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Adverse Effects of Gestational Diabetes Mellitus on Growth and Development of Children

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Abstract: ***Gestational Diabetes Mellitus (GDM) is a condition where the pregnant woman experiences rise in the blood glucose level, which adversely effects mother and the child. The prevalence of GDM is increasing day by day. This review paper briefly highlights the most common adverse effects of Gestational Diabetes on infants, which includes, Pre term birth, Macrosomia, Low birth weight, Hyperglycemia, long term effects like Obesity and Diabetes Mellitus. The risk of developing future Diabetes Mellitus is high in women who have already been diagnosed with GDM. With proper diet counselling and lifestyle management, during the course of pregnancy, GDM can be prevented and the risk of adverse effects can be greatly reduced.***

Keywords: GDM (Gestational Diabetes Mellitus), adverse effects, lifestyle management.

1. Introduction

Gestational Diabetes Mellitus (GDM) is defined as a condition where the pregnant women have elevated blood glucose levels and which is usually diagnosed in the second or third trimester of pregnancy [1]. Infants born to mothers who have Gestational Diabetes are at an increased risk of adverse effects like, Growth abnormalities (large for gestational age (LGA), Hyperglycemia, Congenital malformations, etc [2].The infants of Gestational Diabetic mothers are likely to be born by caesarean delivery. It is clear that GDM is associated with adverse pregnancy outcomes and the risk of cesarean delivery was higher among pregnant women with GDM than in women without GDM by 67% [3].

Some studies done on children born to GDM mother's showed deficits in fine and gross motor function, lower verbal IQ, language impairment, greater inattention and hyperactivity, and poorer general cognitive function.[4]. Children born to mother's who had gestational diabetes showed a strong prediction of impaired glucose tolerance (IGT) and obesity of adolescence in their children.[5]. Infants of Diabetic Mother's (IDMs) experience high or fluctuating blood glucose during gestation, which causes other metabolic anomalies in late gestation and immediately after birth, which may be effect their brain structures in late gestation and early development [6].

The risk of developing type 2 diabetes in the Gestational Diabetic Mother is considerably high. Around 40-50% of GDM mother's tend to develop type 2 Diabetes within 5-10 years after delivery [7]. Modifiable factors like, lifestyle modification, adequate exercise and appropriate diet changes play a significant role in decreasing the risk for abnormal glucose tolerance during pregnancy. The studies show that low in-take of vegetables and high animal origin food among pregnant women of lower socioeconomic strata was associated with an increased risk of GDM[8].

Prevalence of GDM

The prevalence of GDM has been increasing worldwide and is having a negative impact on mothers and neonates [3]. Gestational diabetes mellitus (GDM), is one of the most common pregnancy complications, even in developing countries and the incidence of GDM has increased by more than 30 % within the past couple of decades [9].

In India also the prevalence of gestational diabetes mellitus (GDM) is increasing and it is estimated to be high in urban populations than in rural population[10] .Women who were in the highest income group had the highest prevalence of GDM when compared with the other income classes like upper income, middle upper income and low income. The studies suggest that gestational diabetes may affect between 5 and 8 million pregnant women in India annually [11].

Macrosomia

Recent experimental research study done in Jordan by Reema A. Karasneh, et al,2021 reports that babies born to GDM mother's tend to be heavier when compared to the babies born to non GDM mother's. One retrospective study conducted at the hospital of Saudi Arabia, on 220 patients with GDM who were diagnosed and treated, found that neonates born to women with GDM had a significantly higher mean birth weight than babies born to mothers from the control group. The neonates were also large for gestational age (LGA) babies when compared with the neonates born to mothers from the control group [**12**].

Premature birth

Premature birth may occur in as many as 20% of diabetic pregnancies, compared with a 10% incidence in infants born to mothers without diabetes [2]. Preterm birth also alters immune function including T cell response. [13].GDM carries an increased risk of spontaneous preterm

birth. Preterm birth is one of the leading cause of perinatal morbidity and mortality in developed countries. [14]

Hyperglycemia

Mothers with GDM have high glucose levels which easily crosses the placenta leading to intrauterine hyperglycemia, which induces fetal hyperinsulinemia and causes possible modifications in the growth and metabolism of the fetus [15]. In utero exposure to hyperglycemia as measured by amniotic fluid insulin levels, has been found to be a strong predictor of insulin resistance during childhood, and these effects of maternal diabetes on offspring appear to extend into the adult life. [16].

Congenitalmal formation

The rate of birth defects among women with poor control of diabetes during pregnancy ranges from 4.5% - 35.3%. However, with good glycemic control, these risks are greatly reduced with a range from 0% - 10.7%. As most of the anomalies of the fetus occur between $4^{th}$to 7^{th}weeks of gestation after conception, making periconceptional diabetic control important. [17]. Central nervous system (CNS) malformations are 16 times more likely in IDMs. In particular, the risk of anencephaly is 13 times higher, whereas the risk of spina bifida is 20 times higher. The risk of caudal dysplasia is up to 600 times higher in these infants. Neurologic immaturity, demonstrated by immature sucking patterns, has been found in infants born to insulin-managed mothers with diabetes. In developing countries like India these are more important due to unavailability of good neonatal care which a infant of diabetic mother badly needs. Studies showed the outcome of infant born to gestational diabetes in developing countries is poor because of inadequate medical facilities. This study was conducted in the medical college in one of the remote districts of Karnataka which caters mainly to rural population. Therefore, this study will represent the rural population. [2]

School age children younger than 9 years, born to mothers with gestational diabetes, had a higher rate of attention deficit, lower cognitive scores, and lower gross and fine motor achievements when matched with the control children. These divergences were highest in the young children and tended to diminish with age.[18]

Birth injuries

Hyperinsulinemiain GDM mother promotes the increase of fat and protein synthesis in the fetus, causing excessive growth of the fetus, which in turn leads to increased risk of brachial plexus nerve injury and shoulder dystocia. [7]

Fetal Outcomes	• LGA (birth weight ≥2 SD above the mean) • Macrosomia ° Fetal weight> 4,000g • Increased Birth weight • Apgar score at 5 minutes • Neonatal hypoglycemia ° Serum glucose<40mg/dL • Premature birth ° Birth before week 37 • Neonatal jaundice ° Total serum bilirubin level >5mg/dL • Shoulder dystocia

Sara W.Reece,et al,2018 [19].

The **Apgar score** is a clinical bedside test given done on newborns soon after birth. This test checks a baby's heart rate, muscle tone, and other signs to see if extra medical care or emergency care is needed. The test is usually done twice: once at 1 minute after birth, and again at 5 minutes after birth.

Long term complications of GDM

Obesity

Maternal GDM is an independent risk factor of childhood overweight and obesity, and it is associated with children's faster growth of BMI (Basal Metabolic Index). Children with intra-uterine exposure to gestational diabetes had increased overall adiposity and higher SBP (systolic blood pressure)at the age of 3 years. Charmaine S. Wright, et al. reported that GDM was associated with child adiposity when assessed by skin fold test but not by the BMI z-score. Maternal gestational diabetes results in fetal hyperglycemia which, in turn, induces fetal hyperinsulinemia. Fetal hyper insulinemia during critical periods of fetal development might induce insulin and leptin resistance and fat cell overgrowth, which may increase risk of obesity in postnatal life of the child.[5] In an retrospective cohort study, done by Cu¨neyt Ardıc,et al, reported that gestational diabetes to be a causative factor for obesity or overweight in children who were 2 and 3 years old. Because maternal obesity often appears as a precursor of GDM, it is difficult to differentiate the causative effects of maternal obesity and GDM on childhood obesity separately. Therefore, GDM can be a factor leading to child obesity. The relative weight in the children of mothers with GDM increased dramatically after 5 years of age, and half of the GDM mothers' children were >90th percentile after 8 years of age. [20]

Diabetes Type 2

Preterm birth was more strongly associated with type 2 than type 1 diabetes in adulthood of children born to GDM mother's [13].At 5 years of age, female offspring of diabetic mothers exhibited increased skin fold thicknesses and higher insulin concentrations and were more likely to develop impaired glucose tolerance than control subjects. Female neonates have been shown to have similar cord glucose to males yet increased insulin levels at birth [16].

Risk of developing Diabetes Mellitus in GDM mothers

Women with a history of GDM at first Pregnancy have a 2.25 times increased incidence of GDM when they become pregnant again. [7].

A study done in one of the hospital in UK from 1995-2003 and followed up till 2009 reports the risk of developing diabetes in women who had Gestational Diabetes in the past was 6.9 % at 5 years and 21.1 % at 10 years, from the start of initial diagnosis of GDM [21].Another study done in Sri Lanka also reports the risk of developing diabetes type 2 is 10 fold higher when compared to a woman with no prior diagnosis of GDM [22].

It has been estimated that GDM is the best-known predictor for type 2 diabetes, and that approximately one-third of women with type 2 diabetes may have had previous GDM [23]. A cohort study done on South Indian women for five

years after the incidence of GDM, reports that the incidence of diabetes, IGT/IFG and metabolic syndrome is considerably higher in women who had GDM when compared to non-GDM women. [24]

Management of (GDM) Gestational Diabetes Mellitus

After the intervention by diet and exercise, the blood glucose and HbA1c levels in pregnant women 2 hours after meals were significantly lower than before intervention.[7]Western dietary pattern was positively associated with the risk of GDM, whereas the prudent dietary pattern was inversely associated. The prudent dietary pattern consisted of a high consumption of fruit, green leafy vegetables, poultry and fish, while the western pattern represented a high consumption of red meat, processed meat, refined grain products, sweets, French fries and pizza. It is reported that healthy dietary patterns were significantly associated with a lower risk of GDM. Mediterranean diet was associated with a lower incidence of GDM. It was also found that the sweets and excessive consumption of seafood was associated with an increased risk of GDM.[25]

Table 2: The prudent dietary pattern

Dietary Pattern Food	Factor Loading Coefficient[a]
Vegetables	0.58
Eggs	0.56
Vegetable oils[b]	0.47
Seafood[c]	0.47
Soft Drinks[d]	-0.45
Breakfast Cereals	0.40
Fruit and berries[e]	0.39
Nuts and seed	0.36
Pasta/ Couscous	0.34
French fries	-0.33
Tea, Coffee, Cocoa Powder	0.33

[a]The factor leading coefficient describes the correlation (*r*) between intake of the food groups and the extracted factor. [b]Includes all vegetable oils, peanut and seed butter. [c]Includes all fish, shellfish and seafood products. [d]Includes soda- and sports drink sugar sweetened and sugar free). [e]Includes all fruit, berries and jams.

EA Tryggvadottir, et al, 2016 [26]

An Indian study by R. Deepa, et al 2020 done on lower socioeconomic strata, shows that GDM is related to the consumption of red meat. Few studies have shown that heme iron in red meat may be causing GDM, excess iron has been implicated in increasing the insulin resistance and the risk of type2 diabetes. It is important to consider here that all public hospitals in India supplement pregnant women with Iron tablets irrespective of their iron status. Increased iron supplements in pregnant women without iron deficiency was related to an increased risk of GDM. Thus, high red meat consumption and indiscriminate iron supplementation may be related to GDM.[8]

The adverse outcomes of GDM can be reduced, by dietary consultation during pre-pregnancy and early pregnancy. In addition, the traditional dietary pattern characterized by 'light-colored vegetables, fine grain, red meat and tubers' was associated with increased risk of GDM. Red meat might have a different effect when combined with different foods. Therefore, caution should be taken to balance the different dietary patterns when providing pregnant women with dietary guidance [27].

In one of the prospective cohort study, it was observed that a pre-pregnancy dietary score that represented a low-carbohydrate, high animal protein and animal fat dietary pattern was significantly and positively associated with GDM risk. And on the other hand, a pre-pregnancy dietary score that represented a dietary pattern low in carbohydrate and high in vegetable protein and vegetable fat/oil was not significantly associated with GDM risk. So women, in their reproductive age who follow a low-carbohydrate dietary pattern must consider consuming vegetables rather than animal sources of fat and protein (in particular red meat) to minimize their risk of developing GDM[28].A study done by Ruben Barakat, et al on randomly assigned 510 healthy pregnant women, reported that moderate- intensity exercise which includes aerobic exercise performed on regular basis in the second-third trimester of pregnancy can be an important way in reducing GDM related adverse outcomes on both neonate and mother [29].

It has been estimated that GDM is the best-known predictor of type 2 diabetes, and that approximately one-third of women with type 2 diabetes may have had previous GDM. Some Epidemiological studies indicate that women who are physically active or do not gain weight after pregnancy with GDM have a reduced risk of progressing to overt diabetes. By the lifestyle management and medical treatment, developing Diabetes after GDM in women can be reduced up to 50%. [30]

Lifestyle changes may be challenging during pregnancy and mothers with GDM must be advised to a lifestyle modification as part of their post partum follow-up care. Such an intervention might reduce the risk of recurrent GDM with a subsequent pregnancy as well as improve overall health of both the mother and child. [31]

2. Conclusion

This review paper emphasizes the ill effects of Gestational Diabetes on the mother and baby. Education for management of GDM is the need of the hour. With good dietary practices and adequate exercise the risk of GDM and future Diabetes in mothers who have already been diagnosed with GDM can be significantly reduced.

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