Risk Factors for Gestational Diabetes Mellitus: A Case-Control Study

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Abstract-
Introduction: The basic causes of gestational diabetes mellitus (GDM) are vital as they are effective for the diagnosis and prevention of this condition. The aim of this study was to identify the risk factors for GDM and the possible etiological parameters.
Materials and Methods: This case-control study was conducted with 100 women with GDM and 100 healthy pregnant women at – Himagiri Medical Center in association with tertiary hospital – KIMS Hospital and – Pronto Diagnostics in Hyderabad. GDM was acknowledged by impaired oral glucose tolerance test based on the Carpenter and Coustan criteria. Healthy women were randomly selected from the medical center and were matched to gestational age of 24 to 28 weeks at Diagnostic center. Descriptive and inferential statistics were used for data analysis via the SPSS software.
Results: After adjusting variables, multivariate analysis identified 4 significant risk factors of GDM, including pre-pregnancy low physical activity (odds ratio [OR] = 2.85, 95% confidence interval [CI]= 0.97-8.34), advanced maternal age (OR = 1.24, 95% CI = 1.13-1.35), body mass index ⩾ 30 kg/m^2 (OR = 1.10, 95% CI = 1.02-1.20), and family history of diabetes mellitus (OR = 5.62, 95% CI = 2.26-13.96).
Conclusion: We observed significant associations between low pre-pregnancy physical activity and obesity with GDM risk. Thus, the finding of this study can help devise strategies for the prevention of GDM.

Keywords: **gestational diabetes mellitus, physical activity, body mass index, risk factors.**

INTRODUCTION

'Hyperglycaemia has several consequences in pregnancy and is estimated to impact approximately 16.9% of all pregnancies.'

Gestational diabetes mellitus (GDM) is defined as "carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy."[1] The incidence of GDM has been reported to be 1% to 20% using various diagnostic methods and indicates a mounting trend in current years.[2]

The Asia-Pacific region has the largest number of individuals with GDM, as Asian populations are more prone to abdominal obesity and low muscle mass with augmented insulin resistance compared to Western counterparts,[3] the Asia-Pacific region has the highest prevalence of GDM.

Hyperglycaemia has many consequences in pregnancy and is estimated to influence approximately 16.9% of all pregnancies. The highest prevalence is in the Southeast Asia, where 1 in 7 births is affected by GDM.[8] GDM is associated with some short- and long-term health-related consequences for both women and their children.[9] The clinical recognition of GDM is important, because it often requires diet therapy and drug therapy, such as insulin and antepartum foetal surveillances, to reduce GDM-associated perinatal morbidity and mortality. Hyperglycaemia during pregnancy is commonly identified with the oral glucose tolerance test (OGTT). Screening by the use of OGTT is recommended in pregnancy for high-risk woman at their initial prenatal visit and for all pregnant women between the 24th and 28th weeks of pregnancy.[10]

The risk factors of GDM are obesity, physical inactivity,[2] advanced maternal age,[8] multiparous, family history of type 2 diabetes mellitus, and certain ethnicities, including Asians,[11] a previous macrocosmic child, GDM in the previous pregnancy,[10] and polycystic ovarian syndrome.[12] These factors increase the risk of GDM among pregnant women.

A sedentary lifestyle is the fourth most important risk factor of mortality in the world.[13] Physical inactivity is a risk factor for a noncommunicable disease and influences women's overall health.[14,15] The International Physical Activity Questionnaire (IPAQ) was administered to allow classifying of pregnant women as active and inactive. The cutoff point of 450 METs (metabolic equivalents) is defined from the multiplication of the minimum consumption of 3 METs of moderate physical activity for 150 minutes weekly that a pregnant woman must meet to be physically active.[16] Physical

activity is a dependable strategy to bring about constructive changes in human health. Studies have found that physical activity provides major health-related benefits such as improvements in cognitive,[17] cardiovascular,[18] respiratory,[19] and muscle functions[20] and reduces the incidence and severity of type 2 diabetes mellitus and GDM.[21]
Since GDM represents a major threat to public health, international health organizations have accentuated the necessity of devising national plans to progress the quality of care. However, the unremitting monitoring of the pointers of quality of care remains a challenge in various countries.[22] A meta-analysis of randomized controlled trials on prenatal physical activity showed that physical activity during pregnancy provided a 28% lower risk of GDM compared with those in a control group (relative risk [RR] 0.72, 95% confidence interval [CI 0.58-0.91].[13] GDM prevention interventions that are started during pregnancy may have less effectiveness due to less intensity with concerns about its effects on the foetal growth and biological changes such as craving, nausea, edema, and weight gain in pregnancy as barriers to physical activity and short duration of interventions prior to the diagnosis of GDM. Notably, limited literature, variability in interventions, and lack of adherence to interventions by samples[23] have reduced the generalizability of the findings of previous studies. Therefore, the aim of this study was to identify the risk factors for GDM and the possible etiological parameters.

MATERIAL AND METHODS

This case-control study was performed at KIMS Hospital, a tertiary care hospital in association Himagiri medical center and Pronto Diagnostics set in the Hyderabad from September 2021 to February 2023. This study was carried out on 100 pregnant women with a definite diagnosis of gestational diabetes as a case group and 100 healthy pregnant women as a control group of similar gestational age were selected from the same hospital.
Exclusion criteria included pre-pregnancy diabetes (type 1 or type 2 or both types of diabetes); recurrent miscarriages; child with congenital abnormalities or neonatal mortality in previous pregnancies; smoking before and during pregnancy; multiple gestation; known chronic illnesses such as hypertension, chronic renal diseases, collagen or vascular diseases, endocrine disorders, chronic hepatic diseases; and current use of corticosteroids. Inclusion criteria for the recruitment of the women were age 18 to 40 years, pregnancy at the gestation age of 24 to 28 weeks, and willingness to take part in this study.

RECRUITMENT

The diagnosis of GDM was made using a 2-step approach. All pregnant women who visit a Himagiri Medical Center for prenatal care are routinely screened for GDM by 50-g 1-hour glucose challenge test (GCT) at 24 to 28 weeks of gestation. The control group consisted of those who had normal GCT. An OGTT was performed on the subset of females whose plasma glucose concentrations exceeded the glucose threshold value (140 mg/dL). The diagnostic criteria for GDM were the Carpenter and Coustan conversion as recommended by the American Diabetes Association. The Carpenter and Coustan's criteria are as follow: fasting blood glucose 95 mg/dL, 1-hour blood glocuse180 mg/dL, 2-hour blood glucose 155 mg/dL, and 3-hour blood glucose 140 mg/dL.[24]
Fasting blood glucose was tested after 12 to 14 hours of fasting. If the pregnant women had a positive GCT test and 2 or more abnormal OGTT readings, they were diagnosed with GDM. The women with an abnormal GCT but a normal OGTT and the women with a single abnormal OGTT were excluded from the study. The laboratory tests were performed at the Pronto Diagnostics laboratory. Measurements were made by using the glucose oxidase method via the Hitachi 704 auto-analyzer.
The women with GDM were enrolled in the study and received required care for the management of GDM. However, the sampling was performed by a trained lab techinician and continued till the required sample size was reached. The informed written consent form was signed by the participants before starting the study. Ethical approval was obtained from the Ethics Review Committee of Faculty of Medicine, KIMS Hospitals.

DATA COLLECTION

Anthropometric characteristics, including weight, were measured with the least amount of clothes to the nearest 100 g. Height was measured using a tape measure in the standing position with shoulders in a normal alignment. Pre-pregnancy body mass index (BMI) was calculated using reported height and pre-pregnancy weight and categorized according to standard cutoffs (underweight <18.5 kg/m^2, normal 18.5-24.9 kg/m^2, overweight 25-29.9 kg/m^2, obese ⩾30 kg/m^2).[21] Gestational age was calculated based on the first day of the last menstrual cycle (LMP) for the women with regular menstrual cycles. Also, transabdominal ultrasonography was used for those women with irregular menstrual cycles or those who did not remember their LMP. The family history of diabetes mellitus was defined as the history of type 2 diabetes among the first-degree family members.
Physical activity in the 3 months before pregnancy was assessed at the time of enrolment, from 20th to 28th week of gestation by using the IPAQ. The IPAQ evaluated the women's participation in 4 domains of activities, including "household/caregiving," "occupational," "sports/exercise," and "transportation." The frequency, intensity, type, and duration of physical activities were calculated in various domains.[23] The physical activity level scores were assessed to

determine whether the woman had a sedentary, moderate, or a vigorously active lifestyle. The IPAQ was modified and validated by a sample of young individuals. The process of translation and cultural adaptation of the IPAQ was performed in studies by Kelishadi et al.[14] The internal consistency of this questionnaire, using the calculation of Cronbach's alpha coefficient for the scale, was reported as .7 indicating a satisfactory internal consistency.[13] Pre-pregnancy physical activity was derived from total MET values. It was estimated for various activities with values 3.3, 4, and 8 for walking, moderate activity, and vigorous activity, respectively, and was categorized as sedentary/low (<600 MET min/week), moderate (600 to <3000 MET min/week), and high (3000 MET min/week).[23]

STATISTICAL ANALYSIS

The study's sample was determined to be 200 women including both the cases and control subjects, based on variables, including 95% confidence interval, 80% power, and 15% difference between the women with GDM and healthy women. The collected data were analysed using the descriptive mean ± SD, number and percentage, and inferential statistics. The baseline and follow-up characteristics of the women were compared between the GDM and non-GDM groups using the student's *t* test or chi-square test. The logistic regression model was used to assess the association (odds ratio [OR]) between covariates age, pre-pregnancy physical activity, BMI, family history of diabetes, and GDM.

The data analysis was performed using the SPSS 23.0 software for Windows (IBM Corp, Armonk, NY, USA). The significance level was set at $P < .05$.

RESULTS

The samples consisted of 100 women with GDM and 100 healthy women. The sociodemographic characteristics of the women are shown in Table 1. No differences were reported in the proportion of illiterate individuals between the groups. Similarly, the women with GDM and the healthy women had almost the same proportion of illiterate husbands. No statistically significant difference was found in the occupation status between the women.

Statistically significant differences were reported between the women with GDM and the healthy women in terms of age, pre-pregnancy BMI, parity, and family history of diabetes. The physical activity characteristics of the pregnant women is shown in Table 2.

Physical activity for out-of-home work was performed by only 5 women, which did not enter statistical analysis. Total physical activity in the 3 months before pregnancy among women with GDM was significantly lower than among healthy pregnant women ($P < .000$).

The logistic regression model was used to determine the severity of the relationship between maternal physical activity before pregnancy and GDM. After entering confounding factors such as age, BMI, the family history of diabetes, and parity in the logistic regression model, the number of parities, vigorous physical activity, and walking were excluded from the model, and the rest of the variables remained in the model. The crude and adjusted ORs for GDM are shown in Table 3.

Table 1.

The Sociodemographic and Fertility Characteristics of the Women With Gestational Diabetes Mellitus (GDM) and Healthy Women (N = 200).

Characteristic	Women With GDM (n = 100), Mean ± SD or n (%)	Healthy Women (n = 100), Mean ± SD or n (%)	*P*
Age, years	30.6 ± 5.9	24.6 ± 5.1	<.01
Maternal weight, kg	75.5 ± 14.3	66.5 ± 12.8	<.01
Body mass index, kg/m^2	29.0 ± 5.1	25.2 ± 4.7	<.01
Fasting blood glucose, mg/dL	127.7 ± 36.9	84.1 ± 7.3	<.01
Previous baby birth weight, g	3649 ± 618.2	3305.5 ± 451.9	<.01
Education, years			
1-5	7 (7)	12 (12)	.27
6-9	41 (41)	38 (38)	
10-12	43 (43)	38 (38)	
>12	9 (9)	11 (11)	
Occupation			
Housework	95 (95)	89 (89)	.09
Employee	5 (5)	11 (11)	
Family history of type 2 diabetes	59 (59)	16 (16)	<.01
Parity			
1	36 (36)	58 (58)	<.01
2	34 (34)	31 (31)	
>2	30 (30)	11 (11)	

Table 2.

The Mean Prepregnancy Physical Activity in the Women With GDM and Healthy Women.

Physical Activity	Women With GDM (n = 100), Mean ± SD METs	Healthy Women (n = 100), Mean ± SD METs	*P*
Walking	571.56 ± 76.46	1423.62 ± 96.70	<.01
Moderate activity	1512 ± 185.91	3498.00 ± 275.17	<.01
Vigorous activity	243.76 ± 86.93	827.20 ± 188.58	<.01
Total activity	2910.76 ± 338.74	5165.38 ± 381.27	<.01

Table 3.

Logistic Regression Model for GDM (N = 200).

Variable	Crude OR	95% CI	*P*	Adjusted OR	95% CI	*P*
Total physical activity (METs)						
<600	6.99	2.81-17.39	<.01	2.85	0.29-4.27	<.05
600-3000	6.32	2.99-13.38	<.01	1.13	0.97-8.34	.80
>3000	Ref					
Family history of type 2 diabetes						
Yes	7.55	3.87-14.71	<.01	5.62	2.26-13.96	<.01
No	Ref		1			
Age	1.27	1.13-1.28	<.01	1.24	1.13-1.35	<.01
Body mass index	1.17	1.10-1.25	<.01	1.10	1.02-1.20	<.01

DISCUSSION

This study was conducted to clarify the importance of risk factors for GDM in a study of 100 women with GDM and 100 healthy women. In our study, family history of diabetes mellitus, low physical activity in the 3 months before pregnancy, advanced maternal age, and obesity were significant risk factors of GDM. In the study by Teh et al,[11] the advanced age of the mother was the most important risk factor of GDM, but in this study family history of type 2 diabetes is the most important factor.

In a systematic review and meta-analysis study in Iran, the potential causes of GDM were gestational age, history of gestational diabetes, family history of diabetes, high BMI, abortions, parity, and history of macrosomia.[5] In this study, women in both groups had gestational age between 24 and 28 weeks. Based on the initial univariate analysis, the rate of parity and history of macrosomia was significantly higher among women with GDM. However, after controlling for potential confounders, factors were not the independent factor of GDM. Low physical activity (<600 MET) during pre-pregnancy tripled the risk of GDM. This held true after the adjustment of a number of possible confounders. This was consistent with the findings of previous studies.[22,25,26] Similarly to this study, a systematic review and meta-analysis study by Tobias et al[22] showed that the total physical activity before pregnancy and during early pregnancy was significantly associated with a lower risk of GDM. The value of this association was greatest for pre-pregnancy physical activity as the women with the highest physical activity experienced a 55% reduction in the risk compared with women with the lowest physical activity. According to Shirazian et al,[27] the increase of age >30 years, BMI >30 kg/m^2, and family history of diabetes were independent risk factors of GDM.

In this study, the increased pre-pregnancy BMI, maternal age, and family history of diabetes were independent predictors of developing GDM. Low physical activity during pre-pregnancy increased the risk of developing GDM (OR = 2.8(. The prevalence of GDM is increasing worldwide in parallel with maternal obesity, sedentary life styles, and the increase in the age of pregnant women.[15,16,28] A study in Iran showed that the prevalence of GDM was 3.4%; the highest and lowest prevalence rates were 18.6% and 1.3% in Karaj and Ardebil, respectively.[5]

While physical activity is important in all stages of life, it is especially important before and during pregnancy, as it can affect the health of women and their children. The maintenance of adequate physical activity during pregnancy depends on pre-pregnancy habits. Pereira et al[29] showed that decline in physical activity during pregnancy was accompanied by a near doubling in the prevalence of insufficiently active lifestyle, from 12.6% during pre-pregnancy to 21.6% during pregnancy. For instance, women with a BMI above the normal range are more likely to remain inactive.[30] Regular physical activity is not contraindicated by the disease, provides pregnant women with better overall fitness, improves cardiovascular and muscular performance, prevents excessive weight gain, improves blood pressure, and protects them against GDM.[17] In a meta-analysis study, the relative risks of GDM were 55% lower for women in the highest pre-pregnancy physical activity quantiles compared with those in the lowest (pooled OR 0.45, 95% CI 0.28-0.75; *P* = .002).[22] Pre-pregnancy BMI was associated with the risk of GDM. These findings are consistent with those reported before.[18-20,31] Therefore the American College of Obstetricians and Gynaecologist's recommended performing at least 30 minutes of moderate daily exercise.[17] Clapp et al[32] and Mata et al[33] conducted review studies and concluded that a personalized physical exercise combining neuromuscular and cardiovascular training is highly recommended in

pregnant women if pregnancy period is free of medical contraindications and problems. They highlighted that the uterine blood flow was reduced during exercise, but this does not affect the blood flow to the foetus.

LIMITATIONS

The main asset of the study is a comparison group, so that we were able to compare outcomes for women without GDM. But our study had limitations which should be addressed in the future work. Race and ethnicity as a risk factor have been stated in the valid scientific references, but in our study has not addressed the effect of this risk factor in GDM. In our study, assessment of physical activity was performed using a questionnaire, self-reports that were prone to recall bias because the women with GDM remembered physical activity differently than controls. Further research also needs to be done to better understand the mechanisms of the apparent benefits of physical activity in pre-pregnancy and during pregnancy in prevention of GDM.

CONCLUSION

According to the findings of this study, low amount of physical activity prior to pregnancy, advanced maternal age, obesity, and family history of diabetes mellitus were significant risk factors of GDM. GDM is one of the main health problems in the world that requires effective prevention and control strategies. Therefore, having accurate and reliable information about the causes of GDM is very helpful in planning the prevention of GDM.

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