LUMEN ET VIRTUS
ISSN: 2177-2789

IMPACT OF GESTATIONAL DIABETES MELLITUS ON THE MOTHER-INFANT BINOMIAL: A SYSTEMATIC REVIEW OF THE MAIN COMPLICATIONS AND MANAGEMENT

https://doi.org/10.56238/levv16n45-060

Submitted on: 28/01/2025 **Publication date:** 28/02/2025

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ABSTRACT
Objective: The main objective of this study is to analyze the scientific literature on gestational diabetes mellitus (GDM), highlighting the associated complications and the methods of management of this condition. Methodology: This is a systematic review focused on understanding the key aspects of gestational diabetes mellitus. The research was guided by the question: "What are the most common complications associated with Gestational Diabetes Mellitus and what are the most effective management strategies according to scientific evidence?" To find answers, we searched the PubMed Central (PMC) database using four descriptors combined with the Boolean operator "AND". This resulted in 408 articles. After applying the inclusion and exclusion criteria, 31 articles were selected for analysis, of which 13 were used to compose the review. Results: GDM significantly increases the risk of the mother developing type 2 diabetes after pregnancy. Without appropriate interventions, a considerable portion of women with GDM can be diagnosed with diabetes mellitus within a few years of giving birth. The insulin resistance and

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increased inflammation seen in GDM are key factors contributing to this prolonged risk. In addition, GDM is associated with complications such as macrosomia, neonatal hypoglycemia, respiratory distress syndrome, among others. Conclusion: Gestational Diabetes Mellitus (GDM) is a condition characterized by glucose intolerance during pregnancy, increasing the risk of complications such as preterm birth and macrosomia. GDM occurs due to insulin resistance, and can lead to the development of type 2 diabetes in the future. Effective management involves continuous monitoring, dietary control, and medical interventions, which are essential to protect the health of the mother and fetus.

Keywords: Gestational Diabetes Mellitus. Obstetric Complications. Clinical Management.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a frequent condition that occurs during pregnancy, characterized by hyperglycemia, that is, high blood glucose levels. Unlike type 1 or type 2 diabetes, GDM is first detected during pregnancy and tends to disappear after delivery. However, its occurrence during pregnancy can result in lasting effects for both the mother and the newborn. GDM is commonly defined as "any degree of glucose intolerance with onset or first recognition during pregnancy." This condition affects a significant portion of pregnant women, with an overall prevalence ranging from 1% to 14%. In the Latin American context, the prevalence was estimated at 8.5% (Calvo et al., 2024).

METHODOLOGY

This study is a systematic review that aims to understand the main aspects of gestational diabetes mellitus (GDM) and to highlight the associated complications and management strategies. To develop this research, we formulated a guiding question using the PVO (population, variable and objective) strategy: "What are the most common complications associated with Gestational Diabetes Mellitus and what are the most effective management strategies according to scientific evidence?"

Searches were performed in the PubMed Central (PMC) databases. We used four descriptors in combination with the Boolean operator "AND": Diabetes Mellitus, Gestational, Pregnancy, Prenatal Diagnosis. The search strategy applied in the PMC was: Diabetes Mellitus, Gestational AND Pregnancy, Diabetes, Gestational AND Prenatal Diagnosis. We found 408 articles, which were subsequently submitted to the selection criteria. The inclusion criteria were: articles in English, Portuguese and Spanish; published between 2018 and 2024 and that addressed the themes proposed for this research. In addition, we considered review, observational and experimental studies, available in full. The exclusion criteria were: duplicate articles, available only as abstracts, that did not directly address the topic studied, or that did not meet the inclusion criteria.

After applying the descriptors in the searched databases, we found a total of 408 articles. After applying the inclusion and exclusion criteria, we selected 31 articles from the PubMed database, of which 13 studies were used to compose this review.

DISCUSSION

Gestational Diabetes Mellitus (GDM) is a condition characterized by the development of hyperglycemia during pregnancy in women without pre-existing diabetes. The pathophysiology of GDM involves a complex interplay of hormonal, metabolic, genetic, and environmental factors that result in the maternal body's inability to properly regulate glucose levels during pregnancy. This condition not only affects the mother's health during pregnancy, but can also have long-term consequences for both the mother and the fetus.

During pregnancy, significant changes occur in the mother's metabolism to ensure an adequate supply of nutrients to the fetus. In early pregnancy, there is an increase in insulin sensitivity to promote energy storage in the form of fat and glycogen. However, as pregnancy progresses, especially in the second and third trimesters, progressive insulin resistance occurs (Calvo et al., 2024).

IMPACT OF THE GDM ON THE MOTHER

The association between initial HbA1c levels and adverse obstetric complications is a topic of considerable clinical relevance, given the increasing prevalence of impaired glucose metabolism during pregnancy (Mañé et al., 2024). Glycated hemoglobin (HbA1c) is a measure of long-term glycemic control, reflecting average blood glucose levels over the past two to three months. During pregnancy, hyperglycemia is identified as a significant risk factor for various obstetric complications, and early detection through HbA1c measurement emerges as a promising tool for intervention.

The study by Mañé et al. (2024) reinforces the importance of early screening for hyperglycemia. HbA1c, due to its pre-analytical stability and convenience of not requiring fasting, is a practical and effective method to identify hyperglycemia in the first weeks of pregnancy. This allows for early intervention, which can mitigate obstetric complications throughout pregnancy. By establishing a relationship between initial HbA1c levels and adverse obstetric outcomes, the study provides evidence that elevated HbA1c levels, even below the diagnostic threshold for diabetes, can predict complications.

The article examines several HbA1c thresholds and their correlations with adverse obstetric outcomes. For example, an HbA1c threshold > 39 mmol/mol is associated with an increased risk of complications such as macrosomia, large for gestational age (LGA), preeclampsia, and preterm birth. These findings suggest that elevated HbA1c levels are correlated with an increased risk of obstetric complications, highlighting the need for close monitoring and control of GDM during pregnancy.

The meta-analysis conducted by Mañé et al. (2024) reveals that women with elevated HbA1c levels are at higher risk of complications such as macrosomia, LGA, preeclampsia, and preterm birth. The strength of these associations is greater in studies that employed an HbA1c threshold > 39 mmol/mol, suggesting that this threshold is a critical cutoff point for the identification of obstetric risks.

As mentioned above, GDM is associated with several complications during pregnancy. One of the main ones is gestational hypertension, which can progress to preeclampsia, a potentially fatal condition characterized by high blood pressure and damage to organs, usually the kidneys and liver (Bucci et al., 2024). In addition, exacerbated insulin resistance and hyperglycemia can lead to a higher risk of urinary tract infections and vaginal candidiasis.

Women with GDM are more likely to require obstetric interventions, such as cesarean delivery, due to the increased risk of fetal macrosomia (large baby). Macrosomia can cause shoulder dystocia, where the baby's shoulders become trapped after the head comes out, necessitating emergency obstetric maneuvers (Calvo et al., 2024).

After delivery, most women with GDM return to normal blood glucose levels. However, they remain at increased risk of developing type 2 diabetes in the future. Studies indicate that about 50% of women with GDM develop type 2 diabetes within 10 years of pregnancy (Calvo et al., 2024).

GDM is also associated with a significantly higher risk of long-term cardiovascular events, including heart failure, myocardial infarction, and ischemic stroke. This risk is even higher in women who also experienced gestational hypertension during pregnancy (Bucci et al., 2024). These conditions require continuous monitoring and preventive interventions to mitigate cardiovascular risks.

GDM can also negatively impact women's mental health. Studies demonstrate a strong association between GDM and perinatal depression, with affected women having nearly twice the risk of developing depressive symptoms compared to those without GDM (Jin et al., 2024). This risk is particularly high in low- and middle-income countries, where access to mental health care is limited.

Gestational Diabetes Mellitus (GDM) is associated with an increased risk of rectovaginal colonization by group B streptococci (GBS). This association has significant implications for perinatal health, as GBS colonization can lead to severe neonatal infections. Women with GDM are 16% more likely to be colonized by GBS compared to women without GDM, which poses an additional concern during pregnancy (Mercado-Evans et al., 2024).

GBS is a type of bacteria that can be present in the genital and gastrointestinal tracts of pregnant women without causing apparent symptoms. However, during vaginal delivery, GBS can be transmitted to the newborn, increasing the risk of neonatal sepsis, pneumonia, and meningitis. These infections can be potentially life-threatening or cause long-term complications in the baby's neurological development.

The presence of GBS in pregnant women with GDM requires constant surveillance and strict preventive measures. Screening for GBS is usually performed between the 35th and 37th weeks of gestation. If colonization is detected, intrapartum antibiotic prophylaxis is recommended to prevent vertical transmission of GBS to the newborn. This prophylaxis involves administering intravenous antibiotics to the mother during labor, significantly reducing the likelihood of neonatal infection.

In addition, the increased risk of GBS colonization in women with GDM may be related to changes in the immune and metabolic environment associated with hyperglycemia. Hyperglycemia can compromise the body's immune response, facilitating the colonization and proliferation of pathogens such as GBS. Therefore, close control of blood glucose levels is essential not only to reduce complications directly associated with GDM, but also to minimize the risk of GBS colonization and its perinatal consequences.

In summary, rectovaginal colonization by group B streptococci is a significant concern in pregnant women with gestational diabetes mellitus. Proper management of GDM, including glycemic control and antibiotic prophylaxis, is crucial to prevent serious neonatal infections and ensure the health of the newborn (Mercado-Evans et al., 2024).

For mothers, one of the main challenges is insulin resistance that often persists after pregnancy. Insulin resistance is a key factor in the pathogenesis of Nonalcoholic Fatty Liver Disease (NAFLD), resulting in the accumulation of fat in the liver (FOO et al., 2024). Additionally, GDM is associated with elevated levels of inflammatory adipokines, such as interleukin-6 (IL-6) and TNF-α, which can exacerbate liver inflammation and promote progression to NAFLD (FOO et al., 2024). Another risk for mothers is altered lipid metabolism, a condition that can aggravate liver fat accumulation (FOO et al., 2024). Not least, women with a history of GDM have a substantially higher risk of developing type 2 diabetes in the future, further increasing the risk of NAFLD (FOO et al., 2024). In addition, GDM elevates the risk of cardiovascular complications, such as hypertension and heart disease, which are often associated with NAFLD (FOO et al., 2024). Children of mothers with GDM may have altered liver development, with a greater propensity for liver fat accumulation and liver inflammation throughout life (FOO et al., 2024). In addition, studies indicate that children of mothers with GDM have a significantly higher risk of developing type 2 diabetes and metabolic syndrome, conditions strongly associated with NAFLD (FOO et al., 2024).

These risks highlight the need for continuous monitoring of the liver health of women with a history of GDM and their children, implementing early interventions to mitigate these risks (FOO et al., 2024). Healthcare providers should integrate regular liver function assessments into postnatal care for mothers and children affected by GDM, promoting early interventions to mitigate the risk of NAFLD and other metabolic complications (FOO et al., 2024). Lifestyle recommendations, such as a balanced diet and physical activity, are crucial for women with a history of GDM (FOO et al., 2024). Medical interventions may be necessary to control glucose levels and reduce the risk of liver complications (FOO et al., 2024). Additional studies are needed to explore specific interventions that may reduce the risk of NAFLD in mothers and children (FOO et al., 2024). Clinical trials focused on lifestyle modifications and pharmacological therapies can provide valuable insights (FOO et al., 2024).

IMPACT OF GDD ON THE FETUS

One of the most common complications associated with GDM is fetal macrosomia, which is defined as a birth weight equal to or greater than 4,000 g. Maternal hyperglycemia leads to an increase in glucose transfer to the fetus, resulting in fetal hyperinsulinemia. This condition promotes the overgrowth of the fetus, especially adipose tissue, leading to macrosomia. This disproportionate growth of the fetus can cause a number of complications during childbirth, including shoulder dystocia, where the baby's shoulders are trapped behind the mother's pubis, requiring specific maneuvers for release. In addition, macrosomia is associated with brachial plexus injuries, which are damage to the nerves that control the movements of the baby's arm and hand. These injuries can range from temporary to permanent, depending on the severity. The additional effort required to deliver a macrosomic baby can result in bone fractures, such as the collarbone or humerus. Difficulty in delivery can lead to asphyxiation, where the baby does not receive enough oxygen, resulting in possible neurological damage. Although less common, subdural hemorrhage and facial paralysis can occur due to the traumatic delivery of a macrosomic baby (Calvo et al., 2024).

Neonatal hypoglycemia is another frequent complication in infants born to mothers with GDM. After birth, the maternal glucose source is stopped, but fetal hyperinsulinemia persists, leading to a rapid drop in the newborn's blood glucose levels. Symptoms of neonatal hypoglycemia include tremors, irritability, lethargy, and, in severe cases, seizures and permanent neurological damage if not treated promptly. Neonatal hypoglycemia requires close monitoring of the newborn's blood glucose levels and immediate interventions such as intravenous glucose administration (Calvo et al., 2024).

Respiratory Distress Syndrome (RDS) is more common in infants of mothers with GDM due to delayed lung maturation. Fetal hyperinsulinemia interferes with the production of surfactant, a substance essential for keeping the pulmonary alveoli open. A lack of surfactant can lead to significant breathing difficulties after birth, necessitating immediate ventilatory support. Infants with RDS often need intensive care to monitor and manage their respiratory function. Treatment of RDS may involve the administration of exogenous surfactant and ventilatory support to help the newborn breathe (Calvo et al., 2024).

Babies of mothers with GDM have an increased risk of developing hyperbilirubinemia, which is elevated levels of bilirubin in the blood. This is due to the higher rate of destruction of red blood cells and the immaturity of the newborn's liver in processing bilirubin. Hyperbilirubinemia can cause jaundice, where the baby's skin and eyes turn yellow. In severe cases, it can lead to kernicterus, a serious neurological condition that can cause permanent brain damage (Calvo et al., 2024).

Polycythemia, or increased red blood cell count, is another complication associated with GDM. Maternal hyperglycemia leads to fetal hyperinsulinemia, which increases the production of red blood cells to compensate for intrauterine hypoxia. Consequences of polycythemia include circulatory problems, where increased blood viscosity can cause circulatory problems, and a higher risk of blood clot formation (Calvo et al., 2024).

Babies of mothers with GDM also have an increased risk of hypocalcemia (low levels of calcium in the blood) and hypomagnesemia (low levels of magnesium in the blood). These conditions can cause tremors, irritability, and, in severe cases, seizures, which require immediate treatment (Calvo et al., 2024).

Iron deficiency is common in infants of mothers with GDM due to inadequate iron transfer across the placenta. Iron deficiency can affect the neurological and cognitive development of the newborn, impairing the development of the brain and cognitive abilities (Calvo et al., 2024).

In addition, infants of mothers with GDM have an increased risk of neurological abnormalities, including delayed motor and cognitive development. Maternal hyperglycemia and fetal hyperinsulinemia can affect the development of the central nervous system, resulting in delays in motor and cognitive development (Calvo et al., 2024).

Gestational Diabetes Mellitus (GDM) is a recurrent complication during pregnancy, adversely impacting the development of the Central Nervous System (CNS) of the offspring, especially in the cerebellum. Experimental studies, predominantly conducted in animal models, have shown that GDM alters the morphogenesis of the cerebellar cortex, reducing the volume and thickness of the cerebellar layers, in addition to negatively affecting the density of granular and Purkinje cells. These findings are supported by the stereological investigation conducted by Hami et al., who observed a significant disruption in cerebellar cortex morphogenesis due to GDM (BORUJENI et al., 2024).

In addition to structural changes, GDM interferes with cellular and molecular processes essential for cerebellar development. Alterations in the expression of synaptophysin, insulin and IGF-1 receptors suggest a dysfunction in the signaling pathways necessary for neurogenesis and synaptogenesis, which are fundamental for the motor and cognitive development of offspring. Maternal hyperglycemia and neonatal hyperinsulinemia resulting from GDM contribute to mitochondrial dysfunction in neuronal cells, leading to inadequate cellular energy production and increased oxidative stress, both of which are detrimental to neurogenesis and neuronal function (BORUJENI et al., 2024).

Apoptosis, or programmed cell death, is an essential process during development, responsible for eliminating damaged or unnecessary cells. However, GDM increases the incidence of neuronal apoptosis, which can lead to significant loss of neurons in the cerebellum and other CNS regions, impairing normal development (BORUJENI et al., 2024). Oxidative stress, resulting from excessive production of free radicals due to GDM, damages lipids, proteins, and DNA in developing brain cells, compromising the integrity and functionality of cell membranes and synapses. In addition, there is a significant increase in the concentration of inflammatory molecules, such as tumor necrosis factor alpha (TNF-alpha) and interleukin-6 (IL-6), in fetuses of mothers with GDM. These inflammatory molecules interfere with neurogenesis and synaptogenesis, processes critical for normal brain development (BORUJENI et al., 2024).

Behaviorally, the offspring of diabetic mothers demonstrate anomalies that go beyond the cerebellar structures, influencing cognitive and motor functions. The literature points to a negative correlation between GDM and performance on cognitive and memory tests, indicating that neurophysiological changes have far-reaching consequences. Research highlights the importance of universal screening strategies during pregnancy to identify early and manage GDM, potentially reducing the risk of CNS abnormalities in the offspring (BORUJENI et al., 2024).

Gestational diabetes mellitus (GDM) is a condition that can cause serious complications during pregnancy, including significant effects on the development of the central nervous system (CNS) of the fetus. Studies have shown that GDM can impair the development of the cerebellum, leading to morphological and molecular changes. Maternal hyperglycemia causes hyperglycemia in the intrauterine environment, affecting the fetus and resulting in fetal hyperinsulinemia, which in turn compromises the morphogenesis of the cerebellar cortex. This affects the function of glial and neuronal cells, which are crucial for neuronal migration. (BIETE; VASUDEVAN, 2024).

Oxidative stress caused by GDM increases the production of reactive oxygen species (ROS), damaging proteins, lipids, and DNA, and resulting in apoptosis of neuronal cells. In addition, chronic inflammation associated with GDM increases inflammatory molecules such as TNF-alpha and IL-6, aggravating neuronal damage. MicroRNAs dysregulated in DMG also negatively affect neurogenesis and synaptogenesis, while dysregulation of proteins such as synaptophysin and insulin and IGF-1 receptors compromises the formation of cerebellar synapses. (BIETE; VASUDEVAN, 2024).

Clinical studies and animal models demonstrate that these changes result in reduced cerebellar volume, thickness of the cortical layers, and number of neuronal cells, highlighting the importance of glycemic control during pregnancy. GDM is also associated with neurobehavioral problems in offspring, such as learning disabilities and memory impairment. (BIETE; VASUDEVAN, 2024).

In summary, GDM represents a significant challenge for maternal and fetal health, with direct implications for the neurological development of offspring. Early interventions, especially through insulin administration, show promise for minimizing adverse impacts on cerebellum development and subsequent cognitive and motor functions. Therefore, continued clinical attention and ongoing research are crucial to fully understand and mitigate the effects of GDM on fetal development (BORUJENI et al., 2024).

In conclusion, Gestational Diabetes Mellitus has a significant impact on the health and development of the fetus. Complications associated with GDM, such as macrosomia, neonatal hypoglycemia, respiratory distress syndrome, hyperbilirubinemia, polycythemia, hypocalcemia, hypomagnesemia, iron deficiency, and neurological abnormalities, highlight the importance of tight glycemic control and adequate follow-up during pregnancy to reduce the risks associated with GDM and improve outcomes for the infant.

The treatment of Gestational Diabetes Mellitus (GDM) is essential to minimize the risks for both the mother and the fetus. Proper management of GDM involves a combination of non-pharmacological and pharmacological interventions, with the aim of keeping blood glucose levels within a healthy range and preventing associated complications.

NON-PHARMACOLOGICAL INTERVENTIONS

Nutritional therapy is the first line of treatment for GDM. A balanced diet that is high in fiber and low in simple sugars can help control blood glucose levels in women with GDM (Sánchez-García et al., 2023). The inclusion of polyunsaturated fatty acids, such as DHA and EPA, from food sources such as fish and vegetable oils, has also been shown to be beneficial in the prevention and management of GDM (Sánchez-García et al., 2023). In addition, supplementation of specific micronutrients, such as vitamin D, magnesium, and selenium, can improve insulin sensitivity and reduce the incidence of complications associated with GDM (Long; Liang, 2024).

Regular exercise is another important nonpharmacologic intervention in the management of GDM. Physical activity helps improve insulin sensitivity and control blood glucose levels. It is recommended that pregnant women with GDM perform at least 30 minutes of moderate physical activity on most days of the week, unless there are medical contraindications (Calvo et al., 2024).

Regular monitoring of blood glucose levels is critical for the management of GDM. Pregnant women are encouraged to monitor their glucose levels several times a day, including fasting and after meals. Goals for glycemic control typically include fasting glucose levels below 95 mg/dL and postprandial glucose levels (one hour after a meal) below 140 mg/dL (Calvo et al., 2024).

Health education is a crucial part of managing GDM. Pregnant women should be informed about the importance of glycemic control, available treatment options, and strategies to prevent complications. Diabetes education programs can provide additional support and help pregnant women develop self-care skills (Calvo et al., 2024).

The management of Gestational Diabetes Mellitus involves a multifaceted approach that includes non-pharmacological interventions, regular glycemic monitoring, and, when necessary, pharmacological therapy. Nutritional therapy and exercise are critical for glycemic control, while insulin and other oral hypoglycemic agents may be necessary to achieve glycemic goals. Health education and ongoing support are essential to help pregnant women manage their condition and prevent complications. Implementing these strategies can significantly improve health outcomes for both mother and baby.

Treatment of gestational diabetes mellitus (GDM) may include the use of oral medications, such as metformin and glibenclamide, especially when nonpharmacologic interventions and insulin are not sufficient or feasible. These medications offer effective alternatives for glycemic control during pregnancy.

PHARMACOLOGICAL INTERVENTIONS

Insulin treatment is a crucial part of the management of gestational diabetes mellitus (GDM) when non-pharmacological interventions, such as nutritional therapy and exercise, are not sufficient to keep blood glucose levels within the desired range. The administration of insulin aims to control hyperglycemia and prevent complications associated with GDM for both the mother and the fetus.

Insulin is indicated for pregnant women with GDM who cannot reach target glycemic levels with changes in diet and physical activity alone. Goals for glycemic control usually include fasting glucose levels below 95 mg/dL and postprandial glucose levels (one hour after a meal) below 140 mg/dL. If glucose levels persist above these targets despite non-pharmacological interventions, insulin therapy becomes necessary (Calvo et al., 2024).

There are different types of insulin that can be used in the management of GDM, each with specific characteristics regarding the onset of action, peak of action, and duration of effect. The main types include:

- Rapid-Acting Insulin: This insulin is given before meals to control postprandial glucose spikes. Examples include insulin lispro, insulin aspart, and insulin glulisine. These types of insulin begin to act in about 15 minutes after injection, peak in 1 to 2 hours, and last 3 to 4 hours.
- Short-Acting Insulin: Also known as regular insulin, it is given before meals. It starts working in 30 minutes, peaks in 2 to 3 hours, and lasts 4 to 6 hours.
- Intermediate-Acting Insulin: Examples include NPH (Neutral Protamine Hagedorn) insulin, which is used to provide basal glucose control. It starts working in 1 to 2 hours, peaks in 4 to 12 hours, and lasts 12 to 18 hours.
- Long-Acting Insulin: This insulin is used to provide basal control throughout the day and night. Examples include insulin glargine and insulin detemir, which have an action duration of up to 24 hours without a pronounced peak.

The insulin administration protocol is individualized based on the specific needs of each pregnant woman. The initial dosage is usually calculated based on body weight and blood glucose levels. The dose is then adjusted as needed to achieve and maintain target glycemic levels. Frequent monitoring of blood glucose levels is essential to adjust insulin dosing and avoid both hyperglycemia and hypoglycemia (Calvo et al., 2024).

Insulin dosage may need frequent adjustments during pregnancy, due to hormonal changes and metabolic needs. Dosage adjustment is based on the results of glycemic monitoring and the clinical response of the pregnant woman to treatment. It is common for insulin needs to increase as pregnancy progresses, especially during the second and third trimesters, when insulin resistance typically increases due to the action of placental hormones (Calvo et al., 2024).

Health education is a key part of insulin treatment at GDM. Pregnant women need to be instructed on how to administer insulin correctly, including the injection technique, the sites of application, and the importance of site rotation to avoid lipodystrophy. In addition, it is important for pregnant women to know how to recognize and manage the signs of hypoglycemia, which include tremors, sweating, palpitations, intense hunger, and mental confusion (Calvo et al., 2024).

Continuous glucose monitoring (CGM) is a useful tool for pregnant women with GDM who are using insulin. CGM provides real-time information on blood glucose levels, allowing for immediate adjustments to insulin dosing as needed. This technology can help prevent episodes of hyperglycemia and hypoglycemia and improve overall glycemic control (Calvo et al., 2024).

Insulin treatment is an effective and safe approach for the management of Gestational Diabetes Mellitus when non-pharmacological interventions are not sufficient. Insulin administration, along with close monitoring of blood glucose levels and health education, is crucial for achieving glycemic control and preventing maternal and fetal complications. Individualization of treatment and frequent adjustments in insulin dosage are essential to meet the specific needs of each pregnant woman and ensure positive health outcomes.

Metformin is an oral antidiabetic that exerts its hypoglycemic action by decreasing hepatic glucose production, inhibiting gluconeogenesis. In addition, it increases insulin-mediated glucose uptake in peripheral tissues such as muscle and liver. In pregnancy, the potential benefits of using metformin include lowering blood glucose and insulin resistance. Metformin is often used as an alternative to insulin, especially in women who prefer to avoid injections or who require very high doses of insulin to achieve adequate glycemic control (Calvo et al., 2024).

Studies have shown that metformin is effective in controlling blood glucose levels in pregnant women with GDM. For example, the MiG (Metformin in Gestational Diabetes) study compared the use of metformin with the use of insulin in women with GDM and found that metformin was associated with lower maternal weight gain from baseline to 36 weeks of pregnancy. In addition, women who used metformin had lower HbA1c levels, required lower doses of insulin, and were less likely to require cesarean delivery (Calvo et al., 2024).

However, metformin crosses the placenta, and fetal concentrations of metformin are similar to or higher than those of the mother. Although studies have not found significant differences in fetal and neonatal outcomes, there are potential safety concerns that have yet to be fully clarified. The guideline of the Brazilian Diabetes Society recommends the use of metformin in cases of GDM as an alternative in case of unfeasibility of insulin use, especially in those patients who require high doses of insulin (> 2IU/kg/day) without adequate glycemic control, in addition to cases of excessive maternal or fetal weight gain (Calvo et al., 2024).

Glyburide is another oral hypoglycemic agent that can be used in the management of GDM. Glyburide works by stimulating insulin secretion by the beta cells of the pancreas. While glibenclamide is effective in glycemic control, its use is less common compared to metformin and insulin due to some limitations and safety concerns. Studies have shown that glibenclamide may be effective in controlling blood glucose levels in pregnant women with GDM. However, glibenclamide crosses the placenta to a lesser extent than metformin, but there is still a potential risk of neonatal hypoglycemia. In addition, glibenclamide may be associated with a higher risk of maternal weight gain and maternal hypoglycemia (Calvo et al., 2024).

The Brazilian Diabetes Society guideline recommends considering the use of glibenclamide in cases of GDM when insulin is not a viable option and metformin is not sufficient to achieve adequate glycemic control. However, it is important to closely monitor both the mother and fetus to avoid complications associated with the use of glibenclamide (Calvo et al., 2024).

The study by Zhang et al. (2024) highlights the comparison between metformin (MET) and insulin (INS) in the treatment of gestational diabetes mellitus (GDM), addressing both the efficacy and safety of these interventions. Metformin emerges as a viable and convenient alternative to insulin, which requires injection administration and continuous dosage adjustments based on factors such as BMI and glucose levels (Zhang et al., 2024). While insulin is effective, it presents compliance and convenience challenges that make metformin attractive to many patients. Study results indicated that metformin was associated with a significant reduction in the incidence of excessive pregnancy weight gain (PPG) and neonatal hypoglycemia compared to insulin ($P < 0.05$), which is clinically relevant as excessive weight gain can lead to complications for both mother and baby, while neonatal hypoglycemia is a potentially dangerous condition for newborns (Zhang et al., 2024).

In addition, the efficacy of metformin in glycemic control of GDM was evaluated, with no significant differences in fasting plasma glucose (GPJ) and glycosylated hemoglobin (HbA1c) levels between the groups treated with metformin and insulin, suggesting that both interventions are effective in managing blood sugar levels (Zhang et al., 2024). However, approximately 10-40% of patients may require insulin when metformin does not adequately control glycemic levels, indicating the need for insulin in more severe cases of GDM (Zhang et al., 2024). Metformin has also demonstrated advantages such as reduced weight gain and a lower incidence of neonatal hypoglycemia, reinforcing its safety in the treatment of GDM (Zhang et al., 2024). Although the analysis did not reveal significant differences in neonatal conditions such as jaundice, macrosomia, and respiratory distress syndrome between the treated groups ($P > 0.05$), the limitations of the study, such as the relatively small sample size and the exclusivity of English-language studies, were pointed out. Therefore, further studies are needed to confirm these results and explore the long-term effects of metformin in pregnant women with GDM (Zhang et al., 2024).

CONCLUSION

Gestational Diabetes Mellitus (GDM) is a significant condition that affects the health of mothers and babies during and after pregnancy. This systematic review highlights the complexity of the pathology and the wide range of complications that can arise due to maternal hyperglycemia. Among the most common complications are fetal macrosomia, neonatal hypoglycemia, respiratory distress syndrome, and increased maternal risk for type 2 diabetes and cardiovascular disease in the future.

The study highlights the importance of effective management of GDM, which includes close monitoring of glucose levels, dietary control, physical exercise, and, when necessary, pharmacological interventions such as the use of insulin or metformin. Health education and ongoing support are key to enabling pregnant women to manage their condition and prevent complications.

In addition, early identification and tight control of GDM can mitigate its adverse effects and significantly improve health outcomes for mothers and infants. Future studies are needed to deepen the understanding of the mechanisms underlying GDM and to develop more effective interventions. Therefore, continuous attention and scientific research are crucial to reduce the impact of GDM and promote maternal and fetal health.

To address the challenges associated with Gestational Diabetes Mellitus (GDM), a variety of social and community interventions are essential. Health education programs, such as workshops, lectures, and educational materials, are essential to inform pregnant women and women of childbearing age about GDM prevention and management. Support groups, both face-to-face and online, provide a space for exchanging experiences and emotional support. Community physical activity programs, such as specific classes for pregnant women and partnerships with gyms, encourage the practice of exercises that help with glycemic control. Awareness campaigns and free glucose testing events increase early detection and awareness of GDM. Nutritional support, through consultations and health food fairs, promotes a balanced diet. In addition, the continuous training of health professionals and the integration of multidisciplinary teams ensure effective and up-to-date care. These collective interventions can significantly improve health outcomes for mothers and infants, highlighting the importance of a holistic and community-based approach in managing GDM.

REFERENCES

1. BIETE, Michelle; VASUDEVAN, Sona. Gestational diabetes mellitus: Impacts on fetal neurodevelopment, gut dysbiosis, and the promise of precision medicine. Frontiers in Molecular Biosciences, v. 11, p. 1420664, 2024.

2. BORUJENI, Mohammad Javad Saeedi et al. Gestational Diabetes Mellitus and its Effects on the Developing Cerebellum: A Narrative Review on Experimental Studies. Iranian Journal of Child Neurology, v. 18, n. 2, p. 9, 2024.

3. BUCCI, Tommaso et al. Five-year risk of all-cause death and cardiovascular events in women with gestational diabetes and hypertensive disorders of pregnancy. Current Problems in Cardiology, p. 102698, 2024.

4. CALVO, María José et al. The Placental Role in Gestational Diabetes Mellitus: A Molecular Perspective. touchREVIEWS in Endocrinology, v. 20, n. 1, p. 10, 2024.

5. FOO, Ru Xun et al. Gestational diabetes mellitus and development of intergenerational non-alcoholic fatty liver disease (NAFLD) after delivery: a systematic review and meta-analysis. Eclinicalmedicine, v. 72, 2024.

6. JIN, Yuqing et al. Gestational diabetes and risk of perinatal depression in low-and middle-income countries: a meta-analysis. Frontiers in Psychiatry, v. 15, p. 1331415, 2024.

7. LONG, Bin-Yang; LIANG, Xin. Dietary management of gestational diabetes: A review. Medicine, v. 103, n. 28, p. e38715, 2024.

8. MAÑÉ, Laura et al. Early HbA1c Levels as a Predictor of Adverse Obstetric Outcomes: A Systematic Review and Meta-Analysis. Journal of Clinical Medicine, v. 13, n. 6, p. 1732, 2024.

9. MERCADO-EVANS, Vicki et al. Gestational diabetes as a risk factor for GBS maternal rectovaginal colonization: a systematic review and meta-analysis. BMC Pregnancy and Childbirth, v. 24, n. 1, p. 488, 2024.

10. SÁNCHEZ-GARCÍA, Juan Carlos et al. Advancements in Nutritional Strategies for Gestational Diabetes Management: A Systematic Review of Recent Evidence. Journal of Clinical Medicine, v. 13, n. 1, p. 37, 2023.

11. XU, Ya-Hui et al. Association between sleep duration during pregnancy and gestational diabetes mellitus: a meta-analysis. Sleep medicine, v. 52, p. 67-74, 2018.

12. YI, Yan et al. Epigenetic modifications of placenta in women with gestational diabetes mellitus and their offspring. World Journal of Diabetes, v. 15, n. 3, p. 378, 2024.

13. ZHANG, Li et al. Comparative Study of the Impact of Metformin Versus Insulin on Adverse Pregnancy Outcomes in Women Diagnosed with Gestational Diabetes Mellitus: A Meta-Analysis. Alternative Therapies in Health & Medicine, v. 30, n. 1, 2024.