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Original Article

Maternal glycemic status in GDM patients after delivery

Hossein-nezhad A, Mirzaei k, Maghbooli Z, Larijani B*

Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background: Women with history of gestational diabetes mellitus (GDM) have higher risk for developing diabetes in the future life. The aim of the current study was to examine the association between GDM and susceptibility to type 2 diabetes and Impaired Glucose Tolerance (IGT) after pregnancy.

Methods: As a cohort study, 2416 women who had consecutively referred to five university educational hospitals in Tehran, Iran for antenatal care, were recruited. The universal screening was performed with a GCT-50g and those with plasma glucose level ≥ 130mg/dl were diagnosed as GDM if they had an impaired GTT-100g based on Carpenter and Coustan criteria. All participants followed by 6-12 weeks after delivery for OGTT-75g. Concerning American Diabetes Association criteria was diagnosed post-partum diabetes mellitus and IGT.

Results: The prevalence of overt postpartum diabetes mellitus and IGT were 8.1% (CI 95%: 3.5-15.4) and 21.4% (CI 95%: 13.7-30.8), respectively. We found a significant difference in the prevalence of hyperglycemia (FBG>105 mg/dl during pregnancy), necessity to use insulin during pregnancy and BMI≥27 kg/m2 before pregnancy in patients who developed diabetes after delivery as compared with normal controls. Results of multivariate analysis suggested that gestational necessity for insulin prescribing and BMI≥27 kg/m2 were the two best predictors for developing postpartum diabetes. As well our findings demonstrated that the best predictors for postpartum IGT were history of abortion, gestational insulin therapy and BMI≥27 kg/m2. This correlation was present after adjusting for the age.

Conclusion: It seems that high glucose levels during pregnancy, necessity for insulin therapy during pregnancy, history of abortion and BMI≥27 kg/m2 are the best predictors for postpartum development of diabetes and IGT.

Keywords: Gestational diabetes mellitus, Type 2 diabetes, Predictive factors, IGT

*Corresponding Author: Endocrinology and Metabolism Research Center,5th Floor, Shariati Hospital, North Kargar Ave.,Tehran 14114, Iran, Tel: +98(21) 88220037-8, Fax: +98 (21) 882220054, Email: emrc@sina.tums.ac.ir

Introduction

Type2 diabetes is a major contributory factor in middle and old age morbidity and mortality which imposes a tremendous burden on patients and health care systems (1, 2). The prevalence of diabetes has been dramatically increased, as 1.3 million new cases diagnosed annually. Women with GDM are at increased risk for developing overt diabetes later in the life (3, 4). Accordingly, the timely diagnosis and subsequent management of gestational diabetes after delivery have important implications for the prevention of type 2 diabetes.

Gestational diabetes, the most common medical complication of pregnancy, is defined as glucose intolerance that its onset or first recognition is during pregnancy (4) and complicates approximately 4-8% of pregnancies (5,6). Shortly after delivery, glucose homoeostasis is restored to before pregnancy status, but affected women remain at high risk of developing type 2 diabetes mellitus in the future (7,8). However, evidences from previous studies demonstrated that the majority of patients regain the normal glucose tolerance levels during a few weeks after delivery, but some reported emerging insulin resistance and insulin secretory dysfunction in these women (9, 10). Therefore, women with a history of GDM are faced to an 18–50% increased risk of developing type 2 diabetes mellitus within 5 years following pregnancy (11, 12).

Early postpartum screening measures and detection of predictive factors for subsequent developing type 2 diabetes, provides an opportunity to decrease the risk of diabetes progression in women with a history of GDM (13). For population of any ethnic group, emerging of gestational diabetes indicates the underlying susceptibility to type2 diabetes (14, 15). The results of a recent study in Iranian women showed that 23% of participants who had previous history of GDM, developed to impaired glucose tolerance (IGT) or overt diabetes later in the life (16). The main predictive factors in anticipation of later developing type 2 diabetes in women with history of GDM were reported as following: advanced maternal age (17), prior obesity (18), necessity for insulin therapy during pregnancy (19), severity of IGT during pregnancy (20), history of macrosomia (21), number of parities (19, 22), presence of islet cells autoantibody (23), early diagnosis during pregnancy (24) and elevated fasting blood glucose in response to the glucose tolerance challenge.

The relationship between gestational diabetes and type 2 diabetes mellitus has implications for clarification of the etiology of these disorders and, subsequently, implementing methods for early diagnosis and warranting preventive measures to manage possible ramifications. However, type 2 diabetes is the most common metabolic disorder in Asian population; but, there is a dearth data on the prevalence of IGT in women with history of GDM. Therefore, we designed the current study to evaluate the maternal glycemic status in GDM patients after delivery and to identify the predictive factors which make GDM patients susceptible to subsequently developing impaired glucose tolerance and T2DM.

Methods

Study design and population

As a cohort study, 2416 women who had consecutively referred to five university educational hospitals in Tehran, Iran for antenatal care, were recruited. The study protocol was approved by ethics committee of Endocrinology and Metabolism Research Center (EMRC). After taking written informed consent, participants' information was collected, using a standard questionnaire that included demographic data, information regarding current pregnancy including calculation of gestational age according to the date of the last menstrual period confirmed by ultrasound early in the pregnancy,

infections and medications, and previous medical, obstetric and family history. Primary screening was done at the first clinical visit for prenatal care in whom with risk factors of gestational diabetes. These risk factors included: age ≥ 30 years, pre-gestational body mass index (BMI) ≥ 27 kg/m2, polyuria, glucoseuria, proteinuria, parity ≥5, previous history of gestational diabetes, family history of diabetes mellitus, prior macrosomia, pregravid obesity and unfavorable obstetric outcomes in previous history. The rest of participants were evaluated via universal screening for GDM between 24th and 28th weeks of pregnancy using standard protocol.

Protocol

GDM was diagnosed by the two-step diagnostic procedure using a 50 gr glucose challenge test and a 75 gr oral glucose tolerance test (OGTT). We performed an oral glucose challenge test-50 gr for all participants. Women with increased fasting glucose or with at least one risk factor for GDM are referred to early diagnostic tests; otherwise, screening tests were performed at 24–28 weeks of gestation. The screening for diagnosis of GDM was performed with an OGCT-50gr and a plasma glucose threshold value of 130 mg/dl one hour after glucose load intake in non-fasting state. All women with plasma glucose values greater or equal than 130 mg/dl were given an 100gr-3hours glucose tolerance test to diagnose gestational glucose intolerance using Carpenter and Coustan criteria (25). Plasma glucose levels were measured using the glucose-oxidase enzymatic method, with a coefficient of variation (CV) <5%.

Examination after delivery

All participants followed until 6-12 weeks after delivery. All women with GDM were recommended to have an early 75 g OGTT after delivery. During this time after pregnancy, fasting blood samples were collected for measurement of glucose. Concerning American Diabetes Association criteria (31), Fasting Blood Sugar (FBS) ≥126 mg/dl was considered as diabetes mellitus. IGT was diagnosed if 2-h postprandial glucose was between 140 mg/dl and 199 mg/dl (7.8–11.0 mmol/l) and IFG was diagnosed if fasting glucose was between 100 mg/dl and 125 mg/dl (5.5–6.9 mmol/l) (26).

Statistical analysis

Student t-test and Analysis of Vanance (ANOVA) used for comparing of variables. Chi-square test was used to compare the frequency of variables and the restrictive factors between two groups. Univariate and multiple logistic regression models were used for assessing relationships between the probability of occurrence of postpartum impaired glucose tolerance and T2DM at 6-12 weeks after delivery and pregnancy-related risk factors. The results of the analyses were expressed as odds ratios (OR) and 95% confidence intervals (CI). The level of significance was set at a probability of ≤0.05 for all tests.

Results

A total number of 114 out of 2416 pregnant women have been diagnosed with GDM. The prevalence of GDM in the present study was estimated 4.7% (95%CI: 3.91-5.64). As shown in Table 1, women with GDM had significantly more parities and higher values in body mass index (BMI) than non-diabetic women. Subsequently, 85.9% of women with GDM were followed during postpartum period and in 16.3% insulin therapy initiated, whereas others were managed with diet only. We found no significant differences in BMI, age, parity and FBS levels between referred and non-referred groups. The prevalence of overt diabetes and IGT after pregnancy were estimated 8.1% (95%CI: 3.5-15.4) and 21.4% (95% CI: 13.7-30.8), respectively; while 70.5% restored normoglycemic state.

The analysis suggested that there were a significant differences in FPG levels (>105

mg/dl) (P=0.012), necessity for insulin therapy during pregnancy (P=0.001), before pregnancy BMI (>27 kg/m^2) (P=0.018), number of parities (>4) (P=0.001) and maternal age (>34 years) (P=0.024) between diabetic and non-diabetic women during postpartum period. In contrast, pregnancy-related risk factors like history of abortion, number of parities, maternal age, multiparity, gestational week at GDM diagnosis (>24), and history of type 2 diabetes in the first degree relatives had not significant differences between two groups (Table 2).

As demonstrated in Table 3, pregnancy-related risk factors such as FBG>105 mg/dl (P=0.001), necessity for insulin therapy during pregnancy (P=0.001), number of parities (P=0.001), maternal age (P=0.001), and history of abortion had significant difference between women with IGT and healthy women during postpartum period. Contrarily, before pregnancy BMI>27 kg/m^2, gestational week at GDM diagnosis, and history of type 2 diabetes in the first degree relatives had not significant differences between two mentioned grous.

We found no significant differences between diabetic and healthy women about glucose concentrations at the first and second hours after standard test for assessment of IGT during pregnancy; however, it was significant at the third hour (P=0.003).

Multiple logistic regression model was used to determine the relationships between probability of developing diabetes at 6 weeks after delivery and the presence of before pregnancy and/or pregnancy-related risk factors. Our findings demonstrated that history of abortion, gestational necessity for insulin therapy and BMI≥27kg/m2 were the best predictors of developing IGT after parturition. Also, the best predictors for prediction of further developing diabetes were necessity for insulin treatment during pregnancy and before pregnancy BMI>27 kg/m2. This relationship remained constant after adjustment for the age.

Table 1. Study population characteristics during pregnancy ∗

characteristics	GDM group	Healthy group
Age (year)	29±6	25±5
Before pregnancy BMI (kg/m^2)	27.4±4.3	24.8±2.1
Parity†	1(3)	1(1)
Family history of diabetes	33.3	11.2
History of abortion	25.4	9.8
History of macrosomia (>4000 g)	25.4	4.3

Data are means±SD and %, †interquartile range, ∗ differences were significant (P<0.05), GDM: Gestational Diabetes Mellitus , BMI: Body Mass Index

Table 2. Frequency of risk factors in diabetic and None-diabetic women after GDM complicated pregnancy

Risk factors	Diabetic women	None-diabetic women
GDM diagnosis gestational week†	25	18.8
Before pregnancy BMI¶*	87.5	37.7
Parity§*	37.5	7.2
Insulin requirement during pregnancy*	87.5	2.9
History of abortion	50	18.8
Age>34 years*	50	13
FPG>105 mg/dl*	62.5	17.6
Family history of diabetes	50	39.1

Data are %, †24 weeks≥, ¶≥27 kg/m^2, §≥5, * P-values were significant (<0.05), FPG: fasting plasma glucose, GDM: Gestational Diabetes Mellitus, BMI: Body Mass Index

Table 3. Frequency of risk factors in women with IGT and Non-IGT group after GDM complicated pregnancy

Risk factors	Women with IGT	Non-IGT women
GDM diagnosis gestational week†	34.5	18.8
Before pregnancy BMI¶	51.7	37.7
Parity§*	37.9	7.2
Insulin requirement during pregnancy*	48.3	2.9
History of abortion*	48.3	18.8
Age>34 years*	62.1	13
FPG>105 mg/dl*	62.1	17.6
Family history of diabetes	51.7	39.1

Data are %, †24 weeks≥, ¶≥27 kg/m^2, §≥5, * P-values were significant (<0.05), GDM: Gestational Diabetes Mellitus, BMI: Body Mass Index, FPG: fasting plasma glucose, IGT: Impaired Glucose Tolerance

Discussion

WHO and ADA frequently recommend performing OGTT in all women with GDM at 6–12 weeks after parturition; but, just up to 50% of women returned for follow-up. Nonetheless, 85.9% of women in the present study returned for OGTT as in accordance with findings of the American College of Obstetricians and Gynecologists (ACOG) fellows (27); however, reported rate was lower in some other studies (28, 29). This finding may be explained by appropriately designed follow-up plan among GDM patients after delivery in the present study.

Results of the present study, in favor with prior studies, demonstrated high prevalence of type 2 diabetes and IGT in women with GDM. We found that near one-fourth of women with gestational diabetes further developed type 2 diabetes mellitus or IGT. Data on the prevalence of diabetes in two reported studies from North Korean population were 20% (30) and 18.15% (31) early in the course of postpartum and 6 weeks after delivery. The prevalence of diabetes has been estimated 7-57% during the first year after delivery (32, 33). There are conflicting reports regarding the prevalence of postpartum diabetes mellitus after gestational diabetes which may be explained with different analysis methods and various definitions in prior studies.

Various results about maternal risk factors such as BMI, maternal age, history of type2 diabetes in first degree relatives and the number of parities have been reported. In favor with prior studies, our findings revealed that there were significant differences between postpartum diabetic women and healthy subjects in FPG levels, necessity for treatment with insulin during pregnancy, 3-hour glucose level in OGTT, parity, maternal age and before pregnancy BMI; also, the best predictive factors for further developing postpartum IGT included FPG concentrations, history of abortion, gestational necessity for insulin therapy, parity and maternal age (19, 17, 22, 34).

Some previous studies reported that precocious detection of GDM (<24 weeks of pregnancy) may accounts as a strong predictor of postpartum diabetes (35, 24, 36, 37). These findings may be explained, in part, by the presence of other risk factors that persuades early screening during pregnancy. Accordingly, it seems that higher prevalence of postpartum type 2 diabetes may be explained by the presence of much more risk factors in these women. Also, gestational age at the time of diagnosis, depending on planned screening algorithm, may explains the controversial results of previous studies (30, 37-41).

Several studies have estimated FPG concentrations during OGTT-100 gr as a determinant diagnostic tool (18, 30, 34, 38, 41); but no precise threshold has been defined for FPG levels. A few studies such as Steinhort et al. (34) revealed an 11 times

increase in the risk of developing diabetes in women with FPG>105 mg/dl. Other reports suggested the efficacy of comparison between the highest and the lowest quartiles as the best predictive factor for further developing diabetes (38, 39). Catalano et al. (37) followed women with history of GDM and demonstrated lower glucose concentrations during pregnancy in further normoglycemic women as compare to diabetic women (97±13 vs. 137±25 mg/dl, respectively). Similar results reported by Kjos et al. (31). Discrepant findings may be explained by using different diagnostic criteria (19) or IGT classification protocols (30). Various studies demonstrated dissimilar results regarding to the glucose concentrations following GTT. Glucose concentration at the third hour after GTT had significant differences between diabetic and healthy women in the present study, which was in favor with reported studies (37). In conclusion, our results are in agreement with rapidly growing evidences on the positive correlation between severity of GDM and insulin requirement during pregnancy, and further developing diabetes; however, we found no significant relationship between FPG levels during pregnancy and postpartum emerging diabetes. Necessity for insulin therapy during pregnancy depends on other factors involved in blood glucose control according to lifestyle, which may explain the controversial findings in studies (18, 19, 30, 34). As elucidated in previous studies, the correlation between FPG concentrations and diabetes was more obvious in patients who had no specific treatment during pregnancy.

Our findings demonstrated a significant correlation between before pregnancy BMI and predisposition to further developing postpartum diabetes. Previous reports suggested that obesity may be a strong predictor for emerging of postpartum diabetes (18, 19, 42-47); however, this result was in contrast to some earlier reports (18, 38). These discrepancies may in part be explained by shorter duration of postpartum follow-up and recruitment of patients with various clinical characteristics.

Univariate analysis in previous studies revealed significant correlation between maternal age in GDM patients and postpartum emerging diabetes, except in Australian population (19, 46); in contrast, multivariate analysis has reported different results (18, 24, 30, 39, 40). We observed a significant correlation between maternal age and postpartum developing IGT which is in favor with other studies. We found no significant relation between parity and postpartum diabetes in GDM women; however, discrepant results have been reported (19, 22, 48). Previous observations, along with the results of the present study, did not suggest parity as an independent risk factor for postpartum developing type 2 diabetes in GDM women (19,48), although some reported inconsistent results (19,22). These contradictions may be explained by different ethnical contexts and diagnostic criteria (4).

Multivariate analysis in previous studies except Henry et al. (19), did not show significant correlation between history of type 2 diabetes in the first degree relatives of GDM patients and postpartum developing diabetes (38, 39, 18, 30); in contrary with results of univariate analysis (37, 39, 49) which was similar with our results.

Taken together, high prevalence of postpartum glycemic disorders in patients with GDM emphasizes on the importance of GDM screening programs during pregnancy.

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