

CARDIOVASCULAR CONSEQUENCES IN NEWBORN TO PREGNANT WOMEN WITH GESTATIONAL DIABETES MELLITUS: AN INTEGRATIVE REVIEW

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Abstract: Among maternal physiological changes during the gestational period, one of the most favorable characteristics to be developed is hyperglycemia which, in the case of mothers with a predisposition to Diabetes Mellitus, can generate Gestational Diabetes Mellitus (GMD) which can negatively affect fetal development in as a result of metabolic changes. **Objective:** To identify possible cardiovascular alterations in the offspring as a consequence of Gestational Diabetes Mellitus in pregnant women. **Methodology:** An integrative literature review was carried out, based on the following databases: National Library of Medicine and National Institutes of Health (PUBMED), Embase via PUBMED and Cochrane Library, selecting articles from the last 7 years, of the type of studies randomized and randomized clinical trials, with the full text freely available, except for two articles, one from 2007 and 2015, which contributed to the discussion of this integrative review. Not including reviews, duplicates, studies that did not fit the guiding question or with inconclusive results. The following descriptors in English were used: "Effects", "Results", "Consequences", "Associations", "Cardiac", "Children", "Newborn", "Offspring", "Gestational diabetes" and "Gestational diabetes mellitus" In the search, 11,227 articles were found, of which 9 studies were considered relevant to answer the guiding question. **Results and Discussion:** For discursive purposes, the research highlighted the indispensability of glycemic control in pregnant women and proposed that the alteration in the offspring of diabetic mothers has very significant consequences on the cardiovascular development of the intrauterine fetus and the newborn, resulting in dysfunctions in the cardiac cycle. Changes in myocardial contractility and delay in conduction of electrocardiographic waves converge the significance of the relationship

between Gestational Diabetes Mellitus and cardiovascular pathologies to be evolved with child development. Furthermore, the association between cardiac morbidities and the birth of larger-for-gestational-age fetuses, both as a result of MGD, is extremely relevant, as macrosomia is found to be a precursor factor for heart disease. **Final considerations:** Therefore, clinical trials showed the importance of glycemic monitoring during pregnancy, in which the present research gathered studies with scientific relevance that intersect with the understanding of the increased risk of morbidity and mortality due to cardiovascular metabolic changes due to the occurrence of Diabetes Mellitus during pregnancy. Therefore, it is important that the newborns of mothers with this clinical condition are assisted, in addition to greater foundation of the theme with prospective scientific data for the evaluation of other possible cardiovascular alterations that children may acquire posteriori as a result of cardiac alterations in physiology of the newborn.

Keywords: Gestational diabetes. Newborn. Pediatrics.

INTRODUCTION

The clinical condition of Gestational Diabetes Mellitus refers to resistance to carbohydrates developed during pregnancy, in which, in the 2009 epidemiological data based on the US population, it was estimated that in 7% of pregnancies with complications, 86% of cases were of cases reported for gestational diabetes in women (CORREA et al., 2018). It is worth mentioning that regarding this clinical condition, several studies have also associated the occurrence and worsening of Gestational Diabetes Mellitus with risk factors such as obesity and increasing age. (BOUTHORN et al., 2015).

The pathophysiology of Gestational

Diabetes Mellitus may, in some instances, be related to changes in the function of beta cells in the pancreas, which do not produce enough insulin during pregnancy. Scientific studies suggest that the cause of this gestational resistance has the same mechanisms that cause hyperglycemia in general, including autoimmune or genetic diseases (BUCHANAN et al., 2007). Increased insulin resistance may also result from the combination of increased maternal adiposity and insulin desensitization by direct hormonal influence on the placenta (BARBOUR et al., 2007). This integrative review aims to evaluate the cardiovascular consequences of Gestational Diabetes Mellitus in the offspring of pregnant women who have this clinical condition.

METHODOLOGY

This is an integrative literature review of a descriptive nature, which sought to answer the guiding question: “What are the possible cardiovascular consequences in the offspring of a diabetic mother?”. When searching the databases, the PRISMA protocol was used to systematize the searches:

The following steps were used for the construction of this review: identification of the theme; selection of the research question; data collection by searching the scientific literature. The database was structured in electronic sources, with the establishment of inclusion and exclusion criteria to select the sample, evaluation of the studies included in the mini integrative review by the researchers in the peer modality, interpretation and presentation of the evidenced results.

The search for articles was structured in the following databases: National Library of Medicine and National Institutes of Health (PUBMED), Cochrane, Embase via PUBMED. The health science descriptors used were, via a broad search strategy according to each database: “Effects”, “Results”, “Consequences”,

“Associations”, “Cardiac”, “Children”, “Newborn”, “Offspring”, “Gestational diabetes” and “Gestational Diabetes Mellitus”

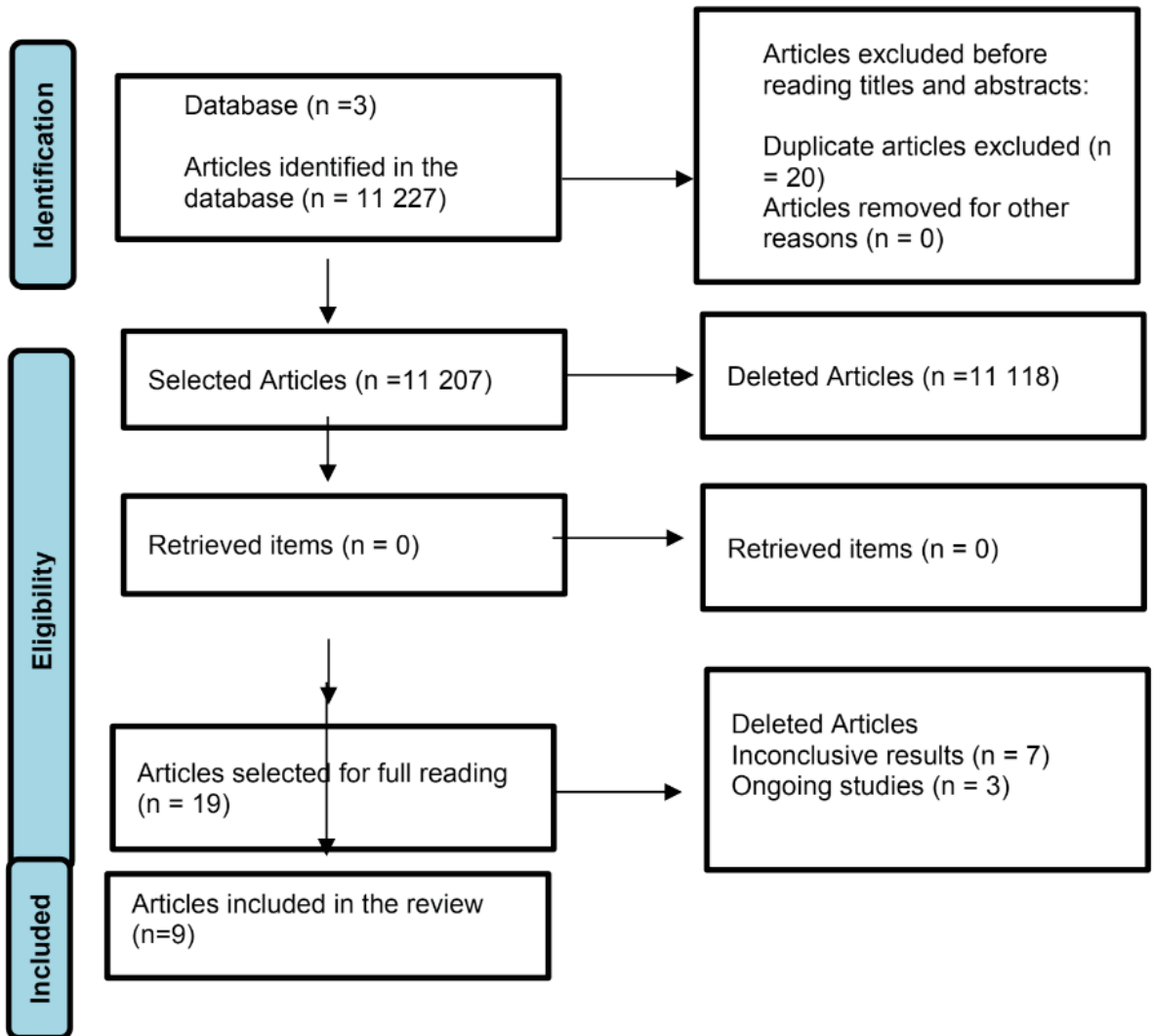
The inclusion criteria of the studies were: freely available full-text articles; studies published in the English language that brought clinical data, and articles published and indexed in the aforementioned databases and the relationship between Gestational Diabetes Mellitus (GDM) and congenital alterations. Also, articles not available in full and published before 2018 were excluded, in addition to studies not published in the form of articles, abstracts, such as monographs, dissertations and theses; comments and letters to the reader.

RESULTS

A comprehensive survey was carried out with a focus on systematizing the information from the selected articles. The extraction of data from the study was approached in a compiled and descriptive way in a table format by the researchers, a didactic format that facilitates the identification of the proposed variables and results of each primary study.

The final sample consists of 9 articles, which are identified in Table 1, with the systematization of the authors’ names, respective title, research objective, scientific method and results. Thus, the discussion of the articles was guided after reading and analyzing the structuring elements of the articles, of which it is important to mention the relationship between gestational diabetes and congenital alterations in newborns at term. In addition, the results suggest the importance of encouraging the production of relevant scientific studies, so that the association between GDM and cardiological pathologies is inserted in the academic and clinical scope and, also, for practices to be adopted, in order to reduce such incidence in the population of pregnant women in this clinical condition.

Identification of studies and analysis of databases



| AUTHOR/ YEAR | STUDY DESIGN | GOAL | MAIN RESULTS | CONCLUSIONS |
|--------------------------|---|---|--|---|
| Blais, et al. (2018) | Observational prospective study with a control group. | To evaluate myocardial muscle relaxation in unborn 3-year-old children. | The study population consisted of 29 children of GDM mothers, 36 children of IR mothers and 41 children of CTRL mothers. Compared with the CTRL group, we found a greater proportion of children in the IR group and in the GDM group who met the criteria for impaired myocardial relaxation, but this did not reach statistical significance. | Did not detect increased risk of impaired myocardial relaxation at three years of age in children exposed to insulin resistance and gestational diabetes mellitus in utero, compared with children of mothers with glycemic norms |
| Epure, et al. (2022) | Prospective cohort study | Analysis of Gestational Diabetes Mellitus and its association with sub-clinical alterations of atherosclerosis in the offspring. | The difference in CIMT between offspring of women with and without GDM was 0.00 mm (95% CI -0.01 to 0.01; p=0.96) and remained similar when adjusting for possible confounders such as index of maternal pre-pregnancy body mass, maternal education, smoking during pregnancy, family history of diabetes, as well as gender, age and body surface area of the children (0.00 mm (95% CI -0.02 to 0.01 ; p=0.45)) | They found no evidence of increased carotid intima-media thickness in newborns exposed to gestational diabetes mellitus. Longer-term follow-up that includes additional data may shed more light on cardiovascular health pathways in children born to mothers with gestational diabetes mellitus. |
| Wang, et al. (2018) | Population-based cohort study | To compare the BMI of children between children exposed to maternal DMG and those not exposed and to assess the associations between maternal hyperglycemia and the risk of overweight in their children aged 1 to 6 years. | In the results, children born to mothers with abnormal glucose during pregnancy had higher mean values of Z-scores for BMI from 1 to 6 years compared to those born to normoglycemic mothers, with P<0.05 being significant. Abnormal maternal glucose was associated with a higher risk of overweight in childhood. Children whose mothers had normal glucose during pregnancy had lower Z-BMI means (1,2,3,5,6 years). When introducing pre-gestational maternal BMI into the model, the differences were still significant among children aged 1, 2, 3 and 5 years and disappeared among children aged 4 and 6 years. Finally, associated with gender, there was a higher risk of overweight (associated with abnormal maternal glucose) in childhood in girls of all age groups, except for 3-year-olds, and a higher risk of overweight in childhood in girls aged 3 years. | CONCLUSIONS: Abnormal maternal glucose tolerance during pregnancy was independently associated with higher children's BMI and risk of overweight from 1 to 6 years of age. Women with positive GCT results (blood glucose level in mg/dL) but negative OGTT results (oral glucose tolerance test) may be overlooked by the health care system. Therefore, health services must pay more attention to the health of these mothers and to the health of their children. |
| Riskin, et al. (2020) | Retrospective observational case-control study. | Evaluation of perinatal complications in the offspring of women with gestational diabetes and gestational pre-diabetes. | The cesarean section rate was significantly higher in mothers with diabetes, both PGDM (68.1%) and GDM (47.6%) compared to only 25.9% in control women. 80.0% of children with respiratory morbidity in the PGDM group had Respiratory Distress Syndrome compared to only 34.9% in the GDM group and 14.3% in the controls (the remainder were diagnosed with Transient Tachypnea of the Neonate). Of babies born to mothers with GDM, 30% had symptomatic hypoglycemia compared with only 2.9% in babies born to mothers with GDM and none in the control group (=0.037). Rates of significant polycythemia (hematocrit > 70%) were 13.3% and 14.0% in infants born to mothers with significantly higher PGDM and GDM compared with 2.7% in controls (p < 0.001). | The risks of preterm delivery or caesarean section, large-for-gestational-age neonates, respiratory morbidity, hypoglycemia, and polycythemia were increased in infants of mothers with diabetes during pregnancy. Despite all advances in prenatal care, diabetes in pregnancy is still associated with significant morbidities. |

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|-----------------------------|-------------------------------------|---|--|--|
| Aghaei, et al. (2019) | Cross-sectional observational study | Evaluation of cardiac alterations in the offspring of diabetic mothers. | In the results, the preload index (PLI) was higher in the case group (0.57 ± 0.11) than in the control group (0.47 ± 0.11), with $p = 0.001$. The myocardial performance index (MPI) between the right and left ventricles and the cardiac outputs of the right and left sides did not differ significantly between groups. | Fetuses of gestational diabetic mothers had a higher ILP value, representing an early change in the diastolic function of the right heart even before the occurrence of heart failure, indicative of valvulopathies. |
| Bernado, S. D. et al (2017) | Cross-sectional cohort study | The objectives are to evaluate the effect of DMG on the cardiovascular health of offspring in early life using surrogate markers of cardiovascular disease and atherosclerosis. | Cohort performed with the offspring of 100 women with GDM and 100 without this clinical condition. The intrauterine LVMI (Left ventricular mass index) assessment in children of mothers without GDM is 30 g/m^2 compared to mothers with gestational diabetes of 32 g/m^2 in one sample, which promotes an alpha-level statistical significance at 0.05, which is an indicator that reveals the cardiovascular alteration established in the study's alternative hypothesis. | The result of the study, with the measurement of data that include LVMI, proposes a scientific advance that avoids biases and limitations in the study. Understanding the histological changes in tissue that the study proposes will promote greater understanding and factor in maternal glycemic control to prevent cardiovascular and metabolic disease (CVD risk) |
| Jacquemyn, et al (2023) | Observational Longitudinal Study | To evaluate and compare the myocardial function of 40 offspring of mothers with diabetes mellitus and to determine whether cardiac alterations persist during the children's prognosis. | Differences were detected in the echocardiogram (STE) with the following significant values: In global longitudinal tension ($p=0,001$), global circumferential tension ($p = 0.017$), mean radial tension ($p = 0.003$), strain rate mean longitudinal systolic strain ($p = 0.011$) and mean circumferential systolic strain rate ($p = 0.013$) compared with the control group at up to 2 years of follow-up. Minimal differences in MDG were observed over the 2-year period. | The impairment in cardiac function due to the offspring of mothers with Diabetes Mellitus (MDD) persisted during 2 years of follow-up. The assessment made may be useful for promoting changes in the treatment, conduct and screening of patients with congenital heart diseases or hypertrophic cardiomyopathy. |
| Leirgul, E. et al (2016) | Observational retrospective study | To investigate the association between pre-gestational or gestational diabetes and the risk of congenital heart defects in the offspring and the association between large birth weight for gestational age and the risk of heart defects in the offspring of diabetic women. | Of the 914,427 births performed at the hospital center where the research data were collected, 5,618 had complications due to pre-gestational diabetes and 9,726 due to gestational diabetes (GDM). Congenital cardiac alterations were found in 10 575. For pre-gestational diabetes, 561 cardiovascular alterations were found compared to 248 children per 10 000 births without alterations by GDM (In proportion) and for gestational diabetes there were 388 cases of cardiac alterations in compared to 132 per 10 000 unchanged by DMG (Ratio). | Among women with pre-gestational or gestational diabetes, having a large-for-gestational-age newborn was associated with a two- to three-fold increased risk of heart defects compared with normal-weight newborns. |
| Wu, Y et al (2020) | Observational retrospective study | To evaluate the association between Pre-gestational Diabetes and Gestational Diabetes Mellitus in 12 subtypes of congenital abnormalities in newborns. | Of the 29,211,974 live births, 90,061 babies had congenital anomalies identified at birth. The risk ratios (Risk Ratios - RR) adjusted for congenital anomalies at birth were 2.44 for pre-gestational diabetes and 1.28 for GDM. Overall, associations were consistent across subgroups by maternal age, race/ethnicity, prepregnancy obesity status, and baby's sex. For specific subtypes of congenital anomalies, maternal prepregnancy diabetes or GDM was associated with a higher risk of most subtypes, such as: Cyanotic congenital heart disease has a higher (4.61) RR for prepregnancy diabetes and a lower RR (1.50) for DMG. | Pregestational diabetes and, to a lesser extent, GDM have been associated with several subtypes of congenital anomalies in newborns. These results suggest a potential benefit of controlling glycemic indexes in preventing congenital abnormalities. |

Chart 1 - Chart 1: Articles included in the analysis of the mini integrative literature review, separated by author/year, study design, objective, main results and conclusions

According to Blais et al. (2018), understanding the relaxation of skeletal cardiac striated tissue in children is one of the basic elements in understanding the physiological changes that gestational diabetes can affect in offspring, and was addressed in their article, an observational research carried out with a control group of mothers normoglycemic women and two groups of mothers (with ongoing pregnancy) who are insulin intolerant and who acquired GDM. These group cohorts of women were submitted to tests during pregnancy, up to the first three years of their offspring, which was necessary for the purposes of a more accurate evaluation and finally to reach a positive result of influence on the myocardial contraction of the submitted, offspring of diabetic mothers, insulin intolerant and who acquired GDM during pregnancy.

The applied echocardiogram used the evaluative method of counting and timing three beats in the cardiac cycle. The technique included the evaluation of the kinetics of the “A” and “E” waves of diastole. It was concluded that offspring of insulin-intolerant mothers with GDM have a certain delay in the completion of the “E” wave in diastole, resulting in a slight delay in the cardiac cycle as a whole. (BLAIS et al., 2018).

According to Epure et al. (2022), histological changes in newborns contribute to understanding whether possible changes in rhythm, relaxation and tissue contraction are related to glycemic changes during the gestational period. At first, no significant differences were found in carotid intima-media thickness (CIMT) between newborns of mothers with and without GDM. When adjusting for offspring sex and potential confounders, the difference in CIMT between offspring of mothers with and without GDM was 0.00mm and there was no significant difference after other adjustments such as body

surface area and age. This work is a prospective cohort study, which included 137 pregnant women without exposure to DMG and 212 pregnant women with exposure to DMG. Of the study participants, 101 newborns were not exposed to DMG and 117 were exposed to DMG. Of these, 200 newborns were born at more than 36 weeks of gestation.

The study also showed that more mothers with GDM developed obesity, around 16%, and that smoking during pregnancy was more frequent among women with GDM (18%). Most newborns (96% with GDM and 98% without GDM) were born at term, between 37 and 41 weeks, and few were born with macrosomia. (6% with GDM and 5% without GDM) (EPURE et al., 2022).

In view of the metabolic study by Wang et al. (2018), the existence of an association between gestational diabetes and the growth of the offspring (from birth to 6 years of age) guided the study, which aimed to understand whether this systemic alteration in changes in the intrahepatic lipid content of the offspring. The study shows that children born to mothers with abnormal glucose levels during pregnancy had higher values of Z-scores for body mass index (BMI) at ages 1, 2, 3, 5 and 6 years, compared to those born to mothers with normal glucose. It was visualized that mothers with GDM were older and had a high pre-pregnancy BMI. Children whose mothers had normal glucose during pregnancy had lower mean Z-BMI across all age groups. 5.5% of mothers were diagnosed with GDM, these were older and had a higher prepregnancy BMI and lower gestational weight gain 8% of mothers failed the GCT test and passed the OGTT test (gct+ogtt-). The study analyzed the risk of overweight in childhood, and the incidence of GDM in mothers, considering the pre-pregnancy maternal BMI and the child's gender.

In the case of unicentric research, as in the

study by Riskin et al. (2020), which addresses, with sample significance, the current situation of newborns of mothers with diabetes mellitus during pregnancy compared to pregnant women with normal blood glucose levels. In this approach, the authors make a distinction between risk factors for neonatal morbidities in which the specific conditions of children of mothers with GDM and children of pre-pregnancy diabetic mothers (PMDG) are segregated, even before pregnancy, with children of mothers not diabetic. Within this scope, it is concluded that there is a true clinical association with the pregnancy of a diabetic mother, both for the case of pregnant diabetes and for mothers with diabetes diagnosed before pregnancy.

The result is that PMDG mothers are highly likely to have offspring with low weight for gestational age (SGA), with respiratory morbidities, congenital anomalies and intrauterine death, while DMG mothers are more likely to have large-for-gestational-age (LGA) children, polycythemia and hypertrophic cardiomyopathy. In addition, the cesarean rate increased and the incidence of premature fetuses and hypoglycemia occurred for both maternal conditions, compared to pregnancy without GDM (RISKIN et al., 2020).

Still within the analysis, for Aghaei et al. (2019), when understanding the relevance of the investigation of gestational diabetes in the effects of the offspring, a large research that was destined to the evaluation of the cardiac alterations of newborns of diabetic mothers, in comparison with healthy pregnant women. The study was observational and took place at the Children's Medical Center in Tehran, Iran, between March 2016 and 2017. A total of 75 women were recruited, of which 25 were diagnosed with gestational diabetes and 50 were healthy. The evaluations took place from 18 to 23 weeks of gestation and the reference

values for glycemic control were defined using the criteria of the World Health Organization. The myocardial performance index (MPI) between the right and left ventricles and the cardiac outputs of the right and left sides did not differ significantly between groups.

For Bernardo et al. (2017), aimed to evaluate the impact of gestational diabetes on the cardiovascular health of offspring during the first years of life, using surrogate markers for cardiovascular disease and atherosclerosis, since there is an intimate pathophysiological relationship between these changes. Thus, he conducted a cohort involving 100 children born to mothers with gestational diabetes and 100 born to mothers without this condition. The collection of results provided important scientific advances by avoiding biases and limitations in the study. Understanding the histological alterations proposed by the study can contribute to better glycemic control in mothers, reducing the risk of cardiovascular and metabolic diseases in the offspring, supporting the null hypothesis that GDM would be a precursor to cardiac alterations.

The study proposed by Jacquemyn et al. (2023) was guided by the observation that the alterations persisted during the prognosis of up to 2 years. Significant differences were identified in echocardiogram (STE) results for global longitudinal strain, global circumferential strain, mean radial strain, mean longitudinal systolic strain rate, and mean circumferential systolic strain rate compared to the control group. These findings indicate that there is impairment in cardiac function in the offspring of mothers with diabetes mellitus and that this persisted during the 2 years of follow-up. Furthermore, in the study by Wu et al. (2020), the same congruence of results is observed, but with a different approach, in which they evaluated the association between pre-gestational diabetes and gestational diabetes mellitus

in 12 subtypes of congenital anomalies in newborns. Pregestational maternal diabetes and gestational diabetes mellitus increased the risk of several subtypes of congenital anomalies. The results highlighted the importance of controlling glycemic levels in preventing congenital abnormalities in newborns.

Finally, the study by Leirgul et al (2016) in which the association between pre-gestational or gestational diabetes and the risk of congenital heart defects in the offspring was investigated, as well as the association between high birth weight for gestational age and the risk of heart defects in children of women with diabetes, such that they indicated that both pre-gestational and gestational diabetes were associated with a higher risk of heart defects in the offspring. Furthermore, having a large-for-gestational-age newborn increased the risk of heart defects two to three times compared to normal-weight newborns in mothers with diabetes, suggesting greater prenatal glycemic control.

DISCUSSION

In the work by Blais, et al. (2018) allows the discussion that GDM can directly interfere with the relaxation of the musculature of the skeletal cardiac striated tissue in children and can affect the offspring. The mothers' blood glucose test was performed during delivery in the umbilical cord, with maternal permission. In this process, children and their possible congenital or chronic heart diseases were followed up, and they were eliminated from the study, so that only the consequences of insulin intolerance/GDM in mothers and consequences in the offspring could be evaluated.

Another method of making the survey more accurate was the fact that the study was based on women with similar age profiles and similar lifestyles. This mechanism prevents many

factors from being considered in the analysis of cardiac relaxation in children. The initial assessment in neonates and later in children included measurements of C-peptide, insulin in children and standardized anthropometry, with the addition of BMI measurements specific to sex and age. To assess the degree of relaxation, an echocardiogram was used in children, administered by pediatricians (BLAIS et al., 2018)

The applied echocardiogram used the evaluative method of counting and timing three beats in the cardiac cycle. This assessment was thorough for all children in the three groups. The technique was performed with an echocardiogram and included the evaluation of the kinetics of diastole "A" and "E" waves, which confirmed the hypothesis that children born to insulin-intolerant mothers with GDM have the completeness of the "E" wave slower, with a standard deviation of speed of 2.5 on the standardized international scale for measuring the cardiac cycle, which is considered significant for delay in diastole (BLAIS et al., 2018).

It was observed in the study by Epure et al. (2022), the subclinical alteration of atherosclerosis, in which it does not indicate typical signs and symptoms of the pathology. Mothers with GD were analyzed and it was concluded that the difference in the thickness of the carotid intima was minimal and remained similar with the control population used. However, understanding the pathophysiology of gestational diabetes and its histological changes, the authors point out the need for clinical studies that follow the cardiovascular trajectory in children who were born to mothers with Gestational Diabetes Mellitus, which is in line with the objective of the present study.

It was observed in the study by Wang et al. (2018) that abnormal maternal glucose is associated with a higher risk of overweight

in all age groups, especially in girls. However, significant differences disappeared between 4- and 6-year-olds when prepregnancy maternal BMI was considered. The study reinforces the importance of proper monitoring during pregnancy to avoid possible complications and ensure the health of mother and baby.

Some important morbidities were also observed in the study by Riskin et al. (2020), regarding LGA offspring, associated with mothers with gestational diabetes, the higher incidence of cesarean deliveries in these cases is discussed, with risk factors associated with complications in childbirth, such as bone lesions and asphyxia, resulting from fetal macrosomia. There is also an emphasis on the physiology of some morbidities in relation to hyperinsulinism, such as hypoxia, which generates an increase in erythropoietin, causing polycythemia, and the deposition of glycogen and fat in myocardial cells, causing hypertrophic cardiomyopathy. In addition, another interesting inference is made about the physiological feedback relationship of insulin with body growth factors, which cause the fetus of the DMG mother to be born with a weight greater than the standard for gestational age (LGA). It is worth mentioning that this information, such as the fact that GDM mothers are more likely to have cesarean sections, a greater propensity for neonatal morbidity and LGA fetuses, compared to mothers without diabetes, are confirmed by Battarbee et al. (2020).

It was observed in the study by Aghaei et al. (2019), that the impairment of cardiac function in fetuses of diabetic mothers during the second and third trimester is well established. The MPI is increased in fetuses of diabetic mothers, regardless of the onset of diabetes and without differences between the right and left sides. Cardiac output on both sides of the heart was similar to that of healthy fetuses. Comparatively, fetuses of mothers

affected by GD showed, in a deeper analysis, a higher value for ILP. This increase in PLI represents an early change in the diastolic function of the right heart, which warns of future heart failure and the need for clinical attention for the offspring of mothers with GDM (BLASS et al., 2018).

Studies by Jacquemyn et al. (2023), Wu et al. (2020) and Leirgul et al. (2016) highlight the relevance of glycemic control during pregnancy and its association with cardiovascular health and fetal development. The research in question has shown that both pre-gestational and gestational diabetes are linked to a higher risk of congenital heart defects in offspring. The significant differences found in the results of the echocardiograms, such as global longitudinal tension, global circumferential tension and other rates of systolic deformation, point to an impairment in the cardiac function of children of mothers with diabetes mellitus, and this alteration persists for up to two years after birth.

In addition, studies also highlighted the importance of glycemic control to prevent congenital abnormalities in newborns, such as the study by Wu et al. (2020) who classified cardiovascular risks according to abnormalities, which reinforced the importance of glycemic control in which most of the null hypotheses expressed in the articles analyzed in this review addressed. Thus, maternal diabetes, both pre-gestational and gestational, was associated with an increased risk of several subtypes of cardiac anomalies in the offspring. Furthermore, high birth weight for gestational age was also associated with a higher risk of heart defects in children of diabetic women. These findings emphasize the need to closely monitor blood glucose levels during pregnancy, seeking adequate control, which can contribute to the prevention and reduction of cardiovascular complications in newborns. These findings

have important implications for clinical practice and underscore the importance of interventions aimed at effectively controlling diabetes during pregnancy, seeking to promote cardiovascular health in both mother and offspring.

CONCLUSION

Scientific studies, therefore, using the descriptors proposed by the authors, have led to the exploration of a correlation between the occurrence of gestational diabetes mellitus (GDM) and the emergence of various cardiovascular syndromes. The main effects of gestational diabetes on offspring, as elucidated collectively by these articles, from their unique perspectives, include cardiovascular comorbidities, which include delayed completion of the “E” wave in heart rhythm, hypertrophic cardiomyopathy, and increased preload. Furthermore, fetal macrosomia has been associated with the existence of cardiovascular problems in the offspring. In a broad sense, a noteworthy finding in these studies is the considerable increase in morbidity due to physiological changes resulting from gestational diabetes. In addition, the occurrence of premature births may be one of these metabolic alterations provided by the increase in glycemic levels. However, it is essential to recognize that the existing body of research in this field still lacks comprehensive data and prospective follow-up, which highlights the need for further investigations to avoid any congenital pathologies.

In light of these findings, it becomes increasingly evident that the control of glycemic levels in pregnant women during pregnancy is of paramount importance, as it has been shown that uncontrolled gestational Diabetes Mellitus (GDM) can affect not only the mother’s health, but also the well-being of the growing fetus. Therefore, this review study

offers valuable insights into cardiovascular health that must resonate with health care providers and policy makers, leading them to prioritize the development of effective interventions and coping strategies for gestational diabetes.

An effective way to prevent MGD would be glycemic control, since by meticulously controlling blood sugar levels, mothers can significantly reduce the risk of complications for themselves and their children. This strategy can effectively reduce the incidence of congenital heart syndromes, considering that the data converge on the predominance of this type of pathology in children born to mothers with gestational or pre-gestational diabetes. It is critical that healthcare professionals educate pregnant women about the importance of adhering to prescribed dietary regimens, monitoring blood glucose levels regularly, and following medication schedules as needed.

Furthermore, the results of this review study underscore the relevance of initiating more clinical research efforts in this domain. Researchers must look to build on these findings and embark on studies with more extensive datasets and robust, long-term prospective follow-ups. Prospective studies have the potential to reveal deeper insights into the causal relationships between gestational diabetes and associated cardiovascular complications in offspring. Furthermore, by adopting a longitudinal approach, researchers can assess the interaction of various factors, both genetic and environmental, that may influence the development of congenital cardiovascular disorders and their classes in children exposed to gestational diabetes.

Proposal: “Therefore, researchers must adopt a more longitudinal approach in order to evaluate the DGM more comprehensively, which in several aspects may result in greater consequences, in addition to those already mentioned above.”

In conclusion, as the knowledge base expands, it is possible that future investigations may reveal new therapeutic targets or preventive measures to mitigate the adverse effects of gestational diabetes on the health of the offspring. By deepening our understanding of underlying mechanisms, researchers can design interventions that target specific pathways, possibly interrupting the cascade of events that lead to cardiovascular morbidities and other metabolic sequelae. This way, these research results serve as catalysts for further exploration, paving the way for innovative approaches in the management and prevention of MGD and its associated complications.

This study serves as a wake-up call for healthcare professionals, urging them to prioritize gestational diabetes management and patient education. Furthermore, it highlights the urgent need for more comprehensive research with prospective follow-up to deepen our understanding of long-term implications and pave the way for preventive measures and improved therapeutic interventions. By investing in more research and implementing evidence-based approaches, we can work towards a future where the adverse effects of gestational diabetes are minimized, ensuring the well-being of mothers and their precious children.

REFERENCES

- AGHAEI, M. *et al.* Presenting the Preload Index. *Iranian Journal of Pediatrics*, v. 29, n.2, p. 86450, 2019.
- BARBOUR, L. A. *et al.* Cellular Mechanisms for Insulin Resistance in Normal Pregnancy and Gestational Diabetes. *Diabetes Care*, 30(Supplement_2), S112–S119, 2007.
- BATTARBEE N. A. *et al.* The association of pregestational and gestational diabetes with severe neonatal morbidity and mortality. *J Perinatol.* v;40(2), p.232-239, 2020.
- BERNADO, S. D. *et al.* Assessing the consequences of gestational diabetes mellitus on offspring's cardiovascular health: MySweetHeart Cohort study protocol, Switzerland. *BMJ Journals*, v.7, n.1, p. 1- 8, 2017.
- BLAIS, S. *et al.* Effect of gestational diabetes and insulin resistance on offspring's myocardial relaxation kinetics at three years of age. *PLOS ONE*, 13(11), e0207632, 2018.
- BOUTHOOORN, S. H. *et al.* Low-educated women have an increased risk of gestational diabetes mellitus: the Generation R Study. *Acta Diabetologica*, 52(3), 445–452, 2015.
- BUCHANAN, T. A., *et al.* What Is Gestational Diabetes?. *Diabetes Care*, 30(Supplement_2), S105–S111, 2007.
- CORREA, A. *et al.* Trends in Prevalence of Diabetes Among Delivery Hospitalizations, United States, 1993–2009. *Maternal and Child Health Journal*, 19 (3), p. 635–642, 2015.
- EPURE, A. M. *et al.* Gestational diabetes mellitus and offspring's carotid intima–media thickness at birth: My Sweet Heart Cohort study. *BMJ Open*, 12(7), e061649.
- JACQUEMYN, *et al.* Impaired myocardial deformation persists at 2 years in Offspring of mothers with diabetes mellitus. *Pediatric Research*, v. 93, n.1, p. 1-7, 2023.
- LEIRGUL, E. *et al.* Maternal Diabetes, Birth Weight, and Neonatal Risk of Congenital Heart Defects in Norway, 1994-2009. *Obstetrics & Gynecology*, v. 128, n. 5, p. 1116-1125, 2016.
- PEDERSEN J. **A diabética grávida e seu recém-nascido.** 2 ed. Munksgaard: Editora Manole, 1979
- RISKIN, A. *et al.* Perinatal Outcomes in Infants of Mothers with Diabetes in Pregnancy. *The Israel Medical Association journal :IMAJ* vol. 22,9 p. 569-575, 2020.
- WANG, J. *et al.* Gestational diabetes and offspring's growth from birth to 6 years old. *International Journal of Obesity*, v. 43, n. 4, p. 663–672, 2019.
- WU, Y. *et al.* Association of Maternal Prepregnancy Diabetes and Gestational Diabetes Mellitus With Congenital Anomalies of the Newborn. *Diabetes Care*, v. 43, n.12 p. 2 983 – 2990, 2020.