Review Article

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Gestational Diabetes Mellitus: An Updated Review

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ABSTRACT

Gestational diabetes mellitus (GDM) is defined as a glucose tolerance disorder that occurs or is diagnosed for the first time during pregnancy and is one of the most common pregnancy complication. It is a well characterized disease affecting a significant population of pregnant women worldwide. It has been widely linked to undue weight gain associated with factors such as diet, obesity, family history, and ethnicity. The clinical and public health relevance of GDM is widely debated due to its increasing incidence, the resulting negative economic impact, and the potential for severe GDM-related pregnancy complications. Also, effective prevention strategies in this area are still lacking and controversies exist regarding diagnosis and management of this form of diabetes. This article provides an overview of clinical issues related to GDM, including the challenges of screening and diagnosis, the pathophysiology behind GDM, the treatment and prevention of GDM, and the long and short term consequences of gestational diabetes for both mother and offspring.

INTRODUCTION

Gestational diabetes mellitus (GDM), by definition, is any degree of glucose intolerance with onset or first recognition during pregnancy. This definition applies regardless of whether treatment involves insulin or diet modification alone; it may also apply to conditions that persist after pregnancy. GDM affects roughly 7% of pregnancies with an incidence of more than 200,000 cases per year. The prevalence, however, varies from 114%, depending on the population and the diagnostic criteria that have been used.[1,2] GDM is the most common cause of diabetes during pregnancy, accounting for up to 90% of pregnancies complicated by diabetes. Women with GDM have a 40–60% chance of developing diabetes mellitus over 5–10 years after pregnancy.[3]

Gestational diabetes mellitus (GDM) occurs in about 5% of pregnancies but figure varies considerably depending upon the criteria used and demographic characteristics of the population. The prevalence is expected to increase as the epidemic of obesity continues. Pregnancies affected by GDM impose a risk for both mother and child as the risk of caesarean and operative vaginal delivery, macrosomia, shoulder dystocia, neonatal hypoglycaemia, and hyperbilirubinemia is increased. Women with a history of GDM are also at an increased risk of developing type 2 diabetes mellitus (T2DM) in the years following their pregnancy and their children have a higher risk of developing obesity and T2DM early in life.[4,5]

SCREENING AND DIAGNOSIS

Screening and diagnostic testing for GDM is however important in order to identify the women at risk for developing GDM and thereby reduce or prevent the risk of adverse events for both mother and child associated with GDM.

The first screening test for GDM, proposed in 1973, consisted of the 1 hour 50 gm oral glucose tolerance test. While some guidelines recommend universal screening, others exempt those patients who are categorized as low-risk. Evidence suggests that universal screening improves pregnancy outcomes compared to selective screening. However, other researchers argue that screening women based on their clinical characteristics allows for more efficient selective screening for GDM.[6]

Low-risk patients include those women with the following characteristics: <25 years of age; normal body weight; no first-degree relatives with diabetes; no history of abnormal glucose metabolism; no history of poor obstetric outcomes; and not from an ethnic group with a high diabetes prevalence (Hispanic American, Native American, Asian American, African American, and Pacific Islander). Although some experts recommend against screening these low-risk patients routinely, selective screening could miss approximately 4% of patients with GDM.[7,8]

Pregnant women with factors conferring a high risk of GDM (marked obesity, previous history of GDM, glycosuria, or family history of diabetes) should be screened for GDM as soon as possible, preferably during their first antenatal visit. If negative, they should be retested at the beginning of their third trimester between 24 to 28 weeks of gestation. Women who are categorized as average risk (neither high nor low risk) should also be screened between 24 and 28 weeks of gestation. When universal screening is implemented, patients with no recognized risk factors for GDM also undergo a 1 hour glucose challenge test at 24 to 28 weeks of pregnancy.[9]

Fasting plasma glucose and postprandial plasma glucose have been shown to have low sensitivity as screening tests for GDM, and therefore they are not recommended for screening. Pregnant women have a higher physiological turnover of erythrocytes, rendering glycosylated haemoglobin (HbA1c) inadequate as a diagnostic tool, because of underestimation of the average glucose level. In fact, a reduction of HbA1c is seen in normal pregnancy. Instead, a variety of oral glucose tolerance tests (OGTT) have been applied, but a consensus regarding screening for and classification of GDM is yet to be achieved globally. However, a 2 hour 75 gm OGTT at 24-28 week of gestation is now being recommended both by the European Association for the Study of Diabetes, International Association of Diabetes and Pregnancy Study Group (IADPSG), American Diabetes Association (ADA), and World Health Organization (WHO).[10,11]

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study recently demonstrated that no specific threshold for the risk of adverse events for both mother and child associated with GDM can be set as the risk increase is continuous. Other studies have supported the idea of lowering the diagnostic threshold in the diagnostic criteria for GDM, taking the maternal and foetal risks of hyperglycaemia into consideration.[12]

It has been estimated that with this new diagnostic criterion, the prevalence of GDM will increase to nearly 18%, which will have a major impact on the costs, the capacity of the health care systems, and the pathologizing of pregnancies that were earlier categorized as normal. The vast majority of the women diagnosed with GDM will however have mild hyperglycaemia, requiring non-pharmaceutical treatment, including lifestyle modifica- tions.[13]

PATHOPHYSIOLOGY

In normal pregnancy, maternal tissues become progressively insensitive to insulin. This is believed to be caused partly by hormones from the placenta and partly by other obesity and pregnancy related factors that are not fully understood. Skeletal muscle and adipose tissue are the main whole-body glucose disposable sites. In normal pregnancy, insulin-mediated whole-body glucose disposal decreases by 50% and in order to maintain a euglycemic state, the woman must increase her insulin secretion by 200%–250%. GDM develops when the pregnant woman is not able to produce an adequate insulin response to compensate for this normal insulin resistance.

GDM is observed in obese as well as in lean women. However, the pathophysiology behind the disease is believed to differ between these groups. In obese women, the pathophysiology is primarily characterized by the pregnancy-induced insulin resistance being amplified by the already elevated pre-pregnant insulin resistance level. The elevated insulin resistance level is a known factor in the metabolic syndrome. In lean women, the same factors seem to play a role but a defect in the first-phase insulin response contributes to a larger extend.[14]

TREATMENT

Evidence shows that screening for and treating GDM lead to the reduction of perinatal morbidity and the improvement of post-delivery outcomes. As in other types of diabetes, the cornerstone of GDM management is glycaemic control. Glycaemic control has been shown to reduce adverse outcomes in pregnant women with GDM.[15]

Target glucose values:- Experts recommend that women with GDM should maintain the following capillary blood glucose values: pre-prandial glucose <95 mg/dl (5.3 mmol/l), 1-hour postprandial glucose <140 mg/dl (7.8 mmol/l), and 2-hour postprandial glucose <120 mg/dl (6.7 mmol/l).[1] Other recommendations suggest maintaining fasting glucose levels of <90–99 mg/dl (5.0–5.5 mmol/l), 1-hour postprandial glucose levels of <140 mg/dl (7.8 mmol/l), and 2-hour postprandial glucose levels of <120–127 mg/dl (6.7–7.1 mmol/l).[16,17]

Even if it is not possible to achieve the recommended levels of glycaemic control, any improvement can be beneficial given that perinatal complications are inter-linked to increasing serum glucose values. Despite the

benefits of glycaemic control, however, studies have shown that very low target glucose values (<87 mg/dl) are associated with increased rates of intrauterine foetal growth retardation.[18]

Insulin therapy:- Insulin therapy is the most commonly used pharmacotherapy. Insulin regimens often include intermediate-acting insulins such as Isophane and short-acting agents such as regular recombinant insulin (Humulin R). Pharmacotherapy can also involve insulin analogues as Aspart and Lisipro insulin. Insulin therapy decreases the frequency of foetal macrosomia and the risk of perinatal morbidity.[19,20] Positive history of diabetes mellitus in a first-degree relative and multiple abnormal values in the OGTT were strongly found to predict the need for insulin management in women with GDM.[21]

CONCLUSION

Worldwide there has been a dramatic increase in the prevalence of overweight and obesity in women of childbearing age. Overweight and obese women have an increased risk of developing GDM leading to complications during pregnancy, birth, and post-natal. Glycaemic control can safely be achieved with a combination of nutritional and pharmaceutical interventions. Metformin and Glyburide have been shown to be as effective as insulin in management of GDM. Effective communication between physician, patient, and primary care provider is essential, as patients experience increased rates of GDM in subsequent pregnancies and a higher lifetime risk of developing non-gestational diabetes.

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