

The Correlation Between Maternal Diabetes and Birth Defects

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Abstract

Diabetes mellitus is one of the most common health problems in the United States, and it is shown to have negative outcomes in infants born to women who are diabetic. Although gestational diabetes mellitus is linked with a few birth defects, research has shown that women with pre-gestational diabetes mellitus have an increased risk of giving birth to infants with birth defects. Among all the defects studied, cardiac and neural tube defects occur most commonly. Appropriate measures should be taken to provide patient teaching, as well as appropriate and effective prenatal care, to women who are at the highest risk for having pre-gestational diabetes mellitus in order to decrease the risk of associated birth defects.

The Correlation Between Maternal Diabetes and Birth Defects

Diabetes Overview

Diabetes is one of the most prevalent health conditions in America, and not only does it negatively affect the person who has diabetes, it is very harmful to infants born to mothers who have diabetes (“Gestational Diabetes”, 2011). When discussing diabetes and pregnancy, it is important to be able to distinguish between the different types of diabetes mellitus (DM). Pre-gestational diabetes mellitus (PGDM) is the term used for women who were diagnosed with diabetes before they ever became pregnant. There are two types of pre-gestational diabetes mellitus: type I and type II. Type I diabetes occurs in people who have a pancreas that does not produce insulin, whereas type II diabetes occurs when a person’s body does not use insulin properly and is therefore insulin resistant.

Gestational diabetes mellitus (GDM) is the term used for a woman who did not have diabetes before becoming pregnant, but who became diabetic at some point during pregnancy. No matter which type of diabetes the mother has during pregnancy, there are consequences to both the mother’s health as well as the baby’s (Michel, 2011).

There are many factors that are used to predict if a pregnant woman will likely become diabetic in the future. These include an early diagnosis of gestational diabetes mellitus in pregnancy, the necessity for insulin therapy during pregnancy, elevated blood sugar levels at the time of the diagnosis, preterm delivery, macrosomic infants, and having an abnormal oral glucose tolerance test two months after delivery. Gestational diabetes mellitus has been reported to have a strong connection with an increased risk of maternal morbidities as well as very serious perinatal morbidities and mortality (Khan, Ali, & Khan, 2013). There are negative consequences to both the mother’s health as well

as the baby's regardless of the type of diabetes the mother has during pregnancy. Because of this, it is imperative to understand the pathophysiology of the different types of diabetes in order to completely comprehend the effect that this health condition has on a developing fetus (Michel, 2011).

Different Types of Diabetes

Diabetes Mellitus Type I

Diabetes mellitus type I (DMI) is an autoimmune disorder characterized by the destruction of the beta cells in the pancreas and accounts for approximately 5-10% of all people with diabetes. In type I diabetes, the body attacks its own T cells and destroys pancreatic beta cells, which are in charge of secreting insulin, at various rates (Michel, 2011). In this type of diabetes, the rate of the destruction of the beta cells differs, being very fast in some individuals and slower in others (Güven, Matfin, & Kuenzi, 2009). In type I diabetes, the main characteristics are a complete absence of insulin, elevated blood glucose, and the breakdown of proteins and fats in the body. Because people with type I diabetes have a total lack of insulin, they are susceptible to developing ketoacidosis, which, if not treated properly and quickly, can be a life-threatening condition. One of the main actions of insulin is to prevent lipolysis, otherwise known as fat breakdown, and to release free fatty acids from fat cells. When there is no insulin produced, as in patients with type I diabetes, fatty acids are released from fat cells and the liver converts them into ketones, causing ketosis to occur. Because there is no insulin created by the body, it is necessary for all people with type I diabetes to use outside sources of insulin replacement to reverse the catabolic state, control their glucose levels, and to prevent

ketoacidosis (Güven et al., 2009). Survival of people with type I diabetes is dependent on this exogenous source of insulin (Michel, 2011).

Type I diabetes mellitus is an autoimmune disorder, and although not much is known about the cause, it is thought that a genetic predisposition leads to the incidence of this condition in some people (Michel, 2011). Additionally, according to Van Belle, Coppieters, and Herrath (2011), type I diabetes, “Precipitates in genetically susceptible individuals, very likely as a result of an environmental trigger. Current genetic data point towards the following genes as susceptibility genes: HLA, insulin, PTPN22, IL2Ra, and CTLA4” (pp. 79).

Diabetes Mellitus Type II

Diabetes mellitus type II accounts for 90-95% of all cases of diabetes. A heterogeneous condition in which there is insulin deficiency combined with high blood sugar, type II diabetes gradually impairs the beta cells over time (Güven et al., 2009). In type II diabetes, the pancreas usually produces some self-made insulin, however, the insulin produced is either inadequate to meet the needs of the body or is not used well by the tissues (Michel, 2011).

There are a few major abnormalities that have an active role in the development of type II diabetes. The first factor is insulin resistance, which is when the pancreas produces insulin but the body does not use it effectively and the tissues do not respond to the action of insulin when trying to metabolize glucose and lipids (Güven et al., 2009; Michel, 2011). The cause of this is either the unresponsive state of the insulin receptors to the action of insulin, or the insufficiency in the number of receptors. Because most insulin receptors are located on liver, muscle, and fat cells, when the insulin is not used

correctly the glucose is hindered when trying to enter the cells, which results in hyperglycemia. Michel (2011) explained, “In the early stages of insulin resistance, the pancreas responds to high blood glucose by producing greater amounts of insulin. This creates a temporary state of hyperinsulinemia that coexists with the hyperglycemia” (p. 1222). According to Guven et al. (2009), the metabolic irregularities that cause type II diabetes, in addition to the body’s resistance to insulin, includes an unbalanced secretion of insulin from the beta cells in the pancreas and an increase in the production of glucose by the liver. People with type II diabetes can have levels of insulin that range from high, to normal, to low, all depending on a number of factors.

Another factor that contributes to the development of type II diabetes is a substantial decrease in the ability of the pancreas to create insulin due to the beta cells becoming worn-out from the compensatory overproduction of insulin (Michel, 2011). Insulin resistance causes an increase in insulin secretion, also known as hyperinsulinemia, and occurs as the beta cells work to keep a normal level of glucose in the blood. Over time, this increased need for insulin secretion causes the beta cells to become exhausted and fail, which results in elevated glucose levels after meals and an eventual increase in production of glucose by the liver (Guven et al., 2009). It is not known why the beta cells cannot adapt; however it may be linked to the negative effects of long-term hyperglycemia or a high circulating volume of free fatty acids.

Additionally, a third factor in the development of type II diabetes mellitus is the inappropriate production of glucose by the liver. The liver does not accurately control the release of glucose in response to blood levels, and instead does so in a disorganized way that does not match the needs of the body at that time. Type II diabetes is usually a

disease with a gradual onset in which a person may go for years with hyperglycemia that is undiagnosed, and many people are only diagnosed due to the findings on routine laboratory testing (Michel, 2011).

According to the International Diabetes Federation (2014), risk factors for type II diabetes include family history of diabetes, obesity, physical inactivity, high blood pressure, impaired glucose tolerance, and increased age. A number of factors can be linked with the incidence of type II diabetes, but among them, obesity and physical inactivity are most strongly associated with the development of this disease (Guyen et al., 2009).

Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) refers to any degree of glucose intolerance that is discovered during pregnancy (Guyen et al., 2009). Gestational diabetes mellitus occurs in about 7% of pregnancies in the United States and usually affects women who are obese or women with a family history of diabetes (Michel, 2011). This type of diabetes occurs due to the development of the placenta and the role it has in impairing insulin in the mother's blood stream during pregnancy. As the baby grows, the placenta introduces increased amounts of insulin-blocking hormones, thus raising the mother's blood sugar and causing the mother to have diabetes during her pregnancy (Michel, 2011). Usually, women with GDM do not have noticeable signs or symptoms; however, on occasion, they may have polydipsia, which is excessive thirst, or polyuria, which is increased urination ("Gestational Diabetes", 2011). Because gestational diabetes mellitus is considered a disorder of carbohydrate metabolism, the main focus for controlling and

directing treatment in the pregnant population focuses on controlling the amount of glucose in the blood (Khan et al., 2013).

Risk factors. Any woman can develop gestational diabetes, but there are certain risk factors that increase a woman's chance of developing GDM. These risk factors include women of advanced maternal age, women with a previous history of gestational diabetes mellitus, women with a family history of diabetes, women who are obese, women with recurrent urinary tract infections (UTIs), women who had infertility treatments, women who had an unexplained neonatal death, women who had a macrosomic baby, women who had pre-eclampsia, and women who are of African American, Hispanic, American Indian, or Asian descent (Khan et al., 2013; Michel, 2011). Although the effects of poorly controlled gestational diabetes mellitus are well known, there has not been any official agreement among professionals on the diagnostic criteria for gestational diabetes (Khan et al., 2013).

Associated birth complications. Although gestational diabetes mellitus is linked with fewer birth defects than pre-gestational diabetes, it still has the propensity to harm the fetus (Lale, Yu, & Ahmed, 2011). During a pregnancy in which the mother has gestational diabetes mellitus, the fetus is exposed to an increased amount of glucose, which results in the fetus having excess growth, a larger birth weight, impaired secretion of insulin, and a decreased sensitivity to insulin. Additionally, some of the negative neonatal outcomes such as stillbirth, jaundice, and birth trauma are more common in infants born to women with gestational diabetes as compared to infants born to healthy pregnant women (Khan et al., 2013). Some of the short-term complications of an infant who has an excess birth weight are shoulder dystocia and infant hypoglycemia (Khan et

al., 2013). Increased maternal glucose levels in pregnancy can cross the placenta and cause hyperinsulinemia in the fetus. This increase in insulin can lead to macrosomia, which is defined as an infant with a birth weight of more than 8 pounds, 13 ounces (“Fetal Macrosomia”, 2012). This increases the chance of a traumatic delivery because the risk of shoulder dystocia is greatly increased in macrosomic infants (Almarzouki, 2012). The fetal metabolism is altered, also, which can cause an impaired tolerance to glucose during youth and adolescence (Khan et al., 2013).

Maternal complications of GDM. Mothers who had gestational diabetes mellitus had a very large increase in the occurrence of hypertensive disorders, including pregnancy induced hypertension, delivery by cesarean section, large for gestational weight babies, macrosomia, antepartum hemorrhage, premature rupture of membranes, preterm labors, deliveries requiring help using instruments, pre-eclampsia, and neonatal intensive care unit (NICU) admissions compared to mothers without diabetes (Almarzouki, 2012; Khan et al., 2013). Because of the fetal complications, such as shoulder dystocia and elevated fetal weight, associated with gestational diabetes mellitus, cesarean delivery is used as an intervention to prevent complications (Khan et al., 2013). The more the weight of the baby increases above the normal range, the higher the risk of delivering via a cesarean section. One study found that women who had gestational diabetes mellitus and were treated appropriately had a decreased rate of giving birth to macrosomic babies, while women who had untreated gestational diabetes mellitus had two times the chance of delivering by a cesarean section (Khan et al., 2013).

Treatment of GDM. Complications experienced by both the mother and the fetus related to gestational diabetes can be reduced by dietary therapy and lifestyle advice

during pregnancy. Common treatment for gestational diabetes mellitus is nutritional therapy (Khan et al., 2013). Women with GDM should receive very thorough teaching detailing the necessary nutrients for optimum health of both the mother and fetus (Güven et al., 2009). According to Güven et al. (2009), the nutrition plan should focus on the proper nutrients and should result in normal glucose levels and proper weight gain. For women with GDM, it is necessary to monitor blood glucose levels throughout pregnancy. Additionally, gestational diabetes can be controlled by oral hypoglycemic medications or insulin, which both prove useful in avoiding negative fetal outcomes (Khan et al., 2013). Therefore, if nutritional therapy does not work in controlling the mother's glucose level, medication therapy is usually then initiated (Michel, 2011).

Statistics

The statistics of birth defects in children born to diabetic mothers is staggering. Of all the pregnancies, about 1-10% of them have glucose that is not regulated properly. Gestational diabetes mellitus affects 90% of diabetes mellitus cases during pregnancy, and about 7% of the population is diagnosed with some type of diabetes each year. Additionally, about six million people are reported to have type II diabetes mellitus that is not diagnosed (Khan et al., 2013). Women who are diagnosed as diabetic before they become pregnant are three to four times more likely to deliver a baby with birth defects than a non-diabetic woman is (Currie, 2008). Presently, diabetes type II affects 8% of cases of diabetes mellitus in pregnancy while type I diabetes mellitus makes up about 1% of all pregnancies (Khan et al., 2013).

Birth Defects

Diabetes is the most common chronic medical condition in the pregnant population (Dunne, Brydon, Smith, & Gee, 2003). Data from The National Birth Defects Prevention Study (NBDPS) analyzed the links of pre-gestational diabetes mellitus and gestational diabetes mellitus, noting a risk for a larger range of birth defect categories than has ever been studied before. Of these, neural tube defects (NTDs) and cardiac defects occurred most commonly. Birth defects occur in every 1 out of 33 babies born in the United States, and they are also the leading cause of fetal deaths in America (Correa et al., 2008). Correa et al. (2008) notes that the mechanisms that cause the link between diabetes mellitus and birth defects are not well understood, but it is widely supported that maternal hyperglycemia has a critical role in this. Correa et al. (2008) stated, "There is a positive correlation between hyperglycemia during embryogenesis and a risk for congenital malformations among infants of diabetic mothers" (p.237.e1). Research has shown that pre-gestational diabetes mellitus is an identified risk factor for cardiovascular, central nervous, and musculoskeletal system defects (Correa et al., 2008). Women with preexisting diabetes mellitus are six times more likely to have a baby with a congenital heart defect than women without diabetes mellitus (Oakley, 2012). More research is required regarding the effects of maternal diabetes mellitus on other organ systems such as the genitourinary and gastrointestinal systems because the link is still not well understood. The study concluded that the frequency of birth defects occurring in children born to diabetic women, who had good control of their blood sugar, was similar to that of the general population (Correa et al., 2008).

There were many associations noted between pre-gestational diabetes mellitus and isolated cases of seven non-cardiac defects, including hydrocephaly, anotia/microtia, anencephaly and craniorachischisis, cleft lip with or without cleft palate, bilateral renal agenesis/hypoplasia, anorectal atresia, and longitudinal limb deficiencies (Correa et al., 2008). In addition, of the 16 possible cardiac defects, 11 of them were positively associated with pre-gestational diabetes mellitus. These defects include tetralogy of Fallot, dextro-transposition of the great arteries, atrial ventricular septal defect (VSD), total anomalous pulmonary venous return, aortic stenosis, left ventricular outflow tract obstruction associations, right ventricular outflow tract obstruction associations, perimembranous VSD, atrial septal defect (ASD) secundum, ASD not otherwise specified, and VSD with ASD. Pre-gestational diabetes mellitus was linked with about 50% of all the categories of birth defects that were studied, which included 7 out of 23 isolated non-cardiac defects as well as 11 of 16 isolated cardiac defects (Correa et al., 2008). Researchers found that risk factors such as having a first-degree family member with a history of a cardiac heart defect and a woman who had multiple pregnancies were both strongly correlated with the risk for having a child with a cardiac heart defect (Gilboa et al., 2010).

In regards to defects caused by gestational diabetes mellitus, there were three non-cardiac defects that showed a correlation with this type of diabetes. These were cleft palate, anorectal atresia, and cleft lip with or without cleft palate. Furthermore, many of the cardiac defects that were linked with pre-gestational diabetes mellitus were not linked to gestational diabetes mellitus. In fact, only three cardiac defects including tetralogy of Fallot, ASD secundum, and pulmonary valve stenosis were shown to correlate with

gestational diabetes mellitus. The researchers found that 3 of 23 isolated non-cardiac defects, 3 of 23 multiple non-cardiac defects, and 2 of 16 multiple cardiac defects were also linked with gestational diabetes (Correa et al., 2008).

In one specific study, researchers found that women with type I diabetes mellitus who received intensive management had a decrease in congenital anomalies and miscarriages. In a study done by Dunne et al. (2003), information on 182 women who had type II diabetes during their pregnancies was analyzed. The duration of their diabetes ranged from under one year to 19 years, with an average of four years. Of the 182 women studied, 12 of them were treated with diet therapy alone during their pregnancies while the remaining women received insulin therapy to control their diabetes during their pregnancies. There were 26 unfavorable outcomes that occurred out of the 182 pregnancies, which included 16 miscarriages, two stillbirths, three terminations, two early neonate deaths, one late neonate death, and two postnatal deaths. Out of these pregnancies, 33% of women had normal control of their blood sugar levels, 38% of the women had average control, and 29% had poor control of their glucose levels. According to Dunne et al. (2003), most of the negative outcomes happened in those pregnancies with moderate and poor glucose regulation. Congenital abnormalities happened in 18 of the pregnancies, and most of these occurred in the pregnancies where the glucose was poorly controlled. Additionally, of the congenital abnormalities, eight were cardiovascular (Dunne et al., 2003).

Heart Defects

Congenital heart defects, including complete atrioventricular canal defects (CAVC) and non-isolated atrioventricular septal defects, are the leading cause of birth

defect-related death. A higher risk for heart defects is associated with maternal obesity, pregestational diabetes mellitus type I and type II, and gestational diabetes. And, because more than one-third of adult women in the United States are obese or diabetic, the prevalence of these birth defects is rising. Because of the malformations caused to the fetus as a result of maternal diabetes, the frequency of congenital heart defects in newborns of diabetic mothers is reported to be five times greater than that of the overall population (Tabib et al., 2013). The tubular heart of the fetus begins to form during the third week of gestation, beats at 28 days, and atrial division has occurred by the end of the fifth week (Davidson, Ladewig, & London, 2012). Research has found that maternal diabetes changes the expression of certain genes that are involved in the embryonic development. This effect, which directly results from maternal hyperglycemia, is toxic to the embryo and can interrupt normal heart development (Lale et al., 2011). As stated above, heart defects are one of the most common types of birth defects, which occur in around 8.5% of cases, which is about ten times more than its occurrence in the general population. There are certain irregularities that appear to be linked to the glycemic control of the mother before conception and during her pregnancy (Tabib et al., 2013).

The highest cause of infant death is birth defects. Complete atrioventricular canal defects are a type of heart defect that frequently occurs. In their study, the researchers found an increase in the occurrence of non-syndromic CAVC in infants born to women with pregestational diabetes, gestational diabetes mellitus, unmarried status, or obesity (Agopian, Moulik, Gupta-Malhotra, Marengo, & Mitchell, 2012). Associations have been made when looking at the link between pregestational diabetes and isolated and non-isolated atrioventricular septal defects. Agopian et al. (2012) stated, "The association

between pre-gestational diabetes and complex heart defects involving conotruncal septation, cardiac looping or the endocardial cushion points towards an early teratogenic effect on cardiac development (3-8 weeks) by an abnormal metabolic milieu in diabetic mothers” (p. 522). There is an association between CAVC in infants born to unmarried mothers, which may indicate the mothers’ participation in other unknown factors of socioeconomic or behavioral nature. Similarly, other researchers have found a link between unmarried mothers and heart defects in their infants (Agopian et al., 2012).

Neural Tube Defects

Neural tube defects are another type of birth defect associated with maternal diabetes mellitus (Lupo et al., 2012). The neural tube is what develops into the brain and spinal cord, so this type of defect is isolated to those areas. The neural tube begins as a small, flat band that develops into a tube by the end of the first month of gestation. If this tube does not close properly or completely, a neural tube defect occurs (“Neural Tube Defects”, 2014). Neural tube defects are also some of the most common and most deadly congenital abnormalities. Neural tube defects encompass a wide range of abnormalities, such as spina bifida and anencephaly. Two risk factors that have been associated with neural tube defects are pre-gestational diabetes and being obese before becoming pregnant. Even though the mechanism of action linking these risk factors is not perfectly clear, there is evidence that babies who are born to mothers who are obese and babies born to mothers who are diabetics may share some of the same underlying pathogenic exposures, such as a change in glucose homeostasis and hyperglycemia (Lupo et al., 2012). Glucose is controlled by the pancreas and is absolutely essential for oxidative

metabolism. During the early stages of gestation, when organogenesis of the fetus is occurring, there is a very high need for glucose because the embryo is reliant on uninterrupted anaerobic glycolysis before the chorioallantoic placenta starts to form. Research implies that the undeveloped embryo does not have a functional pancreas until beta cells are developed, which takes place after seven weeks of gestation. Therefore, during the time the neural tube is trying to close, which is around the fourth week of gestation, the environment of the uterus will likely be altered if the mother has poorly regulated blood glucose levels, which can then lead to abnormal organogenesis in the infant (Lupo et al., 2012). Because babies born to women with diabetes have a higher chance of developing neural tube defects, the American Diabetes Association backs the recommendation of the United States Public Health Service in the suggestion that all women of child-bearing age take 400 micrograms of folic acid every day, as well as suggesting that women with diabetes mellitus who are expecting to become pregnant increase their folic acid to 600 micrograms a day (Correa et al., 2012).

Obesity as a Risk Factor

One of the greatest risk factors for type II diabetes mellitus is obesity, which is defined as having a body mass index (BMI) of 30 kg/m^2 or more (Martinez-Frias et al., 2005). Correa et al. (2008) found that there is an increased risk of isolated and multiple birth defects if a woman has a body mass index (BMI) greater than or equal to 25 kg/m^2 before she gets pregnant in addition to having gestational diabetes mellitus (Correa et al., 2008). Another study found that gestational diabetes mellitus was associated with a greater risk for some congenital anomalies in babies born to obese mothers, regardless of the mother's age (Martinez-Frias et al., 2005). According to their research findings, the

higher the women's BMI is prior to pregnancy, the higher the risk for congenital defects in their infants. These results suggest that gestational diabetes mellitus in mothers who are overweight and obese have different effects than those of gestational diabetes in normal to underweight mothers. One major difficulty that arises when trying to understand the association between gestational diabetes mellitus and different types of severe congenital malformations is that gestational diabetes is mainly diagnosed during the second trimester of a pregnancy, which is a long time after embryogenesis has occurred. Martinez-Frias et al. (2005) stated, "As most of the related malformations were of blastogenetic origin, the metabolic abnormalities in these women must have been present at the early stages of gestation" (p. 779). Because of this, it is thought that these women might actually have had undiagnosed pre-gestational diabetes, which is what caused the malformations in their infants. The researchers also found that a main predictor of one or more congenital malformation was a high pre-gestational body mass index in the mother.

Obesity is clearly one of the major risk factors in the development of type II diabetes, and it is hypothesized that 30-50% of adults who have type II diabetes are undiagnosed. The results of the study done by Martinez-Frias et al. (2005) show that there is an increased risk of congenital defects in infants born to obese mothers who also have gestational diabetes. They commented that gestational diabetes was linked with congenital malformations only in those infants born to mothers who had a high pre-gestational body mass index. This suggests that in certain populations that have a low occurrence of obesity, gestational diabetes may not be linked with an excess risk of birth defects. Conversely, in groups that have a higher prevalence of obesity, the correlation

between gestational diabetes and congenital defects is very likely (Martinez-Frias et al., 2005).

Obesity during pregnancy has been recognized to be a significant risk factor for development of fetal birth defects (Lupo et al., 2012). In one study, Yazdy, Liu, Mitchell, and Werler (2009) found that women who had the highest dietary glycemic index (DGI) and dietary glycemic load (DGL) were one and a half times more likely to have a baby with a neural tube defect. A dietary glycemic load consists of the amount of carbohydrates and the glycemic index for food, so it is used to measure both the quality and quantity of carbohydrates consumed, whereas a dietary glycemic load only measures the quality of the carbohydrate (Yazdy et al., 2009). The researchers theorized that mothers who consumed a high-glycemic diet in the early stages of their pregnancies would be hyperglycemic and hyperinsulinemic, which would then be spread to the developing fetus and could result in a neural tube defect. The birth defects spanned over several organ systems, and were not confined to one specific body system, but rather, included neural tube defects, gastrointestinal defects, and musculoskeletal defects. There was a high incidence of encephalocele, spina bifida, and gastrointestinal defects in high DGI mothers (Parker, Werler, Shaw, Anderka, & Yazdy, 2012). In one case-control study, Waller et al. (2007) found that women who gave birth to children with spina bifida, cardiac defects, anorectal atresia, hypospadias, limb reduction defects, diaphragmatic hernia, and omphalocele were considerably more likely to be obese. The results from this study imply that there is weak to moderate correlation of maternal obesity with 7 of 16 categories of birth defects (Waller et al., 2007).

Several researchers have studied the correlation of an increased risk for neural tube defects associated with mothers who are obese before they conceive (Watkins, Rasmussen, Honein, & Botto, 2003). However, there have not been very many studies that have looked at the relationship between maternal pre-pregnancy obesity and other birth defects, which is what Watkins et al. (2003) did in their research. It is shown that obesity is associated with complications in pregnancy and negative reproductive outcomes, including an increased risk for birth defects in the infants born to obese mothers. Their study proved that the previously recognized link between spina bifida and pre-pregnancy maternal obesity was valid and additionally found that there is an association for omphalocele, heart defects, and multiple anomalies in infants born to women who are obese. They also discovered a correlation between heart defects and multiple anomalies and mothers who are overweight or obese before conception. Maternal obesity produces a higher risk for certain birth defects, which is another adverse pregnancy outcome associated with maternal obesity. There have been many studies that have looked at the increased risk for abdominal wall defects, specific types of congenital heart defects, and orofacial clefts. However, the results have not been consistent between the different studies. According to Watkins et al. (2003), there are many other defects that they found to occur more frequently in infants born to obese women, which are internal urogenital defects, eye defects, esophageal atresia, Potter sequence, other intestinal defects, and clubfoot. Compared with women who were of average weight, women who were obese were more likely to give birth to an infant with a neural tube defect, spina bifida in particular (Watkins et al., 2003). Additionally, women who were overweight were more likely to have an infant born with a heart defect, mainly left ventricular

outflow tract defects. The more obese the woman, the stronger is the association with infant birth defects.

When considering the link between obesity, pre-gestational diabetes mellitus and birth defects, it is important to understand how these biological factors are all related. The exact mechanism for the association between maternal obesity and birth defects is not well researched or confirmed, but there are several explanations that have been suggested. One explanation could be that obese women have alterations in their metabolisms, such as high blood sugar or increased insulin and estrogen levels, which would also increase their risk for birth defects. Also, hyperinsulinemia has been linked as an independent risk factor for neural tube defects. Another suggested explanation is that obese women are more likely to have diabetes mellitus, which is a well-proven risk factor for fetal birth defects. However, their research did show that the majority of the birth defects related to obese mothers tended to be highest among a certain demographic of women, which consisted of women who were white, smoked, were primigravidas, had fewer years of education, and did not report any occurrence of gestational diabetes (Watkins et al., 2003).

Prevention

Because the correlation between diabetes mellitus during pregnancy and birth defects has been scientifically confirmed, it is necessary to identify the risk factors and focus on prevention of diabetes mellitus. Oakley (2012) stated, “Although the evidence from randomized, controlled trials is sparse, there is strong observational evidence that good glycemic control lowers the risk” (p. 179). If women can have better control of their blood sugar levels before they conceive, it is thought that a significant portion of the birth

defects in children born to these women who have preexisting diabetes mellitus will be prevented (Oakley, 2012). According to Correa et al. (2012), controlled glucose levels before pregnancy and in the early stages of gestation is associated with a lower risk of birth defects. Prevention should be focused on trying to improve glucose control of the women who are of reproductive age who are diabetic, specifically focusing on the women who are planning a pregnancy (Correa et al., 2012). Women who have pre-gestational diabetes or gestational diabetes mellitus with a fasting hyperglycemia have three to four times the risk of having an infant with birth defects compared to women who have mild gestational diabetes (Sheffield, Butler-Koster, Casey, McIntire, & Leveno, 2002).

More focused efforts at glucose control during pregnancy can be concentrated on women who have type I diabetes already. Because this type of diabetes mellitus is an autoimmune disorder and usually occurs in children, these women will most likely already be immersed in the healthcare system. Because of this, efforts should be increased to lower the chance of birth defects in these women. Oakley (2012) suggested that clinical research programs should be set up to identify the type of support and teaching women with type I diabetes need that will ensure that they have good control of their blood sugar levels when they become pregnant. Ideally, because type I diabetes is usually diagnosed in the childhood years, these types of programs would start at the pediatric level and in the pediatric community, when the diagnosis is made. Therefore, once these women reach reproductive age, they will already be educated on how to keep their glucose levels under control, and be aware of the effects their uncontrolled blood sugar levels can have on their baby (Oakley, 2012).

One study performed by Temple, Adlridge, and Murphy (2006) found that pregnant women who had type I diabetes mellitus, and who received pre-pregnancy care, had better glycemic control in the early stages of their pregnancies. Their improved blood sugar control was mostly seen in the first 20 weeks of their pregnancies. This pre-pregnancy care that was provided also reduced the risk of spontaneous abortion and adverse outcomes such as major congenital malformation, stillbirth, and perinatal death (Temple et al., 2006).

There is the possibility that some women who were diagnosed with gestational diabetes mellitus during their pregnancies might have had type II diabetes that was simply undiagnosed before their pregnancies (Splete, 2008). Because of this possibility, and because this type of diabetes is first detected during pregnancy, it is imperative that all women undergo screening for diabetes during their first prenatal visit. Women who have significant risk factors such as obesity, prior history of gestational diabetes, and a strong family history of type II diabetes should have their plasma glucose levels checked as soon as possible (Guyen et al., 2009; Michel, 2011). If the first screening shows no signs of gestational diabetes, women should be retested between the 24th and 28th week of pregnancy. Because hyperglycemia has harmful effects on the fetus, it is imperative that mothers, as well as the fetuses, are monitored closely throughout the pregnancies (Guyen et al., 2009).

According to Dunne et al. (2003), some communities and ethnic groups do not think that type II diabetes is a serious illness. However, in order to decrease the fetal mortality rate and chance of birth defects, it is absolutely necessary to eliminate this misconception pertaining to this type of diabetes. Often, symptoms of type II diabetes

will go unnoticed, thus undiagnosed, for anywhere from months to years before women are diagnosed. This diagnosis usually occurs at their first prenatal visit, which is usually around the 10th week of gestation. This means that organogenesis of the fetus has been completed before the mother even had her first consultation. Therefore, women should be screened for type II diabetes at appropriate times and a more effective approach would be beneficial for those women who are at the greatest risk for having type II diabetes. Special attention should be focused on these women who are in the high-risk groups, such as women who are obese and live sedentary life styles (Dunne et al., 2003).

Khan et al. stated (2013), "GDM is a disorder which can be effectively controlled by decreasing the associated high risk factors and this leading to healthy infant delivery" (p.89). Therefore, accurate monitoring and control of gestational diabetes mellitus during pregnancy will help improve both maternal and fetal outcomes. The prevalence of gestational diabetes mellitus and the likelihood of adverse maternal and neonatal outcomes from this disease process can be reduced by good monitoring and adequate control of the diabetes in the prenatal stage (Khan et al., 2013).

However, in order to prevent birth defects, the mothers must have their blood sugar in control before conception, which means women have to be aware of their medical conditions (Oakley, 2012). According to Oakley (2012), about one third of women who are of reproductive age who have diabetes mellitus are undiagnosed. Additionally, about 60% of unplanned pregnancies are to women who have diabetes mellitus. It seems impossible, and daunting, to screen every woman who is of childbearing age for diabetes mellitus, which is why patient teaching and inclusion of community resources is so important. Education should start early in childhood, in

schools and through community resources, regarding the health effects of unhealthy eating, sedentary lifestyles, and obesity.

Prenatal Care

Preventing birth defects in diabetic mothers requires the provision of effective prenatal care. It is known that women with diabetes during pregnancy have a higher chance of negative birth outcomes. Providing adequate prenatal care can help lower the risk of these adverse outcomes. Educating pregnant women who have diabetes regarding controlling their blood sugar levels is essential. This would increase the chance of these mothers delivering healthier babies as well as decreasing the amount of money spent on difficult deliveries and medical complications that could last the lifetime of the mother and baby. Prenatal care for mothers who are diabetic could save a projected five and a half billion dollars in healthcare expense and lost employment productivity over the span of the affected child's life ("Diabetes; preconception care for diabetic women could potentially save \$5.5 billion", 2014). Because it is well known that diabetes in women who are pregnant is correlated to major complications, like preterm labor and birth defects, access to prenatal care can diminish the occurrence of these negative outcomes by assisting the mothers to improve their glucose levels before they become pregnant as well as during the early stages of their pregnancies.

Not only do the complications of diabetes during pregnancy negatively affect the health and wellbeing of the mother and infant, they cause a large cost to healthcare payers and society in general. The Center for Disease Control and Prevention (CDC) examined the amount of money that could potentially be saved by providing effective prenatal care and thus helping to prevent adverse birth outcomes. According to this study, effective

prenatal care provided to pregnant women who were diagnosed with diabetes could prevent \$4.3 billion in healthcare costs to healthcare payers and society over the lifetime of the children born to these mothers (“Diabetes; preconception care for diabetic women could potentially save \$5.5 billion”, 2014). Additionally, successful prenatal care provided to pregnant women who have undiagnosed diabetes could theoretically save another \$1.2 billion, which would equal a total of \$5.5 billion in avoided costs.

Although saving money is important, another benefit of early and effective prenatal care would be the avoidance of birth complications. This study estimated that every year, with universal prenatal care, 8,397 preterm births could possibly be avoided as well as 3,725 birth defects and 1,872 perinatal deaths.

These statistics show the importance of identifying women who are at risk for having pre-gestational diabetes mellitus and providing them with proper education as well as prenatal care (“Diabetes; preconception care for diabetic women could potentially save \$5.5 billion”, 2014). In order to effectively decrease the number of cases of birth defects caused by diabetes mellitus, it is imperative to improve our methods of patient teaching to at risk groups as well as providing awareness and education to women of childbearing age (“Tips For Preventing Birth Defects”, 2014).

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