enrolled in the current study with informed written consent after ethics approval by local board of medical ethics. All women were in their 24th to 28th weeks of pregnancy and had not any pre-pregnancy history of diabetes, any specific medication consumption, pancreatic diseases, hormonal syndromes and genetic disorders. Mean age of these women was 24.34 ± 7.31 years.

Body Mass Index(BMI)

Body mass index (BMI) was assessed in pre-pregnancy and in the time of oral glucose tolerance test, i.e. 24-27th weeks, by the measurement of weight and height of the subjects using the following formula:

$$BMI = \frac{\text{mass (kg)}}{(\text{height(m)})^2}$$

Blood sampling and biochemical analysis

Blood samples (five milliliter with EDTA-K (1mg/mL)) were taken for each subject and plasma was separated by bench centrifuge, glucose levels were measured by biochemical analyzer (BT-3000, Biotechnica Instruments, Italy) using an enzymatic method .

Oral glucose challenge test (OGCT)

Fifty grams of glucose was dissolved in the cold tap water and consumed by subjects and then the second blood samples were collected after one hour.

Subjects with the plasma blood sugar higher than cutoff point, i.e. ≥130mg/dL, were selected for the next step.

Oral glucose tolerance test (OGTT)

100 grams of glucose was dissolved in cold water and was consumed by the subjects. Fasting and timed (1, 2 and 3 hours) blood sugar was measured subsequently. GDM was diagnosed according to the criteria of Carpenter and Coustan (Table 1) with at least two abnormal test results.

Table 1. Diagnostic criteria gestational diabetes

Sample Type	Glucose Tolerance Test by 100 grams glucose				Criteria
	FBS	1 hours	2 hours	3hours	
Whole Blood mg/dL	90	165	145	125	Osullivan
Plasma mg/dL	105	190	165	145	NDDG
Plasma mg/dL	95	180	155	140	Carpenter and Coustan
Plasma mg/dL	92	180	153	---	IADPSG§

§ plasma glucose levels after consumption of 75 grams glucose.

Statistical analysis

Anthropological data were categorized and analyzed by student t-test using statistical software (SPSS version 14 for Microsoft windows users). p 0.05 were considered as significant.

RESULTS

As shown in Table 1, different criteria have been approved for the diagnosis of GDM that differ in sensitivity and specificity of diagnosis. Several large population studies have been conducted to find the best sensitivity and specificity for OGTT and recently international association of diabetes and pregnancy study groups (IADPSG) has reached to a consensus on accepting the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study for the diagnosis of GDM (10). The advantages of shortening the duration of the test were concluded by Weinert as convenience for the patient, lower cost, and a good diagnostic accuracy in all populations evaluated (22). However, the criterion of Carpenter and Coustan has still been accepted by researchers (23).

Two hundred and fifty pregnant women were studied by OGCT screening test and plasma blood sugar of eighty six subjects was found more than cutoff point (≥ 130 mg/dL) so that they were considered subjects with impaired glucose tolerance (Table 2).

Mean age of the pregnant women with plasma glucose greater than 130 mg/dL after consumption of 50 grams glucose was 26.85 ± 5.16 years (median and 10-90 percentile range: 26 and 21-36.3, respectively), which was significantly higher than healthy group with mean age 23.76 ±3.58 (median and 10-90 percentile range: 23 and 19-29, respectively) ($p<0.01$) (Fig. 1).

OGTT was carried out for 86 subjects who had plasma glucose more than 130 mg/dL after one hour of 50 grams oral glucose consumption. Upon

the criterion of Carpenter and Coustan that is given in the Table 1, twenty four of eighty six subjects with impaired glucose tolerance were diagnosed as GDM with at least two abnormal test results (Table 2).

As shown in Table 2, mean age of the GDM patients was 32 ± 5.02 (median and 10-90 percentile range: 32 and 24-38, respectively) years which is significantly higher than non-GDM cases with mean age of 24.85 ± 3.61 (median and 10-90 percentile range: 24 and 20.3-29, respectively) ($p<0.001$) (Fig. 1). The findings of the current study are in good agreement with others which have revealed a positive correlation between maternal age and prevalence of the GDM(24-27) but the cutoff age still remained controversial.

Pre-pregnancy BMI of the

Table 2. Age, BMI and results of oral glucose challenge (OGCT) and tolerance test (OGTT):

	Subjects n=250 (100%)		
	Normal glucose tolerance 164 (63.6%)	Impaired glucose tolerance (≥130 mg/dL) 86 (34.4%)	
		Non-GDM 62 (24.8%)	GDM 24 (9.6%)
Age (years)	23.76 ±3.58	24.85 ± 3.61	32 ± 5.02 §
BMI Pre-	21.73± 2	23.30±1.32§	23.43±1.05§
BMI 24-27th week	22.47±1.94	24.96±1.78	26.27±1.57§
FBS (mg/dL)	78.24 ± 6.38	81.54 ± 4.38	90.03 ± 14.11
OGCT* (mg/dL)	101.81 ± 17.68	167.3 ± 39.43§	
$OGTT_{1h}$** (mg/dL)	N/A	155.16 ± 5.18	248 ± 39.97§
$OGTT_{2h}$** (mg/dL)	N/A	119.16 ± 3.21	224 ± 38.26§
$OGTT_{3h}$** (mg/dL)	N/A	107.2 ± 4.25	192 ± 27.97§

*Plasma glucose one hour after consumption of 50 grams glucose (mg/dL), **Plasma glucose after consumption of 100 grams glucose (mg/dL), § significant difference between GDM and subjects with normal glucose tolerance ($p<0.01$).

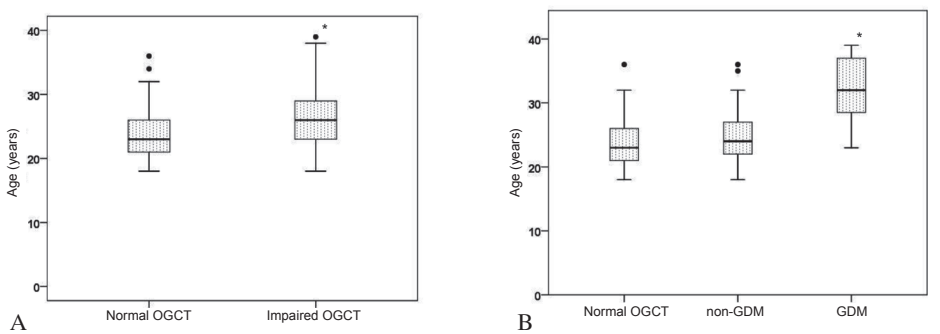

Figure 1. Boxplot showing distribution of age (median, 1st - 3rd quartiles and range) in the different groups. A. comparison of age distribution between subjects with normal and impaired glucose tolerance in 24-28th weeks of Pregnancy, B. comparison of age distribution between the subjects with normal and impaired glucose tolerance who were diagnosed as GDM patients and non-GDM *significant difference ($p<0.05$).

subjects who showed normal glucose tolerance was 21.73± 2 kg/m^2 (median and 10-90 percentile range: 21.76, 18.86-24.23 kg/m^2) and increased to 22.47±1.94 kg/m^2 (median and 10-90 percentile range: 22.65, 19.16-24.87 kg/m^2) once the blood samples were collected for OGCT. Pre-pregnancy BMI in the subjects with impaired glucose tolerance was 23.34±1.25 kg/m^2 (median and 10-90 percentile range: 23.67, 21.55-24.87 kg/m^2) and increased to 25.32±1.82 kg/m^2 (median and 10-90 percentile range: 25.21, 23.07-27.9 kg/m^2) in the 24-28th weeks of pregnancy. A significant difference of pre-pregnancy BMI was found between the subjects with normal and impaired glucose tolerance ($p<0.001$). The impact of pre-pregnancy body mass index on the risk of gestational diabetes was investigated by Singh *et al.* and revealed that pre-pregnancy BMI plays an important role in the risk of GDM occurrence (28, 29) and it is in good agreement with the findings of the current study.

Among the subjects with impaired glucose tolerance, the pre-pregnancy body mass index of the subjects who were diagnosed as GDM patients, was 23.43±1.05 kg/m^2 (median and 10-90 percentile range: 23.49, 22.31-24.81 kg/m^2) and it was 23.30±1.32 kg/m^2 (median and 10-90 percentile range: 23.67, 21.17-25.03 kg/m^2) in the non-GDM subjects. No significant difference was found between pre-pregnancy BMI of the two groups ($P>0.5$). However, the BMI of the GDM patients in the 24-28th weeks of pregnancy raised to 26.27±1.57 kg/m^2 (median and 10-90 percentile range: 26.53, 23.15-28.16 kg/m^2) which is significantly higher than 24.96±1.78 (median and 10-90 percentile range: 24.76, 22.65-27.77 kg/m^2) in the non-GDM subjects ($p<0.01$), (Table 2 and Fig. 2).

Our findings are in good agreement with the other reports that prove the importance of high BMI in the risk of gestational diabetes (30) but the effect of race and ethnicity on the association between BMI and GDM has also been noted (31).

Concerning the effect of higher age and increasing BMI on the risk of

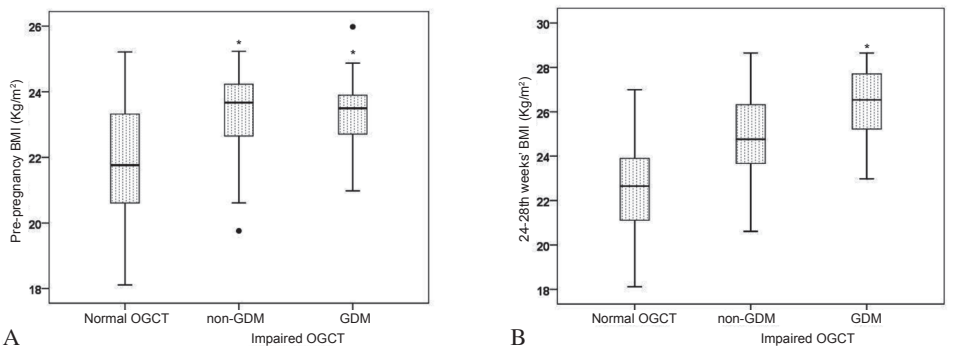

Figure 2. Boxplot showing distribution of Body mass index (BMI) (median, 1st - 3rd quartiles and range) in the different groups. A. comparison of pre-pregnancy BMI between subjects with normal and subjects with impaired glucose tolerance who were diagnosed as GDM patients and non-GDM subjects B. comparison of 24-28th weeks' BMI between subjects with normal and impaired glucose tolerance who were diagnosed as GDM patients and non-GDM subjects * significant difference ($p<0.05$).

development of GDM, we found that the risk of GDM in the older subjects with high pre- pregnancy and 24-28th week's BMI is significantly higher than in young subjects or subjects with low BMI. Similar findings have been reported by others (27, 31).

However, glucose tolerance and gestational diabetes could be affected by several factors such as anti-oxidant and fatty acids (32), and the role of adiponectins in the gestational diabetes has been reported (33).

In the current study GDM was found in 24 of the 250 subjects (9.6 %). It has been reported that the prevalence of GDM in Tehran is 4.7% and one out of every 20 pregnant Iranian women will develop GDM, with significantly increased odds of adverse maternal and fetal outcome (34). A similar result was found in another prospective cohort study in an urban Iranian population living in the central part of Iran, not far from Tehran (16).

The prevalence rate of GDM in southern provinces of Iran is lower than in north west but higher than in Tehran and central provinces (35). It seems that the prevalence of GDM in North West is higher than in Tehran and central provinces of Iran or the incidence of the GDM is increasing in Iran. The observed dissimilarity could be interpreted by increasing rate of GDM as reported in other countries (18-21). Higher rate of GDM was reported in the patients living in northern Quebec, Canada and GDM incidence on swampy women in moss factory was 8.5% (36, 37).

Ferrara and colleagues have studied the incidence of Gestational Diabetes in Asian women using Carpenter and Coustan and found that the 8.3% of patients suffer from GDM (38). Yang *et al.* reported that 24% of pregnant women in Tianjin China are suffering from GDM (39) which is significantly higher than the results of the current study.

Even if different factors such as seasonal variations, methodological differences, differences in race, life style and diets could give rise to the observed variation of the different studies, but global trends of GDM are increasing. It is not clear if early diagnosis and subsequent appropriate dietary and treatment measures really help prevent complications, but there is benefit from targeting a more detailed and focused monitoring of the fetus and mother as increased attention detects complications earlier and permits a reduction in morbidity, especially of the neonate. Hence, assessment of glucose tolerance in the first trimester instead of 24-28th weeks of pregnancy is strongly suggested.

In conclusion, the number of subjects which was included in the current study is not enough to make it an epidemiological study, but it could be considered as a preliminary study showing an increasing rate of GDM in Iran. We believe that epidemiological studies with larger sample size have to be established to provide a clear picture of GDM burden in Iran.

Conflict of interest

All authors disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three years from the beginning of the submitted work that could inappropriately influence, or be perceived to influence our work.

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