REVIEW ARTICLE:

GESTATIONAL DIABETES MELLITUS

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Abstract:

GDM is a form of hyperglycemia. Gestational diabetes (GDM) is a glucose tolerance disorder that occurs or is diagnosed during pregnancy . GDM is a transient type of diabetes that occurs during pregnancy. Most women with GDM will return to normal glucose levels after delivery of the baby. If a woman does not return to normal glucose levels she will be re-diagnosed with type 2 diabetes and will no longer be considered to have GDM. It represents the most common metabolic complication of pregnancy**.** GDM is associated with maternal and fetal morbidities.Early recognition of GDM is very mandatory to prevent maternal morbidity and mortality. GDM may complicate during the pregnancy, intra-partum or post-partum. Birth trauma and poor fetal outcome are important complications. GDM doubles the risk of serious in jury at birth, triples the likelihood of cesarean delivery and quadruples the incidence of newborn intensive care unit admission . Approximately 7% of all pregnancies are complicated by GDM, resulting in more than 200,000 cases annually. The prevalence may range from 1 to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed .

Keywords : Hyperglycemia

Introduction

GDM is a form of hyperglycemia. Gestational diabetes (GDM) is a glucose tolerance disorder that occurs or is diagnosed during pregnancy [1.]. GDM is a transient type of diabetes that occurs during pregnancy. Most women with GDM will return to normal glucose levels after delivery of the baby. If a woman does not return to normal glucose levels she will be re-diagnosed with type 2 diabetes and will no longer be considered to have GDM [2]. It represents the most common metabolic complication of pregnancy**.** GDM is associated with maternal and fetal morbidities [3].

Early recognition of GDM is very mandatory to prevent maternal morbidity and mortality. GDM may complicate during the pregnancy, intra-partum or post-partum. Birth trauma and poor fetal outcome are important complications. GDM doubles the risk of serious in jury at birth, triples the likelihood of cesarean delivery and quadruples the incidence of newborn intensive care unit admission [4]. Approximately 7% of all pregnancies are complicated by GDM, resulting in more than 200,000 cases annually. The prevalence may range from 1 to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed [5-6].

Although the risks associated with GDM are well recognized, the impact on maternal and neonatal health outcomes is less clear and still and matter to think wisely and medically. The factors that have been postulated to influence the risk of GDM among mothers include obesity, a positive family history of diabetes, treatment for infertility, recurrent urinary tract infections, macrosomic infant, unexplained neonatal death, prematurity, pre-eclampsia, diabetes in previous pregnancy, and advancing maternal age [7] Women with GDM have increased risk for potential morbidity and for impaired glucose tolerance, and it identifies a population of women who are at high risk of developing type 2 diabetes in the years following the pregnancy [8]. In addition to higher risk of perinatal

morbidity, the offspring of mothers with GDM face increased risk of childhood obesity and early onset of type 2 diabetes mellitus [9]. So as pregnancy is stage not only related to physiology of a female, is also related to mental psychological and emotional bonding with the offspring. Thus the present article is written to review the etiologies of GDM so that to improve the health of mother and the child to decrease the occurrence of it.

Physiology of pregnancy

The pregnancy involves endocrine and metabolic changes in the body. The physiological changes at the boundary between mother and fetus is known as the feto-placental unit (FPU), this is the major site where protein and steroid hormone production and secretion takes place [10,11,12]. During early pregnancy, glucose tolerance is normal or slightly increased [13,14,15]. Alternation could be caused by the increased in maternal estrogen and progesterone in early pregnancy and causes the increase activity of pancreatic ß-cell hyperplasia (Expansion of beta-cell mass in response to pregnancy) and leads to increased insulin release [16,17]. It increases the rapid increase of insulin level in early pregnancy, in response to insulin resistance. In the second and third trimester, the continuous increase in the FPU or factor will decrease maternal insulin sensitivity. This will stimulate mother cells to use sources of fuels other than glucose such as free fatty acids (FFA), and the supply of glucose to the fetus will be more [13,14,20]. The insulin resistance of the whole body is increased to about three times in pregnant women as compare to the non-pregnant state [20]. Although, during pregnancy there would be increase in insulin level [21]. Some pregnant women are unable to regulate insulin production related to the degree of insulin resistance, and consequently become hyperglycemic, developing GDM [22].

Pathophysiology : Insulin resistance during pregnancy is due to changes in many factors, like alternation in growth hormone and cortisol secretion (insulin antagonists), human placental lactogen secretion (HPL) which is produced by the placenta, promotes lipolysis, and insulinase secretion which is produced by the placenta and facilitates metabolism of insulin. Other hormones related to GDM are estrogen and progesterone causing intolerance of glucose [23].

Pathophysiology of GDM

In the pathophysiology of GDM we have to consider two main points.

1. Role of feto-placental unit in GDM.
2. Role of the adipose tissue in GDM

Insulin resistance and the decrease in insulin sensitivity during pregnancy is mainly associated to the increase levels of pregnancy-associated hormones as estrogen, progesterone, cortisol, and placental lactogen [20,24,25,26,27]. The level of these hormone production will increase as pregnancy progresses and the placenta grows, so the level of insulin resistance also increases. This process usually starts between 20 and 24 weeks of pregnancy. At birth, these hormone production stops when the placenta is delivered and the condition strongly suggesting that these hormones cause GDM [20,28,29].

Diabetic action of steroid hormones (cortisol, estrogen, and progesterone)

Steroid hormones have anti-insulin action [20]. The increase in cortisol level during pregnancy is deliberated as the main hormone which cause decrease in glucose tolerance in normal pregnancy [24,25], estrogen and progesterone which are elevated gradually during pregnancy, main hormones which influence beta cell function in early pregnancy and insulin resistance [20,26,30].

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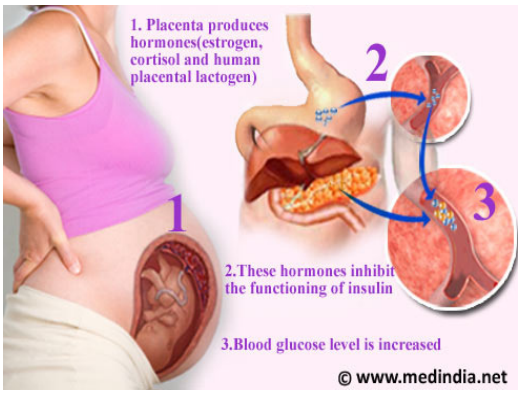

The role of adipose tissue in the development of GDM

Adipose tissue produces numerous factors (adipocytokines), most of them act as hormones. These adipocyte-derived hormones have been involved in the regulation of maternal metabolism and gestational insulin resistance [21,31,32]. Although HPL has often been mentioned as the cause of the decreased insulin sensitivity in pregnancy, because of its production from the placenta and increasing concentrations with advancing gestation [20]. Adipokines (as TNF-alpha and leptin) could impaired insulin signaling and cause insulin resistance [31,33]. TNF-aplha has a latent effect in decreasing insulin sensitivity [21]. While other adipocytokines might increase insulin sensitivity as adiponectin which has been shown to be decreased especially in late pregnancy [33].

Complications of GDM during pregnancy

Women with GDM experience twice the number of urinary tract infections as compare to normal women. This increased infection incidence due to the increased amount of glucose in the urine (glucosuria). There are also leads to increased risk of pyelonephritis, asymptomatic bacteriuria, and pre-eclampsia. There is a 10% risk of polyhydramnios that may increase the risk of abruption placentae and pre-term labor. There is also a 10% per year risk of developing type 2 diabetes after the pregnancy who had GDM. Macrosomia can be occurs at 26 to 28 weeks gestation. Complications allied with macrosomia include operative delivery, shoulder dystocia and neonatal hypoglycemia [13].

There is an increased occurrence of hyperbilirubinemia, hypocalcemia, respiratory distress syndrome, and polycythemia in the neonate. The long-term complications can include obesity, diabetes during childhood, impaired motor function, and hyperactivity [34,35].

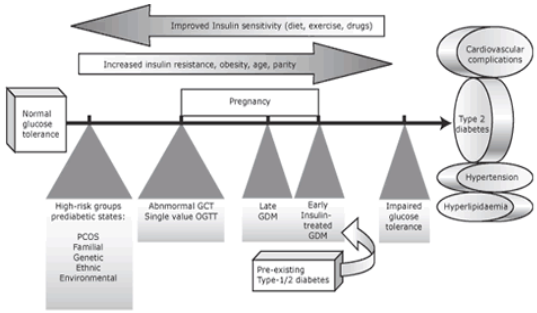

Figure 2.Showing epidemiology of GDM and its association with type 2 diabetes [36]

Effects of GDM on the Mother

• Women with GDM can delivered a heavy weight baby which can lead to increases in birth trauma [37].

• Women who have had GDM are more prone of developing type 2 diabetes [38].

• Women with GDM are more likely to have high blood pressure during pregnancy [39].

Effects of GDM on the Infant

• Gestational diabetes can cause the baby to have a high birth weight [40].

• Infants born to mothers with GDM have three times the risk of shoulder dystocia which can cause temporary or permanent nerve damage in the shoulder [41]. Shoulder dystocia occurs when the baby's shoulder gets stuck behind the mother's pubic bone.

• Newborns born to a mother with GDM are at increased risk for dangerously low blood sugar levels (hypoglycemia) after birth, excessive blood insulin levels (hyperinsulinemia), low levels of calcium in the blood (hypocalcemia), too many red blood cells (polycythemia),

and yellowing of the skin and eyes (jaundice caused by hyperbilirubinemia) [42].

• Babies born to mothers with GDM are at greater risk of becoming obese and having long-term glucose intolerance or developing early onset type 2 diabetes

Summary of reported risk factors for GDM [36,37]

Maternal factors	Family history	Previous obstetric outcome	Pregnancy factors	Protective factors
• Older age • High parity • Prepregnancy weight • Pregnancy weight gain • BMI = 27 • Short stature • Low birth weight • α-Thalassemia trait • Polycystic ovary syndrome • High intake of saturated fat	• Family history of diabetes • GDM in woman's mother	• Congenital malformation • Stillbirth • Macrosomia • Caesarean section • Previous GDM	• High blood pressure in pregnancy • Multiple pregnancy • Increased iron stores	• Young age • Alcohol use

After completion of their study it is found that A positive GCT was observed in 639 women (35.4%). The stimated prevalence of GDM for the whole cohort was 6.8% (124 out of 1804 pregnant women). GDM was more prevalent in women with positive family history of diabetes that is 15.7%. Also the results indicated that GDM was more prevalent in women with history of infertility (12.6%), stillbirth (17%), abortion in previous pregnancies (17%) and macrosomia (23.5%).

According to their study the time of screening was between the 24^{th} and 28^{th} week of gestation. The study indicated that GCT was positive in 35.4% of cases. In their study it is observed that the prevalence of GDM was increased in women with positive history of abortion. The women with positive history of macrosomia in previous pregnancies were found to have more GDM in the current pregnancy. The women with positive history of macrosomia in previous pregnancies were found to have more GDM in the current pregnancy.

Discussion

The above supportive study provides the information about the risk of GDM, which could potentially help to incorporate early intervention measures**.** Their studied women with GDM had a higher risk of adverse health outcomes and were more likely to develop maternal complications. It was reported that socioeconomic status influences the prevalence of GDM in pregnancy. GDM is a problem that affects a significant number of women during pregnancy. Most of the women reverting to normal after

delivery, will suggest that the placenta is the major contributing organ in the development of GDM.

The metabolism of carbohydrates and lipids may lead to hyperglycemia and ketosis. Some hormones produced by the placenta (estrogen, cortisol, and human placental lactogen) can have a blocking effect on insulin, which usually begins about 20 to 24 weeks into the pregnancy. As the placenta grows, the level of these hormones are increased, and insulin resistance becomes greater and when the production of insulin is not enough to overcome the effect of the placental hormones then it results GDM.

The plasma levels of Human Chorionic Gonadotropin (HCG), Human Placental Lactogen (HPL), progesterone and estrogen present during pregnancy increase in the last 20 weeks of gestation. HPL plays a vital role in triggering the changes that lead to glucose intolerance. It has strong anti-insulin and lipolytic effects. The pathogenesis of GDM, are the increase in HPL secretion during pregnancy. It is seen from various study on GDM that women who develop GDM secrete less insulin in response to a glucose load than the normal women.

GDM can leads to type 2 diabetes if it is not diagnosed and treated in the starting time of gestation. The temporary form of diabetes which was started at the time of pregnancy can further cause much complication to mother as well as child.

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Date of submission: 12 March 2014 , Date of Publication : 20 June 2014