

Review Article

Risk factors and screening benefits in pregestational and early gestation diabetes

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ABSTRACT

Gestational diabetes is one of the most widespread complications of pregnancy posing a serious clinical and public health challenge. Globally, 16.5% of pregnancies are affected by the gestational diabetes, and this percentage is expected to rise as the obesity pandemic spreads. It has severe short-term and long-term negative health effects on both the mother and the child, which emphasizes the importance of identifying the risk factors for gestational diabetes and taking steps to prevent the illness. Gestational diabetes occurs when pregnant women who have never been diagnosed with diabetes experience chronic hyperglycaemia caused by impaired glucose tolerance. Obesity, physical inactivity, multiparity, family history of diabetes mellitus, certain ethnicities, birth of a previous macrosomic child are all risk factors for gestational diabetes. Maternal cardiovascular disease, type 2 diabetes, macrosomia, and difficulties in delivery are all some of the complications of gestational diabetes. Additionally, there is a longer-term risk for the child to develop obesity, type 2 diabetes, and cardiovascular disease. Screening and diagnostic tests for gestational diabetes are essential to identify the women who are at risk for developing gestational diabetes and thereafter reduce or eliminate the risk of unfavourable outcomes for both mother and child associated with gestational diabetes. Oral glucose tolerance test is the widely accepted screening test conducted between 24-28 weeks of pregnancy for the diagnosis of gestational diabetes. The purpose of this research is to review the available information about risk factors and screening benefits in pregestational and early gestational diabetes.

Keywords: Gestational, Diabetes, Risk, Screening

INTRODUCTION

Recent decades have seen a sharp rise in the prevalence of gestational diabetes mellitus (GDM), which increases the risk of long-term, foetal, and neonatal complications in the pregnancy. Pregestational diabetes and GDM are two different types of maternal diabetes, diabetes that is diagnosed during pregnancy is known as GDM, however it may already be present or continue after birth whereas diabetes type 1 and type 2 diagnosed prior to conception is considered as pregestational diabetes. If diabetes is diagnosed early in pregnancy as in first trimester it is referred as early gestational diabetes. Children of GDM mothers are more likely to develop hypertrophic cardiomyopathy, macrosomia, hypoglycaemia, jaundice, and respiratory distress. Contrarily, pregestational diabetes is linked to a higher risk of miscarriage, intrauterine growth restriction, and congenital abnormalities, particularly if the mother had poor glycaemic control before conception and early in the first trimester of pregnancy. Approximately 50% of all prenatal morbidity is caused by congenital abnormalities, which mostly affect the cardiovascular, neurologic, and genitourinary systems.^{1,2} GDM has a pooled global standardized prevalence of 14%. GDM was assessed to have a 7.1% regional incidence in North America and the Caribbean, 7.8% in Europe, 10.4% in South and Central America, 14.2% in Africa, 14.7% in the Western Pacific, 20.8% in South-East Asia, and 27.6% in the Middle East and North Africa. South-East Asia and Middle East faces significant huge burden of GDM.³

GDM increases the risk of giving birth to a baby that is large for gestational age and the associated complications, such as surgical delivery, birth canal abrasions, birth trauma, among various others. Pre-eclampsia and early birth are also linked to poor glucose metabolism during pregnancy. About half of women with GDM will eventually develop type 2 diabetes in their later years. Therefore, screening, counselling, and treatment are essential. Currently there is no widely used screening method or gold standard test to determine the presence of a disease. Although the oral glucose tolerance test is used in most nations, but the testing method and diagnostic standards differ.⁴ Higher age and body mass index, prior history of GDM, first-degree relatives with diabetes, and unfavourable obstetric outcomes are the most frequent risk factors for GDM diagnosis. GDM diagnosed pregnant women are more likely to develop obesity, metabolic syndrome, and type 2 diabetes later in life, also their children have an increased risk of the development of these diseases in later stages of life. Asians are more susceptible to developing GDM due to the high prevalence of metabolic syndrome and genetic predisposition. Therefore, with an increase in GDM worldwide, identifying key risk factors and unfavourable fetal and maternal outcomes as well as offering GDM affected women the proper care could have a significant impact on health of many parturient and offspring. There is still disagreement over screening standards, appropriate

screening timing, risk factors and fetal and maternal complications of GDM.⁵ Purpose of this research is to review available information about risk factors and screening benefits in pregestational and early GDM.

LITERATURE SEARCH

This study is based on a comprehensive literature search conducted on October 29, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about Risk factors and screening benefits in pregestational and early GDM. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

O'Sullivan and Mahan established the initial diagnostic standards for GDM 55 years ago. The criteria were created based on the outcomes of a pregnancy-related 100-g oral glucose tolerance test performed on a random sample of pregnant patients receiving prenatal care. In the year 1978, American college of obstetricians and gynaecologists advised screening expectant women for diabetes among those who had previously diabetes related risk factors. Guidelines for the classification of diabetes and different types of glucose intolerance, including GDM, were published by the national diabetes data group in 1979. This classification was only applicable to women whose onset or recognition of diabetes or impaired glucose tolerance occurred during pregnancy. Later on, this emerged as the accepted definition of GDM. It was advised to interpret the oral glucose tolerance test using the extrapolated O'Sullivan and Mahan criteria for plasma levels due to the lack of data linking maternal glycemia to perinatal outcomes. In addition, the World Health Organization reported standards for diabetes and impaired glucose tolerance in pregnant women that were equivalent to those used in non-pregnant people. There are numerous additional GDM detection methods and diagnostic standards available.⁶

Risk factors for GDM

Obesity, physical inactivity, multiparity, family history of type 2 diabetes mellitus, certain ethnicities, birth of a previous macrosomic child, GDM in the previous pregnancy, and polycystic ovarian syndrome are risk factors for GDM. These factors enhance pregnant women's risk of GDM.⁷ The most clearly entrenched non-modifiable risk factor for GDM is ethnicity. Recent data indicate that over the past 20 years, the prevalence rate of GDM has increased by 10-100% among various ethnic groups. Women of particular ethnicities have long been

thought of as having a higher chance of developing GDM. Women from the Middle East, Pacific Islands, and Australian Aboriginal women are among these at-risk ethnic groups. As per various studies, immigrants to western countries experience more GDM than first-generation members of the same ethnic group. Similar to the American, Hispanic, Asian, and African-American women are more susceptible to GDM than non-Hispanic white women. Asian women in Europe are more likely than European women to develop GDM. Although, GDM prevalence among Asian races varies considerably.⁸

Lin et al. revealed in their findings that the comparison between the groups with GDM and those with normal glucose levels revealed that significant risk variables for GDM were advanced age, poorer levels of education, a family history of diabetes, and higher pre pregnancy body mass index.⁹ Results of a retrospective observational study showed that past history of GDM (odds ratio (OR)=10.7; 95% confidence interval (CI): 5.4-21.1), maternal age 40 years (OR 7.0; 95% CI 2.9-17.2), and body mass index 35 kg/m² (OR 6.1; 95% CI 3.0-12.1) were the three biggest independent risk factors for GDM. The three main risk factors for GDM were increasing age, body mass index, and prior GDM.¹⁰ Lee et al. reported in their meta-analysis findings that previous GDM history (OR 8.42, 95% CI 5.35-13.23), macrosomia (OR 4.41, 95% CI 3.09-6.31), and congenital abnormalities (OR 4.25, 95% CI 1.52-11.88) are risk factors for GDM. Body mass index 25 kg/m² (OR 3.27, 95% CI 2.81-3.80); pregnancy-induced hypertension (OR 3.20, 95% CI 2.19-4.68); family history of diabetes (OR 2.77, 2.22-3.47); history of stillbirth (OR 2.39, 95% CI 1.68-3.40); polycystic ovary syndrome (OR 2.33, 95% CI 1.72-3.17); history of abortion (OR 2.25, 95% CI) were all the significant risk factors of GDM.¹¹

Screening for GDM

To identify the women who are at risk for having GDM and consequently lower or eliminate the risk of adverse outcomes for both mother and child associated with GDM, screening and diagnostic testing for GDM is crucial. Most nations use criteria like previous GDM, previous large-for-gestational-age births, diabetes in first-degree relatives, pre-pregnancy adiposity, belonging to a specific ethnic group associated with a high prevalence of GDM, glucosuria and high maternal age when conducting selective screenings. There is chance that cases of GDM will be missed while utilizing selective screening. Selective screening, on other hand, might assist in focusing medical resources on patients who have greatest risk of problems. Additionally, it is recommended to assess fasting glucose early in pregnancy to check for pre-existing diabetes due to increased prevalence of type 2 diabetes in younger age groups.¹²

As per the established guidelines at 24-28 weeks of pregnancy, it is currently advised that all asymptomatic women should be examined. A 75 g, 2-hour oral glucose

tolerance test is advised for screening all females. In the most current literature, there is mounting evidence that all women in the high-risk population should have GDM screening at 24-28 gestational weeks, followed by conclusive testing. It seems sense that the screening and diagnosis of GDM should be done simultaneously using a 75 g oral glucose tolerance test, and this would be the optimum course of action. Most experts agree that monitoring plasma glucose can help high-risk groups identify pregestational diabetes early on, before 20 weeks of pregnancy. Author further stated that there are no randomized controlled trials investigating at how various screening techniques affect health outcomes. The novel screening techniques were only briefly examined in a few research studies. However, the cost-effectiveness of universal GDM screening has been established.¹³

Findings of a retrospective study showed that early screening subjects had higher odds of having hypertension, GDM in a past pregnancy, a greater body mass index, and a higher fasting glucose level. Similarly, caesarean delivery, preeclampsia, large for gestational age, small for gestational age, and macrosomia incidences were seen in early and routine screening groups. Preterm birth rates were greater in the early screening group of subjects. Authors further concluded that early screening for women who satisfied the requirements did not appear to be beneficial which may be due to the retrospective nature of the study hence prospective studies must be conducted to assess the value of early GDM screening.¹⁴ Results of a meta-analysis revealed that there was no difference in risk of large for gestational age at birth between normal care and early detection and treatment of GDM. Risk of large for gestational age reduced in trials with procedure that involved universal screening of participants at their initial prenatal visit and prompt treatment in event that screening test was positive. Overall, risk of large for gestational age at birth not decreased by early detection and treatment of GDM. However, compared to standard care, trials that checked all participants at their initial visit and treated them promptly the majority for a HbA1c of 5.7-6.4% had lower risk of large for gestational age at delivery, indicating a potential advantage of screening all pregnant women.¹⁵

Hillier et al. reported in their findings that 2,672 of the 40,206 patients who underwent GDM screenings developed the disease. Following the intervention, the multivariate adjusted risk for large for gestational age and caesarean birth was generally decreased. Patients with GDM were more likely to experience this difference, and post-intervention insulin/oral hypoglycaemic therapy rates for GDM were also greater than pre-intervention rates. For the other primary outcomes, there were no variations. Only 20% of patients with early GDM diagnoses who underwent postpartum testing had outcomes in the overt diabetes range, indicating a range of diabetes identified in the fetus. Authors further suggested that obese pregnant women should be screened for GDM in the first trimester to enhance GDM-related

outcomes.¹⁶ Benhalima et al reported that there is a significant variation between the various healthcare centers regarding the method of screening for pregestational diabetes in early pregnancy and screening for GDM despite of the fact that most respondents thought it was beneficial to screen for GDM. The different recommendations made by both worldwide and local scientific professional organizations likely have a role in this wide diversity in practices. In order to find the most cost-effective screening method for GDM as well as the most suitable screening method for pregestational diabetes in early pregnancy, more study is required.¹⁷ Hiéronimus and Meaux suggested in their study that limiting false positive rates and focusing medical resources are two benefits of selective screening. However, screening could be more challenging and result in missing up to 45% of GDM patients. Although universal screening increases sensitivity, it also results in more treatment interventions, the benefits of which and their cost-to-benefit ratio in low-risk women must be calculated. Only for women with GDM risk factors have the advantages of GDM screening and treatment been demonstrated. Their applicability to women without risk factors is still debatable.¹⁸

Given the lack of reliable information regarding the advantages and disadvantages of screening and managing GDM in the first trimester of pregnancy, many specialists do not even suggest GDM screening at all. Early testing would primarily seek to identify women who were at low or high risk for developing GDM. The requirement for universal screening and diagnosis after 24 weeks would be lessened by this risk classification, which would also lessen workload and expense. To effectively mitigate the negative short-term and long-term effects of extended intrauterine exposure to hyperglycaemia, the second objective would be to identify women who already have GDM and to begin treatment as soon as possible. Even before the diagnosis of GDM at 24 weeks of gestation, maternal hyperglycaemia appears to accelerate fetal growth. Recent research points to a long-term risk for cardiovascular disease and type 2 diabetes in the offspring. DNA methylation involved in energy metabolism and anti-inflammatory activities appears to be influenced by GDM. Future research is necessary to clarify whether later intervention during pregnancy can change this metabolic programming. Theoretically, by now, after GDM screening in the first trimester, early intervention would be advantageous for women who would be most at risk for unfavourable pregnancies and long-term consequences.¹⁹ Present studies discussing the advantages of screening for pregestational and GDM are quite limited and depict conflicting findings therefore, future research assessing the impact and effectiveness of various screening strategies is need of time.

CONCLUSION

GDM is a prevalent complication of pregnancy with known risk factors and associated with significant

maternal and neonatal complications. Screening for GDM can aid in early diagnosis and prevention of more serious complications however further research focusing on effectiveness of screening for GDM at various stages of pregnancy is essential.

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