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Exploratory Data Analysis: An insight into Gestational diabetes mellitus issue in Pregnancy

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Among the most familiar maternal complications is gestational diabetes mellitus (GDM) and its incidence has increased globally, along with increasing type two diabetes. Every level of dysglycaemia which first arises or has been first detected throughout pregnancy is referred to as gestational diabetes mellitus (GDM). Globally, this has become a public health burden. GDM has become one of the major public health problems for both mothers and children globally. Internationally, the frequency of excess weight and obesity has risen dramatically in women of childbearing age. There seems to be a greater risk of having GDM in overweight or obese women, resulting in problems during pregnancy, birth and neonatal development. Hospital management is a problem for obese pregnant females with GDM and places extra burdens on the healthcare sector. GDM can result in possible risks to the wellbeing of the mother, fetus, and infant, as well as clinically significant negative effects on the mental health of the mother. For females and their developing babies, diabetes may cause problems during pregnancy. Unsatisfactory diabetes control enhances the risk of complications and other birth related issues during pregnancy. It may also cause a woman to suffer severe complications. Numerous maternal and fetal effects are associated with GDM and multiple detection and management methods are also pursued globally in order to reduce the burden of health. An overview of gestational diabetes in pregnancy, its epidemiology, its causes and treatment is given in this review.

Keywords: Pregnancy, diabetes, complications, treatment

Introduction

Gestational diabetes mellitus (GDM) causes several complications during pregnancy. Adverse maternal as well as foetal effects such as elevated risk of pre-eclampsia, caesarean sections, predates, increased fetal weight with related complications and hypoglycemia have been associated with GDM [1-5]. Researches have shown that maintaining glycaemic regulation during course of pregnancy decreases the occurrence of unwanted results substantially. Globally, the incidence of GDM has increased. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) research reports that obesity and GDM are separate and combined risk factors that are involved in poor pregnancy outcomes. A concurrent rise in weight in women of the reproductive age group recorded in India and neighboring countries has been reported. Maternal, foetal, perinatal and neo-natal complications have been associated with an enhanced pre-pregnancy Body Mass Index (BMI) [5-10]. The Indian Ministry of Health has lowered the BMI intervention reference standards for Indians while diagnosing and managing obesity as per World Health Organization (WHO) guidelines [11]. Fortunately, in the study of obesity in pregnancy, many Indian studies continue to use international guidelines. The placenta is exposed to the influence of the intrauterine environment of the mother. The placenta, in turn, has metabolic, structural and functional roles which influence maternal and fetal well-being in the short and long term [11-15].

Increased insulin resistance and endothelial dysfunction in the placenta are pathological changes in GDM and in obesity. These are the consequence of hyperglycemia, lipotoxicity and hyperinsulinemia. As a result of endothelial dysregulation, GDM was characterized by hypoxic stress. Pro-inflammatory states that cause oxidative and nitrative stress are obesity and GDM. The placenta displays functional and/or morphological changes depending on the length and timing of the onset of GDM due to these derangements [15-19]. Pregnancy diabetes is a metabolic condition with severe short- and long-term maternal and fetal health complications. Pregnancy diabetes can be pre-existing or gestational diabetes mellitus. GDM was first identified by O' Sullivan in a group of pregnant women in Boston in the 1960s, while Duncan in London recognized the risk of developing diabetes during pregnancy as early as 1882 [20]. Gestational diabetes mellitus is characterized as 'variable-degree glucose intolerance with onset or first-time awareness during pregnancy'[21]. The disease contributes primarily to countries' healthcare burden [22].

Epidemiology of Gestational diabetes mellitus

The 2016 WHO Global Diabetes Study records a global prevalence of diabetes in 10-25% of pregnancies. Of these studies on the prevalence of hyperglycemia, it has been reported that 75-90% of them are gestational diabetics. The research states that the highest prevalence of gestational diabetes has been observed in regions of South East Asia. The increased frequency of GDM in South Asian populations has also been recorded in other studies. Furthermore, the country of birth also affects the recorded threat of developing GDM even within females of similar ethnicity [22-25]. It was also found that lower and middle-income countries recorded the highest incidence of gestational diabetes. Glucose levels are also shown to be higher in women from economically disadvantaged neighborhoods when diagnosed with GDM. Compared to previous years, GDM prevalence rates have increased significantly worldwide. A substantial increase in the prevalence of GDM has been documented by studies from both developed countries and developing nations. The worldwide rise was due to an increase in obesity and overweight prevalence. Increased prevalence rates of GDM are also recorded in the population composed of multiple ethnic groups in a Colorado study [25-30].

Effects of Gestational diabetes mellitus

In the development of several perinatal and long-term problems in both the foetus and the mother, GDM has been involved. Macrosomia, hypoglycemia in neonates, increased cord C-peptide levels, hyperbilirubinemia, increased neonatal admissions and shoulder dystocia are the fetal outcomes frequently described to be greater in GDM pregnancies [30-35]. The long-term effects have been studied on the offspring of GDM mothers. Increased BMI trends among descendants of GDM mothers are recorded in some studies. A research also explains that in the early years of childhood such an effect on the BMI of offspring is not seen. Treatment of mild hyperglycemia during pregnancy has been reported to improve neonatal outcomes, but does not affect obesity or childhood metabolic disturbances [35-37]. Enhanced danger of cesarean sections, pre-eclampsia and pre-dates are the predominant immediate maternal effects of GDM. Type 2 diabetes development and a predisposition to GDM development in subsequent pregnancies are the long-term risks for the mother [37-40].

Fetal outcomes in Gestational diabetes mellitus

Neo-natal and fetal adverse effects have been associated with GDM. High gestational age (LGA) macrosomia and perinatal mortality in neonatal infants have been found to be correlated with GDM diagnosed by WHO criteria. The most common finding in deliveries of GDM mothers was the excessive growth of the fetus. Cephalopelvic disproportion has been associated with macrosomia and contributes to higher Lower Segment Caesarean Section (LSCS) rates in GDM pregnancies. GDM, gestational weight gain as well as enhanced pre-pregnancy BMI were identified in a multi-

centric Italian study as potential markers in the production of macrosomia [40-42]. Hypoglycemia, increased bilirubin content, feeding problems, hyperviscosity of the blood was other linked perinatal adverse outcomes. In neonates of GDM mothers, clinical neonatal hypoglycemia was seen [42]. The mortality rate is not different from that of the general population for GDM pregnancies under care. In the first trimester, the occurrence of congenital defects and spontaneous abortions had earlier been related to hyperglycemia. Existing guidelines, however, attribute them to overt diabetes [43-46]. There was no correlation of congenital malformations at or later than the second trimester onset of GDM [47].

Treatment of Gestational diabetes mellitus

The primary objective of GDM care is to achieve good glycemic regulation that prevents/reduces fetal as well as maternal complications. A basic change in maternal and fetal outcomes was seen in the timely identification of GDM and treatment intervention with good glycemic regulation [48].

Effects of treatment of Gestational diabetes mellitus

Compared with those in the intervention group (dietary advice / insulin therapy) in a review of pregnancy outcomes among participants in the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), who received routine therapy. The findings showed that counseling substantially decreased the danger of perinatal morbidity as well as showed that maternal anxiety and well-being were alleviated [49-51]. Among the classes, rates of cesarean delivery were similar. An analysis of moderate gestational diabetics in the United States showed that there was a drop in mean birth weight, shoulder dystocia, neonatal fat mass and LGA among the fetal outcomes under care. In either party, no perinatal deaths occurred. Elevated cord blood C-peptide, hyperbilirubinemia, neonatal hypoglycemia, and birth trauma were the criteria which did not show any difference with treatment. The maternal parameters showing a substantial decrease were the number of deliveries by cesarean section and pre-eclampsia [51]. Between intervention and routine care classes, the need for induction of labor was the same. A systematic review and meta-analysis concluded that fetal complications of macrosomia, Broad for Gestational Age (LGA), and shoulder dystocia and maternal hypertension were minimized by GDM therapeutic intervention. No major effects were observed on preterm delivery, labour induction requires, cesarean sections, pre-eclampsia, birth trauma, perinatal or neonatal morbidity and neonatal hypoglycemia [52-54]. Another systematic study involving 12 studies found that the occurrence of macrosomia and shoulder dystocia was substantially decreased by GDM care. No major reductions in the number of small babies in gestational age or perinatal/neonatal deaths were observed. Further studies have shown that the risk of developing type II diabetes in mothers has been minimized by adequate treatment of GDM [11]. Clinical research in females having prior exposure of GDM who were on pharmacological treatment or lifestyle intervention found that diabetes mellitus progression was reduced/delayed by up to 50% relative to those treated with placebo. The need for GDM care is aimed at ensuring minimal/nil prenatal complications as well as avoiding/delaying the production of mother and child metabolic disorder(s). Strict glucose regulation and good glycemic control are involved in GDM management [55]. Glucose levels, i.e. fasting glucose, can be tracked up to 4 times/ day and one hour after having each meal has started. After fasting, the predicted glucose levels are 70-90mg/dl and below 120mg/dl post-prandial. A fasting glucose target of approximately 90 mg/dl and a 2-hour post-prandial glucose target of approximately 120 mg/dl have been reported in the Indian DIPSI recommendations [55].

Medical Nutritional Therapy

The recommendation of medical nutritional therapy (MNT) and lifestyle changes involving physical activity is the first step towards maintaining glycemic control. A research from India on a detailed GDM management protocol, entitled the WINGS project, suggested two weeks of MNT and life-style intervention to follow. If normal glycemic regulation with MNT can be achieved, daily glucose

level monitoring [13] should be followed. In the absence of optimum glucose levels with MNT, it was recommended that insulin or metformin therapy be initiated to treat diabetes. The WINGS project proposed that only insulin be used [54]. A research also indicated that the dosage of insulin should be modified according to the needs of the particular patient. A systematic study on GDM treatment during pregnancy also found that the use of insulin over oral hypoglycemic medication was favoured by several global protocols. MNT requires dietary intake control. The key goal of the MNT was to ensure fetal growth and to avoid ketosis [54-55]. The control of caloric intake during GDM has been modified based on prenatal BMI. For women with normal and increased BMI groups, ACOG recommended caloric intake, composition and distribution. The goal of diet regulation was to maintain optimum gestational weight gain without compromising on fetal nutrition and growth and also without ketosis, as per Institute of Medicine (IOM) guidelines. The caloric intake requirement was similarly suggested by the Ministry of Health and Family Welfare of India. To calculate the daily energy requirement as per BMI and the degree of physical activity, be it sedentary, moderate or strong, a set of formulas has been established. 350 kcal per day was applied to the adult female energy requirement to meet the energy requirement of a pregnant woman. Finally, in the case of underweight BMI, 500kcal/day was added to the regular requirement and in the case of obese women; 500kcal/day was deducted from the requirement. In summary, the Indian recommendation has taken into account the type of physical activity performed by the subject in the calculation of the calories required per day and is also based on Indian BMI cut-off values [55]. The role of exercise was to increase the sensitivity of insulin. Exercise to decrease the need for insulin has been documented and has also helped maintain adequate glycemic control. Exercise regimens adopted by GDM mothers have been found to decrease insulin therapy requirements and doses and also boost glycemic control [56].

Pharmacological management of Gestational Diabetes mellitus

Insulin or other medical pharmacological options should be started in subjects whose fasting and post-prandial glucose levels are not lowered by MNT. A study stated that the majority of studies insist that only insulin is used to control GDM [56-60]. Studies have confirmed, however, that oral hypoglycemic agents such as metformin can be used in GDM and have been successful in preventing complications in pregnancy, and that the protective effects of metformin are comparable to those of insulin. The investigators found that patients preferred to use metformin as opposed to insulin. Studies have been performed on the development of alternative medicinal therapies such as glyburide and glibenclamide in the treatment of GDM. Both therapies have been tested in terms of their success in preventing maternal and fetal GDM complications as well as maintaining tight glycemic regulation [60-64].

Conclusion

Gestational diabetes mellitus (GDM) is a significant pregnancy complication wherein patients without previously diagnosed diabetes experience chronic hyperglycemia during gestation. In most cases, this hyperglycemia is the result of reduced glucose tolerance on the basis of chronic insulin resistance because of pancreatic β-cell dysfunction. Genetic, epigenetic and environmental factors are all likely to contribute to the development of GDM, and over a significant period of time, the processes involved are complex and gradual. The treatment and diagnosis of gestational diabetes is subject to much debate, stressing the significance and validity of clarification and consensus. In order to establish successful therapies and prevention strategies, greater awareness of these processes and their contribution to GDM is needed.

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