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REVIEW ARTICLE

IMPACT OF GESTATIONAL DIABETES MELLITUS ON CHILD BIRTH

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Abstract

Gestational Diabetes Mellitus (GDM) is an irregular glucose tolerance condition that develops first and is recognized during pregnancy. The Oral Glucose Tolerance Test (OGTT) is the gold standard for the diagnosis of this disorder from 24 to 28 weeks. A number of adverse results, including gestational hypertension, cardiovascular disease and preeclampsia, have been associated with pregnant women. As for maternal glucose levels in the second or third trimester the risk of adverse outcomes drastically increases, even within ranges previously considered normal for pregnancy. Excessive gestational weight gain in women with GDM, it is very normal and closely correlated with lifestyle factors during pregnancy. High fat consumption particularly saturated fat, trans fat and cholesterol, increases GDM risk. A higher intake of added sugar and lower intake of vegetable and fruit fiber are independently linked to increased fasting glucose. Animal protein consumption is positive and vegetable protein is inversely related to the risk of GDM. Since fetuses and infants are particularly vulnerable to the effects of toxic compounds, attempts should be made during the years well before childbearing to reduce the exposure of girls and women to dioxins in food, so that fewer quantities of these compounds accumulate in their bodies and are passed on through the placenta and breast milk. The key sources of exposure for most people are fats in meat, food, fatty fish, whole milk and full-fat milk products and their intake should be reduced.

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Introduction:-

Gestational Diabetes Mellitus (GDM) is an irregular glucose tolerance condition that develops first and is recognized during pregnancy. The Oral Glucose Tolerance Test (OGTT) is the gold standard for the diagnosis of this disorder from 24 to 28 weeks⁽¹⁾. GDM is prevalent worldwide and its prevalence in some countries or areas even is higher than 20%⁽²⁾. More seriously, the incidence of GDM, which poses a great threat to maternal and neonatal health, continues to increase. A number of adverse results, including gestational hypertension, cardiovascular disease and

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preeclampsia, have been associated with pregnant women⁽³⁾. The offspring will suffer from fetal macrosomia, respiratory distress syndrome and type 2 diabetes⁽⁴⁾. Proper prenatal care and positive lifestyle changes can improve the adverse maternal outcomes of women with GDM^(5,6). As for maternal glucose levels in the second or third trimester the risk of adverse outcomes drastically increases, even within ranges previously considered normal for pregnancy^(7,8). Given the effects of GDM on the health of the mother and her offspring throughout pregnancy focusing on modifiable risk factors during the pre-, peri and post natal era, namely diet, physical activity, and psychosocial well-being, seems crucial⁽⁹⁾. Excessive gestational weight gain⁽¹⁰⁾ in women with GDM, it is very normal and closely correlated with lifestyle factors during pregnancy⁽¹¹⁾. High fat consumption particularly saturated fat, trans fat and cholesterol, increases GDM risk^(12,13). A higher intake of added sugar and lower intake of vegetable and fruit fiber are independently linked to increased fasting glucose⁽¹⁴⁾. Animal protein consumption is positive and vegetable protein is inversely related to the risk of GDM⁽¹⁵⁾.

Gestational Diabetes Mellitus:

Gestational Diabetes Mellitus (GDM) is defined as a woman has a glucose intolerance with onset and first recognition between 24 to 28 weeks of gestation^(16,17). It usually resolves after childbirth⁽¹⁸⁾, although it carries pre-, peri-, and postnatal risks of adverse outcomes in the mother and the child for example, up to 40% of women with GDM are known to have pre-diabetes a common condition in which the blood sugar level is higher than normal but not yet high enough to be considered diagnostic of diabetes. Prediabetes is considered to be a precursor of type 2 diabetes and increases a person's risk of developing type 2 diabetes, Heart disease or stroke in the early postpartum period⁽¹⁹⁾.

Causes:

Carbohydrate metabolism:

Normal glucose tolerance is maintained because of a balance between adequate insulin secretion and insulin sensitivity. The secretory response of the pancreatic β -cells to glucose (particularly in the early phase) and the sensitivity of the glucose utilizing tissues to insulin determine the ability of insulin to dispose of Carbohydrates⁽²⁰⁾. Pregnancy alters carbohydrate metabolism but adaptation occurs and there is no effect on mother and foetus as insulin secretion increases. When there is abnormal response there is increased foetal risk. Abnormal glucose tolerance occurs when the pancreatic β -cells output does not meet tissues insulin needs in response to changes in insulin resistance⁽²¹⁾. Pregnancy is a diabetogenic, hyperlipidaemic and glucosuric state. After mid pregnancy resistance to insulin develops due to placental reduction of anti-insulin hormones like human placenta lactogen, cortisol, oestrogen and progesterone⁽²²⁾.

The effect of these hormones causes

1. Low FBS (Fasting Blood Sugar) with high PPBS (Post Prandial Blood Sugar)
2. Low renal threshold for glucose and increase in GFR leading to glucosuria
3. Increased production of insulin and high fasting insulin that may lead to functional failure of pancreas.

Fasting blood glucose decreases at early pregnancy and continuously during gestation⁽²³⁾. Insulin sensitivity declines with advancing gestation to reach at late gestation (34–36 weeks) 50–60% of pre-gravid state⁽²⁴⁾. As a reflection of insulin resistance occurrence, fasting insulin concentrations increase. The changes in insulin sensitivity are inversely related to changes in maternal body fat mass⁽²⁵⁾. Hepatic glucose production increases during pregnancy suggest that the defect in insulin action also targets the liver⁽²⁶⁾ found a significant increase in basal endogenous glucose production at the end of gestation in spite of the important increase in fasting insulin concentration⁽²⁷⁾.

First half of pregnancy (Anabolic):

1. Pancreatic beta cell hyperplasia causes hyperinsulinemia
2. Increased uptake and storage of glucose

Second half of pregnancy (Catabolic):

1. Placental hormones blocks glucose receptors and cause insulin resistance by increased lipolysis, increased gluconeogenesis, decreased glycogenesis
2. Increased glucose and amino acid for the fetus.

Glycosuria in pregnancy:

It is an early indicator of gestational diabetes. During pregnancy renal threshold is diminished due to combined effect of increases GFR and impaired tubular reabsorption of glucose, which is most common in mid pregnancy.

Repeat and random urine sample taken on one or more occasion throughout pregnancy reveal glycosuria in 5 to 50% cases. Glycosuria on one occasion before 20 weeks is an indicator for glucose tolerance test.

Inflammatory mediators and their role in pregnancy and diabetes:

Pregnancy has been characterized as a chronic low-grade inflammatory condition because of the increase in activation of circulating blood leukocytes, the inflammation of pregnancy is further enhanced by maternal prepregnancy obesity. This increase in low-grade inflammation, particularly observed in obese women, has been related to increases in macrophage infiltration in both maternal white adipose tissue and the placenta. The increase in inflammation has been associated with increased circulating C-reactive protein (CRP) and interleukin-6 (IL-6). Both of these factors may exacerbate the increased insulin resistance previously noted in obese women with normal glucose tolerance because of effects on the postreceptor insulin-signaling cascade. These inflammatory cytokines may then relate to increased substrate availability for the developing fetus and resultant macrosomia. TNF- α was the strongest independent predictor of insulin sensitivity in pregnancy, accounting for about half of the variance in the decrease in insulin sensitivity during gestation⁽²⁸⁾

Role of adipoinsular axis:

An endocrine feedback loop called the adipoinsular axis connects the endocrine pancreas with adipose tissue and the brain. This axis regulates hunger and fat storage through the hormones named insulin and leptin. Insulin is responsible for promoting the development of fat mass and leptin production. Leptin reduces energy intake and suppresses the insulin secretion via leptin receptors on pancreatic beta cells. Abnormal functioning of this axis may lead to hyperphagia, dysregulation of the energy balance and excessive adiposity⁽²⁹⁾

Growth hormone in diabetes:

Growth hormone may antagonise the peripheral effect of insulin, and may cause it to be utilised in the tissues at such a high rate, that the level of insulin in the blood falls and as a result the islet may be stimulated even more to produce insulin⁽²⁹⁾

Vitamin D3:

The prevalence of type 1 diabetes has inversely correlated. Low vitamin D synthesis may be important in the pathogenesis of type 1 diabetes. Lack of vitamin D3 supplementation in infants has been associated with increased risk of type 1 diabetes later in life⁽²⁹⁾

Anaemia with diabetes:

Occurs due to following reasons:

1. Inflammation which up regulates hepcidin and prevents the release of iron from tissue stores leading to functional iron deficiency.
2. Erythropoietin deficiency due to down regulation of hypoxia inducible factor 1.
3. Sympathetic denervation of kidney due to autonomic neuropathy.

Thyroid disorders and diabetes in pregnancy:

Thyroxine is an anti-insulin hormone. Thyroid hormones raise the rate of hepatic glucose output, increase gluconeogenesis, increase availability of substrates like amino acids and free fatty acids. Thus, hyperthyroidism causes hyperglycaemia and worsens the pre-existing impaired glucose tolerance⁽³⁰⁾

Pathophysiology of Gestational Diabetes Mellitus:

GDM is usually the result of cell dysfunction on a background of chronic insulin resistance during pregnancy and thus both cell impairment and tissue insulin resistance represent critical components of the pathophysiology of GDM. In most cases, these impairments exist prior to pregnancy and can be progressive representing an increased risk of T2DM post-pregnancy⁽³⁰⁾. A number of additional organs and systems contribute to, or are affected by, GDM. These include the brain, adipose tissue, liver, muscle, and placenta⁽³¹⁾

Beta-Cell Dysfunction:

The primary function of cells is to store and secrete insulin in response to glucose load. When cells lose the ability to adequately sense blood glucose concentration, or to release sufficient insulin in response, this is classified as cell dysfunction. Cell dysfunction is thought to be the result of prolonged, excessive insulin production in response to chronic fuel excess⁽³¹⁾. However, the exact mechanisms underlying cell dysfunction can be varied and complex^(32,33)

Defects can occur at any stage of the process: pro-insulin synthesis, post-translational modifications, granule storage, sensing of blood glucose concentrations, or the complex machinery underlying exocytosis of granules. Indeed, the majority of susceptibility genes that are associated with GDM are related to cell function, including potassium voltage-gated channel KQT-like 1 (Kcnq1) and glucokinase (Gck). Minor deficiencies in the cell machinery may only be exposed in times of metabolic stress, such as pregnancy⁽³⁴⁾

Beta cell dysfunction is exacerbated by insulin resistance. Reduced insulin-stimulated glucose uptake further contributes to hyperglycemia, overburdening the cells, which have to produce additional insulin in response⁽³⁵⁾. This loss of cell mass has been linked to epigenetic downregulation of pancreatic homeobox transcription factor (Pdx1), which is essential for normal cell differentiation in the embryo⁽³⁶⁾. Prolactin is also essential for adequate cell proliferation, as demonstrated in mouse knockouts of the prolactin receptor (PrIR)⁽³⁷⁾. In addition, glucotoxicity is also thought to result in cell apoptosis over time. Therefore, reduced cell mass, reduced cell number, cell dysfunction, or a mix of all three contribute to GDM, depending on the individual⁽³⁸⁾.

Chronic Insulin Resistance:

Insulin resistance occurs when cells no longer adequately respond to insulin. At the molecular level, insulin resistance is usually a failure of insulin signaling, resulting in inadequate plasma membrane translocation of glucose transporter 4 (GLUT4)—the primary transporter that is responsible for bringing glucose into the cell to use as energy. The rate of insulin-stimulated glucose uptake is reduced by 54% in GDM when compared with normal pregnancy⁽³⁹⁾. While insulin receptor abundance is usually unaffected, reduced tyrosine or increased serine/threonine phosphorylation of the insulin receptor dampens insulin signalling⁽⁴⁰⁾. In addition, altered expression and/or phosphorylation of downstream regulators of insulin signaling, including insulin receptor substrate (IRS)-1, phosphatidylinositol 3-kinase (PI3K), and GLUT4, has been described in GDM⁽⁴¹⁾.

Neurohormonal Networks:

Neurohormonal dysfunction has been implicated in the pathogenesis of diseases of insulin resistance, such as that present in GDM. This network regulates appetite, active energy expenditure, and basal metabolic rate, and it is made up of a complex network of central (e.g., cortical centers that control cognitive, visual, and “reward” cues) and peripheral (e.g., satiety and hunger hormones) signals⁽⁴²⁾. These contribute to GDM by influencing adiposity and glucose utilization. This network is highly regulated by the circadian clock, which may explain why pathological sleep disorders or those individuals undertaking shift work are correlated with GDM rate^(43,44). Some of the most important regulators of neurohormonal metabolic control are adipokine signalling proteins that are secreted primarily by adipose tissue. These include leptin and adiponectin.

Leptin:

Leptin is a satiety hormone secreted primarily by adipocytes in response to adequate fuel stores.

It primarily acts on neurons within the arcuate nucleus of the hypothalamus to decrease appetite and increase energy expenditure. Specifically, leptin inhibits appetite-stimulators neuropeptide Y (NPY) and agouti-related peptide (AgRP), and it activates the anorexigenic polypeptide pro-opiomelanocortin (POMC)⁽⁴⁵⁾. When leptin was first discovered, it was lauded as a potential treatment for obesity⁽⁴⁶⁾. However, it was soon revealed that the majority of obese individuals do not respond to leptin, and instead demonstrate leptin resistance. While leptin treatment is effective in obesity that is caused by leptin and leptin receptor genetic polymorphisms, these are rare (<5% of obese individuals)⁽⁴⁷⁾. Therefore, obesity is associated with excessive plasma leptin concentration (hyperleptinemia) as a result of leptin resistance, and plasma leptin concentrations are generally proportional to the degree of adiposity⁽⁴⁸⁾. Leptin resistance can occur either as a defect in blood-brain barrier leptin transport, or through intracellular mechanisms that are similar to insulin resistance⁽⁴⁹⁾. Like insulin resistance, a degree of leptin resistance occurs in normal pregnancy, presumably to bolster fat stores beyond what would usually be required in the non-pregnant state. Leptin resistance is further increased in GDM, resulting in hyperleptinemia⁽⁵⁰⁾. However, pre-pregnancy BMI is a stronger predictor of circulating leptin than GDM⁽⁵¹⁾.

The placenta also secretes leptin during human pregnancy. In fact, the placenta is responsible for the majority of plasma leptin during pregnancy⁽⁵²⁾. Placental leptin production is increased in GDM, probably as a result of placental insulin resistance, and this further contributes to hyperleptinemia. This is also thought to facilitate amino acid transport across the placenta, contributing to fetal macrosomia⁽⁵³⁾.

Adiponectin:

Similar to leptin, adiponectin is a hormone that is primarily secreted by adipocytes. However, plasma adiponectin concentrations are inversely proportional to adipose tissue mass, with low concentrations in obese individuals. GDM is similarly associated with decreased adiponectin⁽⁵⁴⁾. In contrast to leptin, there is a stronger association of adiponectin with insulin resistance than with adiposity⁽⁵⁵⁾. This suggests that adiponectin plays an important role in the pathogenesis of GDM, independent of obesity. Adiponectin enhances insulin signaling and fatty acid oxidation, and it inhibits gluconeogenesis⁽⁵⁶⁾. It does so by activating AMP-activated protein kinase (AMPK) within insulin-sensitive cells, which facilitates the action of IRS-1, and by activating the transcription factor peroxisome proliferator-activated receptor alpha (PPAR) in the liver. Furthermore, adiponectin stimulates insulin secretion, by upregulating insulin gene expression and exocytosis of insulin granules from beta cells⁽⁵⁷⁾.

Adiponectin is also expressed at low concentration from the syncytiotrophoblast of the placenta where it is regulated by cytokines, such as tumor necrosis factor alpha (TNF), interleukin (IL) 6, interferon gamma (IFN- γ), and leptin⁽⁵⁸⁾. However, emerging evidence suggests adiponectin impairs insulin signaling and amino acid transport across the placenta, limiting fetal growth. Therefore, adiponectin gene methylation in the placenta is associated with maternal glucose intolerance and fetal macrosomia⁽⁵⁹⁾.

Adipose Tissue:

Adipose tissue actively secretes circulatory factors, including adipokines (leptin and adiponectin) and cytokines (such as TNF- α , IL-6, and IL-1 α), which have wide-ranging metabolic effects⁽⁶⁰⁾.

Factors influencing timing of delivery in GDM:**Biomedical factors:**

The obstetrician considers many obstetric and medical factors while planning the delivery in a woman with GDM. In general, waiting at least until 38 completed weeks' gestation improves fetal outcome, especially in diabetic patients⁽⁶¹⁾. However, if an indication for early delivery exists, GDM should not be considered as a contraindication to proceed with interventions for early delivery. Also, if a spontaneous preterm delivery seems imminent, it should not be postponed⁽⁶²⁾. At times, in fact, an early, planned operative delivery may be appropriate for women with ketosis or ketoacidosis, difficult-to-control diabetes, with frequent episodes of hypoglycemia or hyperglycemia, excessively high insulin requirements, or any other clinical situation which may put the fetus at risk. This may also be true for women with compromised cardiovascular, renal, or retinal function⁽⁶³⁾. Macrosomia refers to a baby who is considerably larger than normal. All of the nutrients the fetus receives come directly from the mother's blood. If the maternal blood has too much glucose, the pancreas of the fetus senses the high glucose levels and produces more insulin in an attempt to use this glucose. The fetus converts the extra glucose to fat. Even when the mother has gestational diabetes, the fetus is able to produce all the insulin it needs⁽⁶⁴⁾. The combination of high blood glucose levels from the mother and high insulin levels in the fetus results in large deposits of fat which causes the fetus to grow excessively large. Macrosomia is a common accompaniment of GDM, especially in women with uncontrolled glycemia. The risk of cephalopelvic disproportion (CPD) and shoulder dystocia increases as fetal weight gain occurs with advancing gestational age. The chances of a normal vaginal delivery, therefore, may recede as gestation progresses in women with refractory GDM cost-effective in reducing maternal complications⁽⁶⁵⁾.

Psychosocial factors:

The Psychosocial factors are depression, panic disorder, drug use, domestic violence, and having two or more medical comorbidities. This issue is important in cultures where a premium is placed upon a woman's ability to have normal childbirth, where the parturient is unable to afford the physical rest required after surgical delivery, or if the financial burden associated with an operative delivery has to be paid by the patient. These realities imply that an earlier, planned delivery at 36–37 weeks gestation, may be indicated in select women, who wish to try and maximize the chances of a normal vaginal delivery. Induction of labor at less than 40 weeks gestation in women with mild GDM does not increase their risk of LSCS. In fact the risk of LSCS rises threefold in women who are induced at 41 weeks, as compared to those who are induced at 39 weeks⁽⁶⁶⁾.

Environmental factors:

In the etiopathogenesis of diabetes, environmental factors play a part. Polluted air, soil water, unhealthy diet, stress, lack of physical activity, vitamin D deficiency, enterovirus exposure, and immune cell damage are all included⁽⁶⁷⁾.

Air pollution:

Air pollution is one of the risks to GDM's environmental health. Endothelial dysfunction, dysregulation of visceral adipose tissue through inflammation, hepatic insulin resistance and changes in autonomic tone that may increase peripheral insulin resistance may be the underlying mechanism⁽⁶⁸⁾ Type 2 diabetes and GDM share common risk factors, and both are characterized by insulin resistance and impaired insulin secretion⁽⁶⁹⁾

Exposure to chemicals:

To improve insulin resistance and diabetes, contaminants from water contamination, plastic packaging, cleaning and beauty care products have all been identified⁽⁷⁰⁾

Persistent organic pollutants (POPs) are pollutants that, due to the widespread use of pesticides and industrial chemical products, persist throughout the setting. Environmental contaminants consumer products and cosmetics can all increase the risk of developing diabetes. Endocrine-disrupting chemicals are substances present in the environment, food and consumer products that have the ability, among other functions, to influence hormone production and metabolism⁽⁷¹⁾

Risk factors for Gestational Diabetes Mellitus:

Risk factors for GDM is physical activity, which decreases insulin resistance, reduces future risk of type 2 diabetes⁽⁷²⁾, and limits gestational weight gain by increasing energy expenditure and altering food intake⁽⁷³⁾. Thus, physical activity has a protective effect on the development of GDM^(74,75). Finally, psychological factors also play an important role in GDM. Higher stress exposure and perceived stress are associated with increased fasting glucose levels in pregnant women, even before they know their diagnosis⁽⁷⁶⁾ Psychological stress and negative life events can be associated with higher salivary cortisol levels during pregnancy, which might influence glucose levels⁽⁷⁷⁾. Depressive symptoms in early pregnancy also increase the risk for GDM. For example, physical activity may reduce symptoms of depression⁽⁷⁸⁾ probably by reducing plasma kynurenine^(79,80) Physical activity increases energy expenditure can influence total food intake reduces stress-induced food intake and can also regulate eating behavior via endocrine mediators such as insulin, leptin, and ghrelin⁽⁸¹⁾ Eating behavior, such as emotional eating or unhealthy habitual eating plays an important role in explaining the depression-BMI relationship. Finally, the higher risk for maternal postpartum depression is also associated with reduced parenting skills, which may have negative consequences for the development of the child⁽⁸²⁾

Complications on delivery:**Fetal effects:****Spontaneous abortion:**

Early miscarriage is associated with poor glycemic control. Up to 25 percent of diabetic gravidas have an early pregnancy loss. Those whose HbA1c concentrations were >12 percent or whose preprandial glucose concentrations were persistently >120 mg/dL had an elevated risk.

Malformations:

The incidence of major malformations in women with type 1 diabetes is at least doubled and approximates 11 percent. Cardiovascular malformations accounted for more than half of the anomalies. The risk of an isolated cardiac defect was fivefold higher in women with type 1 diabetes. Three interrelated molecular chain reactions have been linked to congenital malformations. They are

1. Alterations in cellular lipid metabolism,
2. Excess production of toxic superoxide radicals,
3. Activation of programmed cell death.

Altered fetal growth:

Diminished growth may result from congenital malformations or from substrate deprivation due to advanced maternal vascular disease. That said, fetal overgrowth is more typical of pregestational diabetes. Maternal hyperglycemia prompts fetal hyperinsulinemia, and this in turn stimulates excessive somatic growth. Except for the brain, most fetal organs are affected by the macrosomia. Diabetic women have excessive fat deposition on the shoulders which predisposes to shoulder dystocia or caesarean delivery⁽⁸³⁾

Neonatal effects:

Modern neonatal care has reduced neonatal death rates due to immaturity; however neonatal morbidity due to preterm birth continues to be a serious consequence of pregestational diabetes. Preterm neonates, those born to diabetic women treated with insulin prior to pregnancy were at greater risk for necrotizing enterocolitis and late-onset sepsis than neonates of mothers without diabetes.

Respiratory distress syndrome:

Gestational age rather than overt diabetes is likely the most significant factor associated with respiratory distress syndrome. Indeed, very-low-birth weight neonates delivered between 24 and 33 weeks gestation, rates of respiratory distress syndrome in newborns of diabetic mothers were not higher compared with rates in neonates of nondiabetic mothers.

Hypoglycemia:

Newborns of a diabetic mother experience a rapid drop in plasma glucose concentration after delivery. This is attributed to hyperplasia of the fetal β -islet cells induced by chronic maternal hyperglycemia. Low glucose concentrations—defined as <45 mg/dL—are particularly common in newborns of women with unstable glucose concentrations during labor.

Hypocalcemia:

Defined as a total serum calcium concentration <8 mg/dL in term newborns, early onset hypocalcemia is one of the potential metabolic derangements in neonates of diabetic mothers. Its cause has not been explained. Theories include aberrations in magnesium–calcium economy, asphyxia, and preterm birth.

Complications on childbirth:**Macrosomia:**

Is defined as an estimated fetal weight of more than 4000gms to 4500gms or more than 90th percentile at any gestational age. It occurs in 25% to 42% in hyperglycemic pregnancies. Diabetic macrosomia is characterised by specifically by a large fetal abdominal circumference and decreased head to abdominal circumference ratio because fetal hyperinsulinemia leads to abdominal fat distribution.

Hyperbilirubinemia and polycythemia:

The pathogenesis of hyperbilirubinemia in neonates of diabetic mothers is uncertain. A major contributing factor is newborn polycythemia, which raises the bilirubin load. Polycythemia is thought to be a fetal response to relative hypoxia. According to Hay (2012), the sources of this fetal hypoxia are hyperglycemia-mediated elevations in maternal affinity for oxygen and fetal oxygen consumption. Together with insulin like growth factors, this hypoxia leads to elevated fetal erythropoietin levels and red cell production. Fetal renal vein thrombosis is reported to result from polycythemia.

Cardiomyopathy:

Newborns of diabetic pregnancies may have hypertrophic cardiomyopathy that primarily affects the interventricular septum. In the first trimester, fetal diastolic dysfunction was already evident. In the third trimester, the fetal interventricular septum and right ventricular wall were thicker in fetuses of diabetic mothers. Most affected newborns are asymptomatic following birth, and hypertrophy usually resolves in the months after delivery.

Long-term cognitive development:

Intrauterine metabolic conditions have long been linked to neurodevelopment in offspring. The intelligence quotient of those whose mothers had diabetes during pregnancy averaged 1 to 2 points lower. DeBoer and associates (2005) demonstrated impaired memory performance in infants of diabetic mothers at age 1 year. Results from the Childhood Autism Risks from Genetics and the Environment (CHARGE) study indicated that autism spectrum disorders or developmental delay were also more common in children of diabetic women⁽⁸⁴⁾

Ways to Control Gestational Diabetes Mellitus:

Since fetuses and infants are particularly vulnerable to the effects of toxic compounds, attempts should be made during the years well before childbearing to reduce the exposure of girls and women to dioxins in food, so that less

quantities of these compounds accumulate in their bodies and are passed on through the placenta and breast milk. The key sources of exposure for most people are fats in meat, food, fatty fish, whole milk and full-fat milk products and their intake should be reduced⁽⁸⁵⁾

1. Choose leaner cuts of beef, pork, and poultry; trim the fat and remove skin from chicken before cooking.
2. Choose non fat and low-fat milk and milk products
3. Choose a diet high in fruits, vegetables, whole grains and lean proteins.

These strategies help lower the intake of saturated fats and total fats and therefore help reduce the risk of exposure to dioxins⁽⁸⁶⁾

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