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Introductory Chapter: Gestational Diabetes Mellitus

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1. The condition

Pregnancy, though a physiological condition, involves increased stress on a mother's biological processes. Advanced age, frequent pregnancies with shortened intervals, and several other risk factors may cause one of these processes to buckle under the stress giving rise to a disease state [1].

Gestational diabetes is a typical example which occurs as a temporary condition during pregnancy and is characterized by hyperglycemia and its varied manifestations. The word "gestational" implies exaggerated physiological response in pregnancy. Pregnancy is a state of insulin resistance, which has been designed by nature with the aim to supply the fetus with adequate nutrition at all times, irrespective of the mother's feeding cycles or habits. When this resistance, which is a physiological response to pregnancy, becomes aggravated and overcomes the pancreas capacity to secrete extra insulin, the result is a constant state of hyperglycemia. Risk factors and risk markers for GDM are age (the older a woman the higher her risk of GDM), overweight or obesity, excessive weight gain during pregnancy, a family history of diabetes, and GDM during a previous pregnancy [2].

Human placental lactogen and prolactin, the levels of which steadily increase during pregnancy, also contribute to the phenomena of increased insulin resistance by preventing the intake of insulin into peripheral tissue. A lesser explored hormone adiponectin exerts a protective effect by inhibiting hepatic glucose production. In GDM pregnancies, there is a significant decrease in placental adiponectin from an early stage of pregnancy, which now appears to be another independent risk factor for GDM. Adiponectin levels are also affected by pro-inflammatory cytokines, thus indicating a relationship between inflammation and carbohydrate metabolism or even a gross metabolic dysregulation [2].

2. The magnitude of the problem

According to the International Diabetes Federation (2017), 21.3 million or 16.2% of live births had some form of hyperglycemia in pregnancy, and a majority of these (85.1%) were due to gestational diabetes and one out of seven births is affected by gestational diabetes. The WHO Global Report on diabetes (2016) also gives similar figures: 75–90% of cases of hyperglycemia in pregnancy are due to gestational diabetes and 10–25% of pregnancies are affected by gestational diabetes. To complicate matters, a maximum number of these cases are from the low- and middle-income countries emphasizing the fact that diabetes per se as well as gestational diabetes are not the diseases of the affluent society who have access to quality health care [3]. A large number of these cases are from those sections of the population who do have

access to basic antenatal care, where missing gestational diabetes is common and associated with grim outcomes for the mother and baby.

3. Maternal and fetal complications

Undetected, unmonitored, and uncontrolled gestational diabetes leads to severe maternal and fetal morbidity and mortality. GDM has a spectrum of both short- and long-term complications for both the mother and the fetus [4].

Among the short-term complications, are those that happen in the index pregnancy, hypertension is often associated with type 2 diabetes and so is true for GDM. Women who have GDM often develop hypertension during pregnancy and when compared to women who are euglycemic during pregnancy the difference is significant. Pregnancy-induced hypertension leads to several other problems in terms of preeclampsia and even eclampsia.

Several reasons for short-term morbidity in the mother are related to the increased size of the fetus. Nonprogress of labor and cephalopelvic disproportion due to a large-sized baby may lead to instrumental deliveries, perineal injuries, and C-sections.

For the fetus, the hallmark complication of GDM is macrosomia and the problems resulting from it. These could be sudden fetal demise, shoulder dystocia, obstructed labor, hydramnios, malpresentations, and cord prolapse. Macrosomia also leads to earlier onset of labor, giving rise to a preterm baby with all the associated risks of prematurity. The chief among these is the respiratory distress syndrome (RDS) due to lack of surfactant: this is a combined effect of prematurity as well as the fact that hyperglycemia per se also delays lung maturity.

The baby of a GDM mother has more chances of admission to intensive care due to RDS and also because it is more prone to metabolic derangements which are typical of this condition. Hypoglycemia, hyperbilirubinemia, and hypomagnesemia are significantly more in babies of GDM mothers.

When considering long-term complications of GDM recurrence of GDM in subsequent pregnancies and the development of type 2 diabetes in later life are the ones of major concern. A GDM mother has about 30–60% chance of recurrence in subsequent pregnancies. A systematic review of 28 studies covering the same number of years showed that a GDM mother has a cumulative incidence ranging from 2.6 to 70% of type 2 diabetes. Recurrence of GDM in subsequent pregnancies and the development of type 2 diabetes in later life are linked to risk factors like obesity, interval between pregnancies, and the amount of insulin needed during the index pregnancy.

Long-term complications in the neonate of a GDM mother are obesity and type 2 diabetes in adult life. The girl child also runs the risk of GDM in her pregnancy.

4. The controversies

Screening and diagnosis of gestational diabetes is varied and till date a single universal guideline has been elusive. This is compounded by the fact that both gestational diabetes and type 2 diabetes are very dependent on ethnicity. This often leads to the question as to whether a single mathematical figure would actually reflect hyperglycemia and its complications in different ethnic groups.

International and national bodies advise various ways to screen gestational diabetes. Large numbers of such guidelines confuse the primary health provider and the practicing obstetrician. In this era of evidence-based medicine, there is need

for a single robust, evidence, practical guideline, the use of which would ensure the early detection and adequate management of gestational diabetes at the earliest in different countries and ethnic groups.

5. Recent advances

Although screening for GDM remains the mainstay for early detection, biomarkers for predicting, and monitoring the condition have also been identified. These biomarkers are altered as a result of the underlying pathology of GDM and thus help in predicting the condition before it actually becomes manifest clinically. These biomarkers may be related to insulin resistance, chronic inflammation, and altered placental function all of which are related to the patho-physiology of GDM. Micro-RNAs, one such group of biomarkers are a class of RNAs which are not involved in coding but can modulate gene expression. Thus, particular levels of circulating micro-RNAs can be used as biomarkers to predict GDM.

Efforts are also being made to combine several biomarkers to form a risk score for prediction of GDM. Combining clinical risk factors and biomarkers to predict the condition are also in the process.

6. The way ahead

Gestational diabetes mellitus has a well-documented link with maternal age, family history, diet, obesity, and lack of exercise. Both ethnicity and deprivation are major contributors to an increased risk of GDM. Research has confirmed that a better diet, increased physical activity, an appropriate pre-pregnancy Body Mass Index could reduce the development of gestational diabetes mellitus. The challenge now is to find ways of delivering these benefits in real life rather than in purely research settings. Keeping these things in mind, the first aim should be primary prevention. It plays the most significant role in creating awareness as regards gestational diabetes among public. Awareness should particularly target the groups which are at high risk for developing diabetes. Primary steps in preventing gestational diabetes can delay or halt further developments which in turn reduce both the need for gestational diabetes care and other required treatments. Prevention of gestational diabetes and diabetes per se should be considered a public health priority. The biggest task faced by the medical fraternity is lack of awareness across all segments of society about this epidemic.

A uniform consensus on how to screen for and diagnose gestational diabetes is another focus area for national and international bodies. As both ethnicity and deprivation are major contributors to this disease condition, the guidelines framed should make allowance for both [5, 6].

Another area that needs looking into is the identification of markers which could predict the condition with reasonable accuracy. It is also essential that such markers be cost-effective as both diabetes and gestational diabetes can no longer be considered as the disease of the elite society.

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