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PRE GESTATIONAL DIABETES MELLITUS DURING PREGNANCY AND ITS ADVERSE EFFECTS

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ABSTRACT

Introduction: Gestational diabetes mellitus (GDM) refers to any degree of blood glucose intolerance that occurs or being discovered for the first time during pregnancy, regardless of whether this condition persists after delivery or whether glucose-control treatment is needed during pregnancy. Gestational diabetes does not include diabetes occurred before pregnancy. According to statistics, the incidence of GDM is 3-6%, and it usually occurs after 20-24 weeks of pregnancy. It is a common high-risk metabolic complication. Gestational diabetes increases the risk of adverse pregnancy outcomes. **Materials and Methods:** It was a comparative study this study was conducted from March 2021 to February 2022 at the department of Genecology at Kalpana Chawla Government Medical College **Aims:** To evaluate the effects of Pre-Gestational Diabetes Mellitus (PGDM) and Gestational Diabetes Mellitus (GDM) on macrosomia and birth defects. **Result:** Simultaneously, a control group consisting of 200 pregnant women with normal blood glucose levels (NGT) was randomly chosen. Results from the multivariate logistic regression analysis revealed that age, pre-pregnancy body mass index (BMI), family history of diabetes, 2 h postprandial blood glucose (2hPBG), and glycated hemoglobin (HbA1c) were identified as independent risk variables for gestational diabetes mellitus (GDM) with statistical significance ($P<0.05$). The occurrence of difficult labor and cesarean section, abnormal amniotic fluid, early rupture of membranes, and abnormal pregnancy were substantially more frequent in the GDM group compared to the normal control group ($P<0.01$). The incidence of fetal distress, macrosomia, small for gestational age new-borns, and preterm infants in the gestational diabetes mellitus (GDM) group was considerably greater than in the normal control group ($P<0.01$). The levels of 2hPBG and HbA1c in the GDM group decreased significantly after the intervention compared to before the intervention ($P<0.05$). **Conclusion:** The age of pregnant women and their family's medical history of diabetes are significant factors in the occurrence and development of gestational diabetes mellitus (GDM). Hence, it is imperative for expectant moms to diligently consider the pertinent risk factors that instigate gestational diabetes mellitus (GDM), while undergoing screening and taking preventive measures throughout pregnancy. This will help mitigate and avert the occurrence of GDM, thereby ensuring the well-being of both the mother and the baby.

KEYWORDS

gestational diabetes, risk factors, pregnancy outcomes and intervention measures

INTRODUCTION

Gestational diabetes mellitus (GDM) is a disorder characterized by varying levels of intolerance to blood glucose that is either detected or first appears during pregnancy. It is irrelevant whether this condition continues after childbirth or if therapy for glucose control is required during pregnancy. [1] Gestational diabetes specifically excludes pre-existing diabetes that occurs prior to pregnancy. Based on statistical data, the prevalence of gestational diabetes mellitus (GDM) ranges from 3% to 6%. Typically, GDM develops after 20 to 24 weeks of pregnancy. This is a frequently occurring metabolic issue that carries a significant level of risk. Gestational diabetes elevates the likelihood of unfavorable pregnancy consequences. [2] Research has indicated that individuals diagnosed with gestational diabetes mellitus (GDM) and their offspring have a notably higher likelihood of developing chronic conditions, including diabetes, metabolic syndrome, and cardiovascular disease, in the future. [3] The incidence of gestational diabetes mellitus (GDM) has considerably grown in recent years due to factors such as delayed child-bearing age, changes in food choices, and lifestyle modifications. Gestational diabetes mellitus (GDM) can lead to negative pregnancy outcomes such as miscarriage, preterm birth, fetal distress, fetal abnormalities, fetal death, intrauterine infection, excessive fetal growth (macrosomia), high blood pressure throughout pregnancy, preeclampsia, and excessive amniotic fluid (poly-hydramnios). [4] Gestational diabetes can elevate the likelihood of the mother developing type 2 diabetes. Gestational diabetes patients experience a heightened risk of developing diabetes within five years following childbirth. While most gestational diabetes patients can regain normal glucose metabolism after giving birth, approximately 40-50% of them still acquire type 2 diabetes within 5-10 years after delivery. Consequently, long-term care becomes necessary. [5] In view of the short-term and long-term unfavourable effects of gestational diabetes on mothers and children, it is of great significance to analyze the risk factors of GDM, provide early screening and prevention for pregnant women with high-risk factors, give intervention guidance to actively control blood sugar in the normal range so as to to reduce the incidence of GDM and adverse pregnancy outcomes, as a way to prevent or delay the presence of long-term unfavorable prognosis of mother and child. This study analyzed the risk factors of 378 GDM patients admitted to the hospital from March 2021 to February 2022 at, Kalpana Chawla Government Medical College, analyzed the impact on pregnancy outcomes, and proposed corresponding interventions in order to give a basis for comprehensive prevention and treatment of GDM.

MATERIALS AND METHODS

Clinical data From March 2021 to February 2022, 378 GDM patients awaiting delivery in Kalpana Chawla Government Medical College, were selected as the research subjects. Simultaneously, 200 pregnant women with normal blood glucose (NGT) during the same period were randomly selected as controls.

Inclusion Criteria

Patients who satisfy the diagnostic criteria for GDM have a fasting blood glucose (FBG) level of at least 5.1 mmol/l, a 1-hour blood glucose level of at least 10.0 mmol/l, and a 2-hour blood glucose level of at least 8.5 mmol/l. Gestational diabetes mellitus (GDM) is diagnosed when blood glucose levels above the established diagnostic criteria at any given moment. The study includes patients who are capable of actively participating without assistance, have no previous record of mental disease, and possess comprehensive data on pregnancy examinations and postpartum follow-ups.

Exclusion Criteria

people who have both diabetes and pregnancy; people with serious mental illnesses; patients with significant heart, liver, renal, and autoimmune conditions prior to pregnancy.

Techniques Lab parameters Based on the specified time constraints, a volume of 3 ml of blood was extracted from each participant's elbow vein. Self-coagulation method was employed for blood glucose and blood lipid analysis, while EDTA-K2 anticoagulation method was used for glycated hemoglobin (HbA1c) analysis. The process of centrifugation was carried out at a force of 2,264 times the acceleration due to gravity for a duration of 20 minutes in order to separate the upper layer of serum or plasma. All specimens were tested and found to be free of lipemia or hemolysis. The process is finished within a duration of 2 hours, starting from the collection of the material to the actual testing.

Blood glucose and blood lipids were assessed using the Hitachi 7170S automatic biochemical analyzer manufactured by Hitachi, Ltd. Fasting insulin levels were evaluated using electrochemical immuno-luminescence technology from Roche Diagnostics. HbA1c levels

were studied using the G8 HbA1c analyzer produced by Japan Tosoh Corporation. Oral glucose tolerance test (OGTT): All pregnant women received an OGTT between 24 and 28 weeks of pregnancy. The subjects underwent a fasting period of 8-12 hours prior to the test, after which venous blood samples were collected at 8 am to measure fasting blood glucose (FBG) levels. Subjects were instructed to consume 300 ml of warm water containing 75 g of anhydrous glucose powder within a 5-minute timeframe. Blood samples were collected at 1 and 2 hours after consumption to assess blood glucose levels. Blood lipids and HbA1c were assessed concurrently with the measurement of fasting blood glucose (FBG).

A self-designed questionnaire was utilized to gather comprehensive data on pregnant women, including age, pre-pregnancy body mass index (BMI), weight gain during pregnancy, height, family history of diabetes, menstrual cycle, pregnancy history, polycystic ovary syndrome (PCOS) history, history of adverse pregnancy and delivery, history of gestational diabetes, fasting blood glucose (FBG), blood glucose levels 1 hour after eating (1hPBG), blood glucose levels 2 hours after eating (2hPBG), HbA1c levels, fasting insulin levels (FINS), triglyceride (TG) levels, cholesterol (TC) levels, high-density lipoprotein cholesterol (HDL-C) levels, low-density lipoprotein cholesterol (LDL-C) levels, and pregnancy outcomes. The questionnaires are disseminated and gathered by proficient investigators. The recovery rate and efficiency of the questionnaire are both 100%. Pre-pregnancy overweight is characterized by a pre-pregnancy BMI (Body Mass Index) of 25 kg/m2 or above, whereas a gigantic baby is described as having a body mass of 4 kg or more.

Intervention measures Promote health education: Facilitate community-based education and awareness programs on pre-pregnancy health, offering counseling and training to women of suitable age. Disseminate comprehensive information on gestational diabetes mellitus (GDM), covering its incidence, progression, and potential risks. Foster a heightened sense of self-care among pregnant women. Enhance community healthcare services by conducting comprehensive screenings for blood sugar levels and weight. Enhance the health records of pregnant women in the community and ensure regular monitoring throughout pregnancy. Diet intervention is the main approach to managing weight and promoting a healthy lifestyle. It involves providing guidance on sensible eating habits before and during pregnancy to actively manage weight. Patients with gestational diabetes mellitus (GDM) are advised to create an individualized dietary regimen. The diet consists of 40% carbohydrates, 20% protein, and 40% fat. It emphasizes the consumption of whole grains and suggests substituting fruits with vegetables such as cucumbers and tomatoes. Food items with a high glycemic index were omitted from the well-balanced diet. Exercise intervention: Pregnant women were instructed to engage in suitable physical exercise based on their individual circumstances. Physical activity has the potential to decrease body weight, alleviate insulin resistance, and appropriately engaging in exercise can effectively manage weight increase during pregnancy. Both diet intervention and exercise intervention were applied to the GDM group, and the levels of blood glucose 2 hours after a meal (2hPBG) and HbA1c before and after the intervention were compared.

Quantitative analysis: The data were subjected to statistical analysis using SPSS 25.0 (IBM Corp). The measurement data were presented as the mean value plus the standard deviation (SD). To compare between groups, the Student's t-test was employed. The enumeration data were reported as percentages, and the $\chi 2$ test was used to compare between groups. The risk variables for GDM were examined by logistic regression analysis. The study employed univariate analysis to examine both general data and clinical data. Additionally, multivariate unconditional logistic regression analysis was conducted, with statistical parameters ($P<0.05$) serving as independent factors and GDM as the dependent variable. A significance level of $P<0.05$ was used to determine statistical significance.

RESULTS

Table I. Univariate Analysis Of Risk Factors For GDM [n (%), Mean ±Sd].

Variables	GDM (n=378)	NGT (n=200)	$\chi 2$/t	P-value
Age n (%), ≥35 years	124 (32.80)	32 (16.00)	$\chi 2$=19.378	<0.001
BMI before pregnancy (kg/m2)	28.16±1.38	22.78±1.04	t=6.416	0.004
Weight gain during pregnancy (kg)	16.82±1.46	14.51±1.41	t=1.247	0.259
Height (cm)	163.57±2.67	164.98±2.41	t=0.174	0.868
Family history of diabetes n (%)	132 (34.92)	22 (13.00)	$\chi 2$=31.641	<0.001
Menstrual period (d)	3.62±0.97	3.84±0.88	t=0.235	0.786
Gravidity	2.11±0.63	1.91±0.52	t=0.224	0.831
PCOS history n (%)	113 (29.89)	40 (20.00)	$\chi 2$=6.579	0.010
History of adverse pregnancy n (%)	60 (15.87)	22 (11.00)	$\chi 2$=2.551	0.110
GDM history n (%)	162 (42.86)	10 (5.00)	$\chi 2$=87.679	<0.001
FBG (mmol/l)	6.89±1.20	4.52±0.48	t=3.003	0.024
1hPBG (mmol/l)	12.32±1.65	8.29±0.92	t=3.274	0.017
2hPBG (mmol/l)	9.33±1.42	5.01±0.86	t=7.851	<0.001
HbA1c (%)	8.98±0.42	5.56±0.22	t=7.232	<0.001
FINS (mmol/l)	18.43±3.78	11.26±1.82	t=2.697	0.035
TG (mmol/l)	3.08±0.79	1.92±0.63	t=2.612	0.042
TC (mmol/l)	4.97±1.02	3.89±0.98	t=1.015	0.349
HDL-C (mmol/l)	0.92±0.12	1.53±0.15	t=2.967	0.028
LDL (mmol/l)	3.38±0.82	3.36±0.77	t=0.765	0.432

Table II. Multivariate Non-Conditional Logistic Regression Analysis Of Risk Factors For GDM.

Items	B	S.E	Wald	P-value	OR	95% CI
Age ≥35 years	0.637	0.179	12.078	<0.001	1.891	1.332-2.686
BMI before pregnancy	1.117	0.307	13.261	<0.001	3.045	1.657-5.571
Family history of diabetes	0.738	0.178	16.927	<0.001	2.093	1.472-2.978
PCOS history	0.363	0.655	3.718	0.054	3.536	0.783-6.928
GDM history	1.005	0.728	14.002	<0.001	5.326	2.315-6.489
FBG	0.491	0.405	1.474	0.225	1.634	0.739-3.613
1hPBG	0.553	0.574	0.861	0.354	0.587	0.190-1.809
2hPBG	0.452	0.188	5.801	0.016	1.572	1.008-2.271
HbA1c	0.678	0.312	12.309	<0.001	2.989	1.621-5.509
FINS	0.179	0.153	1.378	0.241	1.196	0.887-1.614
TG	0.238	0.296	0.649	0.420	1.259	0.711-2.266
HDL	0.104	0.329	0.101	0.751	1.110	0.583-2.115

Table III. Comparison Of Adverse Pregnancy Outcomes Between The GDM And The Control Group, N (%).

Groups	Dystocia and cesarean section	Abnormal amniotic fluid	Premature rupture of membranes	Pathological pregnancy	Fetal distress	Macrosomia	Small for date children	Preterm children
GDM (n=378)	170 (44.97) a	51 (13.49)a	65 (17.20) a	105 (27.78)a	55 (14.55)a	78 (20.63)a	34 (8.99)a	64 (16.93)a
Control (n=200)	58 (29.00)	9 (4.50)	11 (5.50)	12 (6.00)	6 (3.00)	8 (4.00)	5 (2.50)	8 (4.00)
$\chi 2$	13.972	11.368	15.667	38.423	18.485	28.578	8.763	20.056
P-value	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	0.003	<0.001

GDM, gestational diabetes mellitus. aP<0.01.

Analysis of the risk variables for gestational diabetes mellitus using univariate methods. An analysis of the two groups of data revealed significant differences in age, family history of diabetes, BMI before pregnancy, history of gestational diabetes mellitus (GDM), history of polycystic ovary syndrome (PCOS), fasting blood glucose (FBG) level, 1-hour postprandial blood glucose (1hPBG), 2-hour postprandial blood glucose (2hPBG), glycated hemoglobin (HbA1c), fasting insulin (FINS), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) ($P<0.05$). These significant differences were also observed in BMI before pregnancy, GDM history, PCOS history, FBG level, 1hPBG, 2hPBG, HbA1c, FINS, TG, and HDL-C ($P<0.05$) (Table I).

Analyzed risk factors for gestational diabetes mellitus (GDM) using multivariate non-conditional logistic regression. A multivariate non-conditional logistic regression analysis was conducted, using the statistically significant ($P<0.05$) parameter identified in the single

factor analysis as the independent variable and the presence or absence of GDM as the dependent variable. The findings indicated that age, BMI, prior history of gestational diabetes mellitus, family history of diabetes, 2-hour postprandial blood glucose, and glycated hemoglobin (HbA1c) were identified as autonomous risk factors for gestational diabetes mellitus (GDM) (Table II).

Comparative analysis of pregnancy outcomes between the gestational diabetes mellitus (GDM) group and the control group. Gestational diabetes mellitus (GDM) has detrimental consequences on both pregnant women and newborn newborns during the perinatal period. This study found that the occurrence of maternal dystocia, cesarean section, abnormal amniotic fluid, premature rupture of membranes, and pathological pregnancy was significantly higher in the group with gestational diabetes mellitus (GDM) compared to the normal control group. These differences were statistically significant (P<0.01). Additionally, the likelihood of fetal distress, macrosomia, small for gestational age infants, and premature infants was significantly higher in the perinatal infants of the GDM group compared to the normal control group. This difference was also statistically significant (P<0.01) (Table III).

Assessment of 2hPBG and HbA1c values in the GDM group prior to and following the intervention. The levels of 2hPBG and HbA1c in the GDM group decreased considerably after the intervention compared to before the intervention (t=2.842, 2.986, P=0.029, 0.020).

DISCUSSION

GDM, or gestational diabetes mellitus, is a condition characterized by high blood sugar levels in women during pregnancy. Worldwide, the prevalence of gestational diabetes mellitus (GDM) has been steadily rising in recent years. The initial clinical manifestations of GDM are atypical. In the absence of timely screening and early intervention, both the mother's and the infant's health would be adversely impacted for an extended duration. Investigating the risk factors associated with GDM, examining the negative impacts on pregnancy outcomes, and suggesting appropriate preventative interventions are highly important in lowering the occurrence and advancement of GDM and maintaining the well-being of both mothers and infants.

Previous studies have shown [6] the occurrence of gestational diabetes mellitus (GDM) is strongly associated with pre-pregnancy obesity and advanced maternal age. There is a positive correlation between pre-pregnancy BMI and the occurrence of GDM, with higher BMI values leading to a higher incidence of GDM. Additionally, an older age at the time of pregnancy is also associated with an increased likelihood of developing GDM. During pregnancy, the placenta releases hormones like prolactin (HPL) and prolactin (PRL) which gradually raise insulin resistance. Additionally, obesity is linked to insulin resistance, and insulin resistance contributes to and worsens obesity. As a result, pregnant women who are overweight or obese are more likely to develop gestational diabetes mellitus (GDM). Kim et al [7] Examined the correlation between BMI and GDM and observed that the occurrence of GDM in pregnant women with normal body weight, overweight, obesity, and severe obesity rose by 2.3%, 4.8%, 5.5%, and 11.5% respectively. This indicates a connection between BMI and GDM prior to pregnancy. Ogonowski et al [8] Case-control studies have revealed a positive correlation between pre-pregnancy BMI and the risk of gestational diabetes mellitus (GDM). Furthermore, advanced pregnancy is presently acknowledged as a significant predisposing factor for gestational diabetes. The study findings indicate that pregnant women who are aged 35 years or older and overweight prior to pregnancy have a higher likelihood of developing gestational diabetes mellitus (GDM). These factors were identified as independent risk factors for the advancement of GDM, aligning with the aforementioned article. The odds ratio (OR) values for GDM were 1.891 and 3.045 for women aged ≥35 years and those who were overweight before pregnancy, respectively.

The presence of gestational diabetes is significantly influenced by a person's family history of diabetes. The field of genetics is potentially linked to susceptibility genes and the presence of high glucose levels in the womb. The prevalence of type 2 diabetes in the maternal lineage of women with gestational diabetes is substantial. It is possible to hypothesize that their mothers also experienced gestational diabetes, resulting in their infants being exposed to high glucose levels in the womb. Furthermore, hyperglycemia stimulates the growth of fetal pancreatic islet β cells and adipocytes, leading to excessive proliferation and an increased likelihood of producing a big infant. These newborns have a higher likelihood of developing obesity and insulin resistance in adulthood, as well as being more susceptible to gestational diabetes mellitus (GDM) following pregnancy. [9]. In addition to this, the risk of GDM is closely related to the postprandial hyperglycemia and high HbAIc of pregnant women [10]. The 2-hour postprandial blood glucose (2hPBG) fails to meet the established criterion, suggesting the presence of impaired glucose tolerance. HbAIc serves as an indicator of blood glucose regulation during the previous 2-3 months, providing a more accurate assessment of blood glucose management compared to FBG. Insulin resistance may occur as a result of the indirect response to prolonged oral glucose tolerance test (OGTT) with 2-hour blood glucose levels and failure to manage HbAIc. The study findings indicated that having a family history of diabetes, gestational diabetes mellitus (GDM), 2-hour postprandial blood glucose (2hPBG), and glycated hemoglobin (HbA1c) were all separate risk factors for developing gestational diabetes. The odds ratio (OR) values obtained from the multi-factor unconditional logistic regression analysis were 2.903, 5.326, 1.527, and 2.989, respectively. These values indicate that having a family history of diabetes, gestational diabetes mellitus (GDM), 2-hour postprandial blood glucose (2hPBG), and glycated hemoglobin (HbA1c) are all risk factors for GDM.

The enduring consequence primarily involves a substantial elevation in the likelihood of post-natal diabetes. The fetus has a short-term effect where the high glucose environment in the uterus stimulates the pancreatic β cells of the fetus to produce insulin, resulting in persistent hyperinsulinemia. Hyperinsulinemia stimulates adipogenesis and protein anabolism, leading to fetal overgrowth. [11], Women with a history of childbirth have a 2.25 times incidence of GDM when they become pregnant again [12]. Obesity can diminish the responsiveness of insulin target organs to insulin and lead to insulin resistance. Hence, women with a higher body mass index (BMI) are more susceptible to gestational diabetes mellitus (GDM) compared to women with a healthy BMI. Additionally, there is an elevated likelihood of experiencing unfavorable pregnancy outcomes. [13] The study findings revealed a considerably increased occurrence of maternal dystocia, cesarean section, abnormal amniotic fluid, early rupture of membranes, and pathological pregnancy in the GDM group compared to the control group. The incidence of fetal distress, macrosomia, full-term infants, and preterm newborns in perinatal infants is much greater compared to the normal control group, with a statistically significant difference (all P<0.01).

Intervention countermeasures: As pregnant women progress in their pregnancy, the levels of hormones that oppose the effects of insulin in the body rise, leading to a decrease in insulin sensitivity. To maintain normal glucose metabolism, increased insulin secretion is necessary. Additionally, it is characteristic of blood sugar metabolism that blood sugar tends to elevate following a meal or after being stimulated by a sugar load. Hence, achieving the criteria for postprandial blood glucose levels is more challenging. Simultaneously, prolonged high blood sugar levels, as shown by elevated HbA1c, are associated with an increased risk of negative outcomes during pregnancy. Therefore, it is crucial to carefully manage postprandial blood glucose levels. The findings of the current study indicate that following dietary and exercise interventions, the postprandial blood glucose and HbA1c levels of pregnant women were measured.

Significantly lower than before intervention, which is consistent with literature reports [14]. Strategically determining the age at which marriage and childbirth occur could help prevent gestational diabetes mellitus (GDM) during pregnancy. It is advisable for the government, society, and families to promote early childbirth as a means of reducing the likelihood of gestational diabetes mellitus (GDM). Non-interventional variables include a family history of diabetes and a previous history of gestational diabetes mellitus (GDM). Individuals with such medical background should promptly undergo blood sugar test. Although a negative result from the OGTT test during early pregnancy does not entirely eliminate the possibility of gestational diabetes mellitus (GDM) developing later in pregnancy. To improve the identification of gestational diabetes mellitus (GDM), it is advisable to carefully choose a few significant high-risk indicators and evaluate pregnant women comprehensively. This evaluation will help determine if there is a risk of GDM and whether repeated oral glucose tolerance test (OGTT) screenings should be conducted. This approach aims to minimize the chances of missing a GDM diagnosis. It is crucial

to prioritize the OGTT screening for pregnant women between 24-28 weeks of gestation. This is because during this period, there is a substantial increase in the secretion of hormones (HPL, PRL) by the placenta, leading to insulin resistance and elevated blood sugar levels. The initial manifestations of GDM may not be readily apparent, and the key approach to managing this condition is to promptly screen, diagnose, and treat it in order to enhance the outlook for both mothers and infants and minimize unfavorable pregnancy outcomes.

CONCLUSION

The current study conducted a thorough analysis of the risk variables associated with gestational diabetes, surpassing the scope of prior investigations. Additionally, matching management strategies were provided. The study examined the influence of BMI and age on GDM, and analyzed the impact of family history of diabetes, GDM history, 2hPBG, and HbA1c on GDM.

The current study investigated the risk variables associated with GDM. Timely screening, prevention, and intervention can enhance the prognosis and result of both the mother and newborn. Nevertheless, it is necessary to conduct long-term monitoring of postpartum mothers and infants.

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