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Management of Gestational *Diabetes mellitus* with Risk Factors and Trans-Generational Prevention

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ABSTRACT

Background: Gestational *Diabetes mellitus* (GDM) has become a pervasive health issue of today's era, leading to be a complicated disorder globally. It has also been proved to be highly accountable for causing an undesired impact on maternal health of patient as well as progeny. The high number of reported cases with consequent complications need appropriate medical care and timely attention.

Objectives: The present study was intended to display the real figure of a high rise in GDM in Pakistan, with all involved parameters, to rectify the real factors either socioeconomic or domestic, accountable for the jeopardizing of disease.

Methodology: The study was conducted in different maternity hospitals of Karachi, Pakistan. Association between GDM with age, family history, co-morbid complications, fetal complications and others were analyzed by Pearson chi-square test using SPSS.

Results: More than 50% of participants belong to the age bracket of 31-45 years and 31.2% having a positive family history of diabetes. No known risk factor regarding GDM was present in 40.6% of women. GDM was observed prevalent and associated with poor health management of mother, and found to increase with elderly mothers (i.e. age of mother at the time of conception) in Pakistan.

Conclusion: GDM should be considered as primary health care for the trans-generational prevention of diabetes and needs to be addressed as a public health issue in order to cure the mother and fetus during pregnancy and to prevent long term effects of this disease.

INTRODUCTION

Pregnancy and parenthood are the state of emotional well-being and account for satisfaction and sense of worth. The creation of new life gives courage and happiness to the marital relations, however, during all the period of pregnancy mother is on the front line during all the state of creation[1, 2]. As a matter of fact, from the beginning of conception till birth and even after birth, a mother faces numerous experiences regarding health, socio-economic burdens, family pressures, health issues etc[3]. Pregnancy is a cluster of physical and psychological alterations, and

interestingly both may affect the health of fetus and mother in either positive or negative manner[4]. According to a research, approximately 20% women face mood swings and anxiety disorders, while those having history of psychiatric illness are even more susceptible for such conditions that cannot be treated by any psychotropic medicine, since as FDA has not approved any such therapy during pregnancy. The handling of pregnancy is a highly sensitive matter therefore, because of having teratogenic effects, neonatal toxicity, and risk of long-term neurobehavioral consequences, the medicines are carefully prescribed during pregnancy[5, 6].

Besides all the possible complications during pregnancy, gestational diabetes itself is a complex matter[7] that is highly accountable for making the pregnancy handling more difficult for mothers[8, 9]. Simply, diabetes has been found to be highly associated with stress and depression with a fact that this anxiety disorder is also accompanied with the pregnancy either early or late. Hence, various factors like social, economic and health related factors enhance the level of stress that may in turn be responsible for the onset of hyperglycemic state during the gestational period. The disorder is thus the state of glucose intolerance[10].

According to the data, the prevalence of hyperglycemia associated with pregnancy is found one in six globally, and among that 84% are GDM. The prevalence frequency of GDM is high among Asian women than white women as in Asia, the prevalence of GDM is increasing over years[11, 12]. The GDM has been found with the progression of Type II diabetes in the future. However, due to GDM, a transitory condition is induced by the metabolic stress of pregnancy which causes carbohydrate intolerance, and can be treated by diet control and by insulin therapy during the period of pregnancy. But the condition may or may not be complicated if it persists after childbirth. This abnormality in glucose metabolism may or may not be normalized after delivery, for a reason that there are 40% chances of gestational diabetics to develop into Non-Insulin-Dependent Diabetes mellitus (NIDDM) within fifteen years after childbirth[13, 14].

The physiological changes during pregnancy correlate the future programming about the metabolism and health in upcoming life, hence childbearing is believed as a window of maternal health in upcoming life. Adequate health care guidance and complete nutrition develop an intrauterine environment that creates an impact on the growth of the baby, and for this purpose, women during pregnancy require medical care and guidance. However, in spite of all significant and essential cure, there is one unavoidable and unpredictable physiological change that happens during pregnancy i.e. hyperglycemia, referred to as Gestational Diabetes mellitus (GDM) or glucose intolerance. This may also occur due to hormonal imbalances, dysfunctioning of pancreatic β-cells responsible for releasing insulin, and distressing insulin sensitivity which normally works as an anabolic hormone, thus enhances glucose uptake by peripheral tissues and maintain glucose equilibrium by controlling the production of glucose from the liver, while antagonizing the adipose tissue to release lipids[15-17]. Insulin resistance is the defined cause of GDM, as a state of decline in insulin concentrations, however, placental hormones trigger the insulin resistance to assure receiving sufficient nutrients by the fetus for vigorous growth. In such situation, the β-cells release more insulin to normalize the maternal blood glucose levels and to maintain glucose homeostasis. Despite insulin resistance, the maternal β-cells create a balance by increasing insulin synthesis and secretion, leading to maternal hyperglycemia[18-22].

GDM is in compliance with various genetic and environmental factors, as family history has a significant impact on the occurrence of diabetes, and as a high-risk factor for the development of GDM[23-25]. Moreover, variations of DNA for diabetes in gene polymorphisms is also responsible for transgenerational inheritance of obesity and glucose intolerance in the offspring from both mother and father. However, the types of genetic variation contribute to genotypic and phenotypic characteristics differently in different ethnicities such as Asian women have the highest GDM rate[26-28]. This associated fact also identify the accountability of climate conditions for GDM, for e.g.: the extremity of weather and cold to hot temperature situations influence the physiologic mechanisms, hormonal balance, fats and lipid regulation, therefore the higher prevalence of GDM has been observed at high temperature regions[29-32]. Along with regional and climate factors[33-35] different socio-economic status, awareness about the disorder, and health care measures significantly distress the occurrence of GDM in a direct or indirect manner, which if not addressed, results

in adverse maternal and neonatal outcomes that will increase drastically. This demands an early antenatal screening irrespective of the presence of risk factors for GDM and thus, it can be controlled by further promoting awareness of GDM and other pregnancy complications through educational sessions with dietician, diabitician or healthcare provider in order to prevent maternal and fetal complications.

MATERIAL AND METHODS

Study Design and Study Period:

This cross-sectional observational study was conducted in different maternity/tertiary care hospitals and clinics of Karachi, Pakistan from October-December, 2020. All the participants were recruited from primary health care clinics and hospitals.

Study Population and Sample Size:

Sample size calculations were performed using Open Epi software to determine the size of sample with 95% confidence interval. Total 1000 pregnant women of fertile age (16-45 years old) were selected for this study.

Exclusion Criteria for Study Population:

Women pre-diagnosed with Type 1 diabetes were excluded from the study.

Study Tool

For the purpose of current study, a questionnaire was designed according the standard DIPSI (Diabetes in Pregnancy Study Group India) criteria[33] that was designed under the guidelines of World Health Organization (WHO) and International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria for the diagnosis of GDM. Accordingly, the study covered following aspects to analyze the frequency of diabetes among the pregnant women in Pakistan along with the associated factors.

The survey questionnaire comprises important objectives including:

1. Socio-demographic details (four items)

2. Risk factors for GDM

3. Fetal complication associated with GDM

4. Disorder association with GDM

5. Treatment choice for GDM

Statistical Analysis:

Data were analyzed using SPSS-20 and the results were expressed in the form of frequency and percentages. The association of GDM with different parameters was analyzed by Pearson Chi-square test. The prevalence of GDM was compared in different groups made with respect to age, ethnicity, trimester, family history, co-morbid disease, maternal complications and fetal complications.

RESULTS

The present study was designed and proceeded through a survey based questionnaire according to the DIPSI criteria to analyze the frequency and related factors for gestational diabetes among Pakistani women[33]. According to the information obtained from Pakistan Fertility and Family Planning Survey (PFFPS) for analyzing the health issues of women during pregnancy, the majority of women faced diabetes during pregnancy, and in recent years, a high jeopardy has been observed. According to the reported data, the different big cities of Pakistan like Karachi, Peshawar, and Lahore have GDM cases ranging from 8% to 26% and interestingly, no regular data was reported from rural areas, that indicates the negligence about this disorder.

During the analysis, different aspects influencing the GDM were included like age of mother matters for GDM. Similarly, a significant correlation was recorded between age of pregnant woman and GDM. Moreover, in women with age bracket of 16-30 years, 45.2% population had diabetes while, in women with age group from 31-45 years, 54.8% were observed having diabetes during pregnancy. The outcome revealed that the women of older age has more chances to suffer with GDM according the significant estimated p-value.

As per weeks of gestation, 8.2% patients were in first trimester, 38.9% patients were in second trimester and 52.9% patients were in third trimester, with increased incidence noted in third trimester (Table **1**). The data showed that maternal age is a traditional risk factor for Gestational Diabetes mellitus (GDM), as according the American Diabetes Association the lowest cut off is 25

years, however no such harmony of the age is stated above which there is significantly high risk of GDM.

Regarding ethnicity in the GDM group, 12.0% participants were Punjabi, 7.9% Pukhtoon, 13.8% Balochi, 6.9% Sindhi speaking and 59.5% participants were Mohajir. As ethnicity relates different demographic facts, cultural background, and socioeconomic differences and consequently affects the behavior and approach towards health and education, and sometimes gender discrimination is observed in some races. All this may also lead to cause unhealthy pregnancy with certain complications.

The family history also found to matter as more cases were of patients who had diabetes, likewise heart diseases and thyroid were also reported with GDM. However, 40% population were reported with no family history but developed GDM. Complicated cases having diabetes and thyroid along with heart problems were observed in 8% pregnant women. According to the study, the most accountable factor for GDM was family history. Furthermore, pregnancy is complicated due to GDM in a variety of manner as like most of the infants of GDM mothers were overweight as compared to the non-GDM mothers (Table **2**).

Table1. Socio-Demographic Data of Women having GDM.

Socio-Demographic Characteristics	Age in Years	Gestational Diabetes mellitus (GDM) (n)	Gestational Diabetes mellitus (GDM) (%)	p-value
Age group of Women	16-30	452	45.2%	0.000
	31-45	548	54.8%	
Ethnicity	Punjabi	120	12.0%	
	Pukhtoon	78	7.8%	
	Balochi	138	13.8%	>0.05
	Sindhi	69	6.9%	
	Mohajir	595	59.5%	
Trimesters	First	61	6.1%	>0.05
	Second	339	33.9%	<0.0001
	Third	600	60.0%	

Table 2. GDM and Associated Fetal / Maternal Complications.

Pregnancy-Related Fetal, and Maternal Complications	Pearson Chi Square Value	Asymptotic Significance
Family history of pregnant women		
Diabetes		
Heart Disease		
Diabetes + Thyroid + Heart Disease	1.777	0.000
Thyroid Disease		
No risk factor		
Fetal complication		
Large Size (more than 9 pound)		
Pre-term labor		
No complications	17.283	0.000
Pre mature birth		
Small size		
Down syndrome		

Contd…

Maternal complications (Comorbidity)		
Obesity		
Hypertension + Obesity		
Abnormal blood lipids		
Liver disease	2.336	0.000
Kidney disease		
Hypertension		
Depression		
Thyroid disease		
No disease		
Treatment Choice for GDM		
Insulin		
Metformin		
Diet controlled only	1.000	0.000
Exercise		
Glyburide		

DISCUSSION

Pregnancy, a distinctive normal physiological condition, is a feeling of completion and happiness and a new life is created. However, normally during pregnancy the body passes through various changes including both physiological and psychological, and most of them normalize after delivery whereas, some account to induce long lasting effects throughout the life as like diabetes. As during the period of pregnancy, fetus development is completely reliant on mother, and to keep the growth of fetus and mother healthy, there are certain pregnancy induced metabolic changes considered as normal. But sometime these disturbances may lead to some pathological conditions like impaired glucose tolerance, leading to GDM[34, 35].

With the progression of gestation, fasting glucose drops off gradually with advancing gestation however, the mechanism is not well defined. But there are some accountable factors like increased plasma volume in the beginning of gestation, high feto-placental glucose utilization, and uptake of carbohydrates (glucose) by mother in second and third trimester. Interestingly, more production of hepatic glucose regardless of a decline in fasting glucose in GDM leads to a simultaneous increase in fasting insulin and decrease in fasting glucose and this may aggravate with prolonged fasting[36]. The hepatic disturbance causes increased glucose concentrations in blood despite high insulin concentrations, and that sustains discrepancy between tissue insulin demands for glucose monitoring and the ability of the pancreatic β-cells to produce the required insulin accordingly.

The increasing frequency of Diabetes mellitus among pregnant women needs the development of preventive strategies. Different socio-economic factors like cast, region, diet intake, stress affects the prevalence of this disorder.

Therefore, the present study was designed to identify and focus on the facts and figures with associated features of GDM among Pakistani women. Unfortunately, the disorder is unnoticed in Pakistan due to unavailability of appropriate data and uncertain data collection, as the major part of population lives in rural areas. Hence, cases form underprivileged areas are not reported or treated, and most pregnancies and deliveries are handled by inexperienced or non-institutional and uncertified experienced obstetricians at home or at local unregistered clinics and small hospitals settings, devoid of basic emergency facilities. Further, lack of facilities for antenatal care and childbirth, and unwanted pregnancies in married women are more accountable in developing complications during

pregnancy, leading to different disorders[37]. The reality states that the awareness and information related to reproductive health including infertility, abortions, and pregnancy handling is inadequate.

In current study, Gestational Diabetes mellitus risk is higher in women with age group of 31-45 years, as compared to the women aged between 16-30 years, with a highly significant p-value. The high risk of GDM in old age is due to the fall in pancreatic beta cells performance with age, while in elderly age, the inadequate pancreatic beta cell response to stimulation develops more insulin resistance as compared to younger age.

One of the strong factor of GDM is family history. Statistical analysis showed highly significant ratio between family history and GDM. Different socio-economic aspects like joint family system, load of responsibilities, and week physical health are most common in Indo-Pak that hinders to live healthy and happy life, and these are the important reasons of antenatal disorders. Consequently, medicines are required to be prescribed to manage the glycemic level in pregnancy and to avoid possible unhealthy effects on both baby and mother before and after delivery[38]. The current study revealed that GDM is managed through diet control, exercise, insulin and medicine including metformin and glyburid, however the insulin therapy was found to be adopted by majority of the population whereas, second option was by medicine at high frequency and metformin was established at higher rate for treatment. Management of GDM through diet control was observed relatively at low level may be due to the ground reality of pregnancy cravings, for fulfilling the nutritional need of the woman and fetus; a principal biological reality. The exercise and work-out like aerobics, yoga, and walk are considered as a best remedy for curing or controlling the diabetes and cholesterol, and also help to reduce stress and depression normally, and in pregnancy significantly. But unfortunately the adaptation of this safe management was observed at very low level as gestating is a lengthy, tiring, and uncomfortable situation and sometime this laborious work induces laziness that does not allow the physical activity and women are more prone to rest[39]. The obesity in pregnancy are inter-related with GDM and according to Royal College of Obstetricians and Gynecologists (RCOG) moderate exercise like yoga and walk for 30-60min three times a week is safe during pregnancy with GDM, and it also significantly reduces the occurrence of GDM and gestational obesity, along with associated hypertension and preeclampsia[40].

The present study was also focused on the other health conditions and disorders already present and account for aggravating the hyperglycemia leading to the GDM. The obtained data revealed that obesity is a prominent cause of GDM at high frequency, and more prevalence and co-morbidity was observed of obesity with hypertension. However, hypertension, lipid disorder, kidney and thyroid diseases were found to be co-morbid with diabetes in pregnancy at equal rate.

Nonetheless, the handling and care of pregnancy is essential right of every woman and immediate relations should be responsible and should play positive role for saving mother and baby both. Firstly, proper meal plan and supplements are basic need for healthy pregnancy. Healthy diet with low glycemic index help to reduce the risk of GDM and hypertension. Various social and economical factors influence the diet and healthy environment for a pregnant women. Unfortunately, in Pakistan, high poverty rate, low income, and more dependence on one income

hinders in providing ideal conditions during pregnancy. Thus, the present study showed that majority of the population is deprived of healthy and good diet and furthermore no essential supplements were consumed after conception, and women are being consulted with gynecologists in second or third trimester. All these factors are cumulative cause to lead to high GDM rate in Pakistani women.

CONCLUSION

The outcomes of this study showed an increasing incidence of GDM at older age pregnancy because of more susceptibility towards hypertension and Type 2 DM. Additionally, different socio-economic factors were also observed to influence GDM rate including family income, lifestyle, stress etc. that directly or indirectly affects the health during and after the pregnancy. To overcome the associated risks during pregnancy, health care programs, plans, and campaigns should be arranged and healthcare professionals should work to give awareness about maternal and fetus health care.

ETHICAL APPROVAL

All procedures were performed in accordance with the ethical principles, and the study approved by the Faculty Research Committee, Department of Pharmacology, Jinnah Sindh Medical University, Karachi, (Ref. No. JSMU/Pharma/151/2020). After verbal consent, the data was collected and firmly preserved for the privacy of all information given by participants. Ethical issues (informed consent, misconduct, data assembly, etc.) have been fully observed by the authors.

CONFLICTS OF INTEREST

None.

LIST OF ABBREVIATIONS

DM	Diabetes Mellitus
GDM	Gestational Diabetes Mellitus
OGTT	Oral Glucose Tolerance Test
SPSS	Statistical Package for Social Sciences

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