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## GESTATIONAL DIABETES AND ITS MATERNAL AND NEONATAL COMPLICATIONS: A REVIEW ARTICLE

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### Abstract

Gestational diabetes is the most common metabolic disorder during pregnancy. Gestational diabetes refers to the conditions in which the increase of blood glucose level is diagnosed for the first time during pregnancy. Gestational diabetes occurs almost in 4% of pregnancies. This study aims to investigate different aspects of gestational diabetes and its complications on the fetus and mother. Given the serious complications of diabetes on the mother and particularly the fetus, this study is necessary to reduce the potential risks of gestational diabetes by identifying gestational diabetes and the methods to avoid and treat it. According to the research objective, this study is a review article and an applied research in terms of methodology which tries to identify and treat gestational diabetes and its complications on the mother and fetus reviewing the previous studies. According to the study results, since some cases of gestational diabetes might have not been in fact diagnosed as type II diabetes, the women with a previous history of gestational diabetes should be screened for diabetes during the weeks 6-12 after the delivery using the oral glucose tolerance test (OGTT) criteria in non-pregnant women. Women with a history of gestational diabetes are at increased risk of future diabetes and should be screened for diabetes or pre-diabetes in the future using the criteria specified for the diagnosis of diabetes in asymptomatic patients.

**Keywords:** Diabetes, gestational diabetes, fetal diabetes.

### Introduction

Gestational diabetes is the most common metabolic disorder during pregnancy with prevalence between 0.15% and 17.7% (1, 2). Its prevalence is reported to be between 1% and 3% in America, an average of 10.9% in Asian countries and 5.2% in Europe (3-5). On the other hand, the prevalence of diabetes in different parts of the world is between 1%

and 6% out of which 15% to 25% are insulin-dependent and 75% to 85% are non-insulin-dependent (6-8). The total prevalence of diabetes in Iran also appears to be 3 to 4 percent out of which more than 7 to 8 percent are insulin-dependent and the prevalence of glucose tolerance test is the same amount and can turn into overt diabetes under physiological conditions such as pregnancy or illness (9, 10). Diabetes can affect the fetus growth during pregnancy. In early pregnancy, maternal diabetes can lead to congenital defects and the increased risk of miscarriage. Most congenital defects have adverse effects on major organs of the body such as the brain and heart (2, 11-13). During the second and third trimester of pregnancy, maternal diabetes can lead to overfeeding and excessive growth of the infant. A large overweight infant increases the risk of painful and difficult deliveries. For example, large overweight infants often need a caesarean section for delivery and they will be at risk of shoulder injury if naturally delivered(14). The infant overweight also leads to delays in delivery time and the risk of infant brain hypoxia. In addition, when the fetus is overfed and blood insulin levels rise accordingly, there will be a risk of sharp drop in the infant blood sugar after the delivery(15). That is because the infant will no longer receive high levels of blood sugar from the mother's blood. According to the above complications, the best measure is to prevent from gestational diabetes. However, if for any reason severe gestational diabetes occurs, a healthy baby could be delivered with a proper treatment, despite the diabetes (16, 17).

### **GDM Diagnosis**

GDM in high or medium risk women can be diagnosed at one or two stages. Plasma glucose is measured an hour after taking 50 grams of glucose in a two-step method regardless of the hours of the day or the last meal. If blood sugar exceeds 140 milligrams per deciliter by an hour after the intake, 50 g (GCT) of glucose will be followed by 100 grams Oral glucose tolerance test (OGTT)(18, 19).

### **Materials and methods**

For this research, English and Farsi-language articles published in the field of gestational diabetes were searched through databases of Google Scholar, PubMed, sid, Magiran and Science Direct. In this search which was limited to the studies from 2000 to 2014, the keywords of gestational diabetes, prevalence, prevalence of gestational diabetes, maternal and neonatal complications and a combination of them were used. As a result of this search, nearly two thousand articles were found through the mentioned databases. According to the titles and abstracts of the articles and the inclusion and exclusion criteria, and after excluding the repeated and irrelevant articles, nearly 35 articles were selected to read their full text. All selected articles were case-control type except one case which was review type.

## Review

### Gestational Diabetes

For every patient with urinary excretion of glucose, positive family history of diabetes mellitus, suspicious history of stillbirth or abortion, family history of fetal diabetes or previous congenital abnormality, and gestational diabetes must be considered. In addition, in the patients previously diagnosed with diabetes, pregnancy may cause changes; for example, it may accelerate retinopathy. The main complications of gestational diabetes include the risk of pre-eclampsia and eclampsia, birth canal injuries caused by the large fetus, polyhydramnios and a higher incidence of bacterial infections. Fetal complications include huge fetus, low blood glucose, low blood calcium and embryonic jaundice, if untreated, as well as the increased risk of major malformations in infants and the increased prevalence of maternal mortality(20, 21). Given that gestational diabetes is asymptomatic and thereby without complaint, it is more important to diagnose the patients. Gestational diabetes occurs in 2 to 5 percent of cases and it gets more likely with increase of mothers' age during pregnancy. A third of the mothers suffering from gestational diabetes will later develop type II diabetes (22). Another opinion in relation to gestational diabetes is that more than half of women with this disease will finally develop overt diabetes and after 5 to 10 years, their disease progresses towards type I or type II diabetes with a higher prevalence(23).

### Etiology and pathogenesis:

Glucose response to insulin and the food eaten in patients is less than ordinary people. Insulin resistance in pregnant women is 3 times as much as non-pregnant ones. This increased resistance is caused by the events affected by pregnancy hormones and free cortisol and is usually seen in muscle tissues(24) .

### Gestational diabetes mellitus

Gestational diabetes mellitus or GDM is a common complication during pregnancy. Gestational Diabetes Mellitus means any non-permitted levels of blood glucose occurring during pregnancy or recognized for the first time during pregnancy. Gestational diabetes mellitus increases the risk for mother and fetus. Some of these risks will remain with the mother and her child even to the end of life. The complications threatening the mother include preeclampsia; crises of increased blood glucose, urinary tract infection which may cause hydronephrosis, the need to perform a caesarean section, pregnancy caused illness, the surgery increasing the risk of developing overt diabetes in the patient, the risk of cardiovascular diseases such as hypertension and hyperlipidemia (25, 26). In the mothers with gestational diabetes mellitus, there will be 50% risk of type II diabetes by 20 years after the diagnosis of gestational diabetes mellitus. High blood sugar in mother carries more sugar to the baby leading to the increased insulin in the fetus blood and

eventually overgrowth of fetus. Numerous dangers in this disease indicate the degree of importance to identify and classify it by appropriate laboratory tests and diagnostic and therapeutic interventions to control gestational blood sugar and ultimately achieve the desirable level of blood sugar (27, 28).

### **Epidemiology and pathology:**

Gestational diabetes mellitus is one of the most common metabolic complications of pregnancy. Gestational Diabetes Mellitus occurs in 14% of pregnancies which is approximately 200 thousand cases per year in the United States. As there has been an increase in Type II diabetes in recent decades, more prevalence has been also reported for gestational diabetes mellitus. The prevalence of gestational diabetes mellitus has doubled between 1994 and 2002 . GDM occurs when the insulin secretion in the mother's body is not as required during pregnancy. The reasons for the proper functioning of pancreatic  $\beta$ -cell along with decreased insulin secretion in GDM are divided into the three following groups:

1. Autoimmune
2. Monogenic
3. The subject's insulin resistance(14)

### **Identification and diagnosis:**

Statement by ADA (America Diabetes Association) in 2004 suggests some standards for review and diagnosis of GDM which are in fact standards of medical care in diabetes-2009. Given the risks GDM creates for the health of mother and fetus, GDM risk should be examined and estimated during the first examinations of pregnancy and before child birth. GDM risks are divided into three categories of very high risk, high or medium risk and low risk. Medium-risk women are those who do not have low risk criteria including high risk women with no GDM signs in their early examinations and reviews (11) .

### **The impact of diabetes on pregnancy**

Today, most women with gestational diabetes give birth to healthy children. The doctor monitors the patient and keeps blood glucose at normal range using diet, exercise and, if necessary, insulin injections. However, diabetes can have serious complications for both mother and child if not properly controlled. In most pregnant women, the most important concern is that their high blood sugar causes high blood sugar levels in their fetus. As a result, the fetus pancreases should secrete more insulin to burn excess glucose. All these events cause the body to produce more fat and lead to fetal overweight, especially in upper body. Because of these risks, caesarean may be recommended if the doctor is suspected of large fetus. Fortunately, if gestational diabetes is controlled, only a small percentage of fetuses

get too large. In these infants, the risk of neonatal jaundice, polycythemia (high red blood cell count) and hypocalcaemia (low blood calcium) are also higher. Gestational diabetes may also affect fetal heart function if not well controlled. Some studies showed that there is a relationship between severe gestational diabetes and the increased risk of stillbirth in the last two months of pregnancy and that gestational diabetes finally doubles the risk of pre-eclampsia (29-32).

### **Fetal monitoring to avoid complications of gestational diabetes**

The doctor may monitor the fetus more closely in the last two or three months of pregnancy according to the severity of illness and whether the mother has other pregnancy related problems or not. The doctor will teach the mother how to count the number of fetal movements in the third trimester of pregnancy and inform the doctor of any decrease in fetal mobility immediately. If blood sugar is not controlled or it is so high that there is a need for insulin or there are other problems, there may be a need to control the fetal heart (non-stress test) or periodic ultrasound about the week 32 (this type of ultrasound is called “biophysical profile”. If the blood sugar limit is controlled without any need for insulin injection and the patient has no other problem, there may be no need for these tests until the last several weeks of pregnancy or at delivery time(33, 34).

### **The effect of gestational diabetes on the fetus:**

The fetus in a mother with gestational diabetes is in an environment quite different from a healthy woman's fetus. Glucose, alanine and free fatty acids are transmitted to the fetus through large amounts of maternal blood circulation (35). As a result, amniotic fluid insulin concentration increases, indicating compensatory response of the fetus to the increase of these materials. Overt hyperglycemia in the first trimester of pregnancy increases the risk of congenital malformations and perinatal mortality. The side effects of gestational diabetes on the fetus include:

The increased risk of macrosomia which leads to complications such as shoulder dystocia and brachial plexus injury: all organs of the fetus except for the brain will develop macrosomia (36). Macrosomia in these infants is closely related with the neonatal hyperinsulinism caused by maternal hyperglycemia. Neonatal hyperglycemia: a sharp drop in plasma glucose concentration after the delivery is among the characteristics of infants of mothers with  $\beta$  diabetes(37). This event is attributed to the embryonic pancreatic cell hyperplasia caused by chronic maternal hyperglycemia. Hyperinsulinism in turn overstimulates the somatic growth. Meanwhile, neonatal hyperinsulinism may cause hypoglycemia in the first few minutes after birth. The incidence of this event is highly variable and depends on the threshold determined to diagnose neonatal hypoglycemia(38). Hyperbilirubinemia: pathogenesis of hyperbilirubinemia in the infants of diabetic mothers is not clear. However, prematurity, polycythemia and hemolysis

are reported to be involved in this issue. Heart hypertrophy: these infants may suffer from hypertrophic cardiomyopathy, which is rarely progressed to congestive heart failure (CHF) (39). The mentioned infants are particularly macrosomic and hyperinsulinism is known to be involved in pathogenesis. Obesity: these infants are at increased risk of obesity, impaired glucose tolerance and diabetes in late adolescence and early youth (17).

## **Treatment**

Usually, if standard nutritional therapy fails to continually keep fasting plasma glucose under 105 or blood glucose two hours after a meal under 140, insulin therapy is recommended. American Diabetes Association recommends insulin therapy when nutritional therapy fails to keep fasting blood sugar at level of 105 milligrams per deciliter or less (40).

**Medical nutrition therapy (MNT):** nutritional consultation is an important point in the care and treatment of these patients. The purpose of such treatment is to supply food for the mother and the embryos, control glucose levels and prevent from Keto-acidosis resulted from food deprivation (fasting). The diet of a pregnant woman who weighs 80 to 120% of normal weight; like a non-diabetic pregnant women, is 30 kcal per kg of body weight in 24 hours, and 40 to 50 percent of calories should be supplied from carbohydrates, and more than 12% of calories should be supplied from 40% of calories with saturated fat and 20 proteins (41).

**Exercise:** a proper exercise in patients with gestational diabetes is recommended. Researchers have shown that an exercise improving cardiovascular performance controls blood sugar more than no-exercise die (12).

**Insulin:** insulin is a pharmacological treatment which, added to nutrition therapy, is most effective in reducing fetal mortality. Insulin therapy can be based on glycemic control with or without fetal growth assessment. American Diabetes Association recommends insulin therapy when nutrition therapy fails to keep plasma glucose levels less than 105 mg per deciliter or less than 155 mg per deciliter an hour after a meal or less than 130 mg per deciliter two hours after a meal. In very obese women, to overcome pregnancy caused insulin resistance and 1/5-2 U/Kg obesity, the initial dose of insulin should be increased (40).

**Oral hypoglycemic drugs:** oral glucose-lowering agents are not recommended for gestational diabetes treatment. However, a randomized clinical study on pregnant women with gestational diabetes who could not reach target glucose level through diet has compared the use of insulin and Glyburide. However, the use of Glyburide during pregnancy is not approved by FDA and further studies are required to prove its suitability during pregnancy (40, 42-45).

**Conclusion :** GDM diagnosis during pregnancy is required for the health of mother and fetus. However, the progress in medical and midwifery care has improved the pregnancy complications. However, in general, both mother and fetus remain at risk of some complications. The studies have shown that most of these complications occur as a result of hyperglycemia. Thus, the best treatment method to prevent from complications is to keep blood sugar at normal level. In addition, women with a history of GDM should be encouraged to use preventive behaviors such as increase of physical activity, use of a suitable diet and maintaining normal weight. Since some cases of gestational diabetes might have not been in fact diagnosed as type II diabetes, the women with a previous history of gestational diabetes should be screened for diabetes during the weeks 6-12 after the delivery using the oral glucose tolerance test (OGTT) criteria in non-pregnant women. Women with a history of gestational diabetes are at increased risk of future diabetes and should be screened for diabetes or pre-diabetes in the future using the criteria specified for the diagnosis of diabetes in asymptomatic patients.

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