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Does gestational diabetes mellitus influence the morphological characteristics of the placenta?

O diabetes mellitus gestacional influencia as características morfológicas da placenta?

¿La diabetes mellitus gestacional influye en las características morfológicas de la placenta?

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Abstract

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance, with a decrease in insulin sensitivity during pregnancy, with recognition in the second or third trimester of pregnancy and disappearing after delivery. This mini-review is to provide a broad view of some recent studies that investigated the placental morphology in cases of maternal diagnosis of gestational diabetes. A literature search was carried out in PubMed, Medline, Google Scholar data sources, verifying the morphological characteristics of the placenta in situations of diagnosis of gestational diabetes, through prospective and observational studies, with the key terms "gestational diabetes", "placenta" and 'morphological". We show, in table format, the studies carried out between 2015 and 2020 with the main placental morphological changes that reflect the condition of pregnant women with diabetes mellitus, the most considered in the literature, increase in placental weight and thickness. It was evident that there are still few studies on placental changes, requiring the encouragement of scientific productions on the approach. In conclusion, understanding the mechanism of placental development allows the assessment of changes when pregnant women are diagnosed with GDM, taking into

account therapeutic strategies that can intervene in glycemic and metabolic control, in order to ensure maternal-fetal health.
Keywords: Gestational; Diabetes; Placenta; Morphological and microscopic findings.

Resumo

O diabetes mellitus gestacional (DMG) é definido como qualquer grau de intolerância à glicose, com diminuição da sensibilidade à insulina durante a gestação, com reconhecimento no segundo ou terceiro trimestre de gestação e desaparecimento após o parto. Esta mini-revisão é fornecer uma visão ampla de alguns estudos recentes que investigaram a morfologia placentária em casos de diagnóstico materno de diabetes gestacional. Foi realizada uma busca bibliográfica nas fontes de dados PubMed, Medline, Google Acadêmico, verificando as características morfológicas da placenta em situações de diagnóstico de diabetes gestacional, por meio de estudos prospectivos e observacionais, com os termos-chave “diabetes gestacional”, “placenta” e “morfológico”. Mostramos, em formato de tabela, os estudos realizados entre 2015 e 2020 com as principais alterações morfológicas placentárias que refletem a condição da gestante com diabetes mellitus, a mais considerada na literatura, aumento do peso e espessura placentária. Evidenciou-se que ainda são poucos os estudos sobre alterações placentárias, sendo necessário o incentivo de produções científicas sobre a abordagem. Em conclusão, compreender o mecanismo de desenvolvimento placentário permite avaliar as alterações quando gestantes são diagnosticadas com DMG, levando em consideração estratégias terapêuticas que podem intervir no controle glicêmico e metabólico, a fim de garantir a saúde materno-fetal.
Palavras-chave: Gestacional; Diabetes; Placenta; Achados morfológicos e microscópicos.

Resumen

La diabetes mellitus gestacional (DMG) se define como cualquier grado de intolerancia a la glucosa, con disminución de la sensibilidad a la insulina durante el embarazo, reconociéndose en el segundo o tercer trimestre del embarazo y desapareciendo después del parto. Esta mini-revisión es para brindar una visión amplia de algunos estudios recientes que investigaron la morfología placentaria en casos de diagnóstico materno de diabetes gestacional. Se realizó una búsqueda bibliográfica en las fuentes de datos PubMed, Medline, Google Scholar, verificando las características morfológicas de la placenta en situaciones de diagnóstico de diabetes gestacional, a través de estudios prospectivos y observacionales, con los términos clave “diabetes gestacional”, “placenta” y 'morfológico'. Mostramos, en formato de tabla, los estudios realizados entre 2015 y 2020 con los principales cambios morfológicos placentarios que reflejan la condición de las gestantes con diabetes mellitus, el más considerado en la literatura, aumento de peso y grosor placentario. Se evidenció que aún existen pocos estudios sobre alteraciones placentarias, siendo necesario el fomento de producciones científicas sobre el abordaje. En conclusión, comprender el mecanismo de desarrollo placentario permite evaluar los cambios cuando las gestantes son diagnosticadas con DMG, teniendo en cuenta estrategias terapéuticas que puedan intervenir en el control glucémico y metabólico, con el fin de garantizar la salud materno-fetal.
Palabras clave: Gestacional; Diabetes; Placenta; Hallazgos morfológicos y microscópicos.

1. Introduction

In 1674, the British physician Thomas Willis introduced the term 'diabetes mellitus' (DM), defining it as 'Pissing Evil', but it was only in 1776 that Matthew Dobson associated the urine of diabetics with an increase in glucose in the body (Vecchio et al., 2018). Understanding DM generated studies related to the anatomy of the pancreas, allowing, in 1921, the knowledge of insulin, a peptide hormone with the function of controlling glucose metabolism, enshrining in the commemoration of the centenary of the discovery of insulin in 2021 (Vecchio et al., 2018; Mbanya & Mba, 2021).

Currently, DM is a chronic disease, described as a group of disorders, whose main characteristic is the elevation of blood glucose (Cho et al., 2018). This increase in blood glucose levels can lead to microvascular complications, affecting the retina, kidneys and peripheral nerves, and macrovascular complications such as clinical conditions of myocardial infarction, stroke and peripheral arterial disease (Egan & Dinneen, 2019; Diabetes Canada Clinical Practice Guidelines Expert Committee et al., 2018).

It has had an impact on people's quality of life, being among the 10 leading causes of death, with global prevalence estimates of 578 million in 2030 and 700 million in 2045, with a greater occurrence in developed countries (Saeedi et al., 2019). This phenomenon is influenced by obesity and unhealthy behaviors, evidenced by poor diet and sedentary lifestyle (Forouhi & Wareham, 2019).

Blood glycemic values associated with the diagnostic status of DM correspond to the following aspects: (1) fasting plasma glucose test (FPG) > 126 mg/dL (7.0 mmol/L) twice; (2) two hours of plasma glucose > 200 mg/dL (11.1 mmol/L) during the oral glucose tolerance test (OGTT); and (3) glucose values > 200 mg/dL (11.1 mmol/L) at any time of day are considered diabetic. Regarding the pre-diabetic condition, glucose levels between 100 and 126 mg/dL in fasting are considered, or > 140 mg/dL, but < 200 mg/dL after 75 g of glucose during OGTT, due to, possibly, present alterations in the metabolism of carbohydrates. Regarding normal glycemic values, consider those below 100 mg/dL in fasting or below 140 mg/dL with two hours of plasma glucose during OGTT (Diabetes Canada Clinical Practice Guidelines Expert Committee et al., 2018).

DM can be classified into four categories, corresponding to: type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes mellitus and other specific types of diabetes (Egan & Dinneen, 2019).

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance, with a decrease in insulin sensitivity during pregnancy, with recognition in the second or third trimester of pregnancy and disappearing after delivery (Arshad, Karim & Hasan, 2014). However, the pathophysiology and effects of GDM remain unclear, mainly related to the extent to which glycemic control can determine placental abnormalities (Huynh et al., 2015).

This antepartum pathological condition affects about 9-25% of pregnant women worldwide (Alejandro et al., 2020). The etiology is multifactorial, involving risk factors such as overweight or obesity, inadequate diet, high blood pressure, micronutrient deficiencies, endocrine dysfunction, advanced maternal age and family history of diabetes, which can influence changes in blood glucose levels, resulting in chronic hyperglycemia during the pregnancy (American Diabetes Association, 2020; Plows et al., 2018; Zaugg et al., 2020).

Studies investigated placental changes related to gestational diabetes due to the prevalence of an increase in large or small-for-gestational-age babies. Women with gestational diabetes are more likely to develop type 2 diabetes mellitus after childbirth (Ehlers et al., 2021; Li et al., 2020).

The proper development of the placenta is essential for the health of the fetus and the mother, but as disorders that promote changes in the organ can compromise pregnancy and childbirth, generating the susceptibility of pre-eclampsia, premature birth, fetal malformation, increased fetal growth, infection, hyperbilirubinemia, miscarriage and stillbirth (Turco & Moffett, 2019).

Studying the morphological changes in the placenta related to GDM becomes pertinent. The main objective of this mini-review is to provide a broad view of some recent studies that investigated the placental morphology in cases of maternal diagnosis of gestational diabetes.

2. Methodology

A literature search was carried out in PubMed, Medline, Google Scholar data sources, verifying the morphological characteristics of the placenta in situations of diagnosis of gestational diabetes, through prospective and observational studies, with the key terms “gestational diabetes”, “placenta” and ‘morphological”.

3. Results and Discussion

3.1 Placenta: morphological characteristics

Placenta is a complex fetal organ, essential for embryo growth, functioning exclusively for the gestational period (Berceanu et al., 2018; Gauster et al., 2012). Placenta maintains nutritional, endocrine and immunological functions, allowing residual elimination and gas exchange between mother and fetus (Berceanu et al., 2018). The human placenta is developed during pregnancy, being completed at the end of the second trimester, with the main function of maintaining a maternal-fetal bonding interface (Silini et al., 2020).

The shape is discoid, measuring 2-4 cm thick, and may maintain locations in the anterior, posterior, lateral or fundal region, as the growth of placental tissue provides migrations to different positions throughout the first 15 weeks of pregnancy (Oppenheimer et al., 2020).

The placenta, at the end of the gestational period, presents weight measurements, approximately 530 g; diameter, approximately 16 cm, with approximately 17 cm of central thickness, 450 cubic cm in volume and 18 cotyledons, being differentiated depending on the type of delivery, position of the umbilical cord and the time of delivery (Carrasco-Wong et al., 2020).

The placenta has endocrine actions, secreting more than 100 peptides and steroid hormones, contributing to the modulation of maternal physiology and metabolism, ensuring protection and safety for the development of the fetus (Burton & Jauniaux, 2015).

The main hormones produced by the placenta are estrogen, progesterone, cortisol, somatotropin, human chorionic, placental lactogenic hormone, prolactin (Edu et al., 2016). As the placenta grows, there is a risk of insulin resistance (Yi-xiao et al., 2020).

3.2 Placenta and Gestational Diabetes: morphological characteristics

Although the effects and pathophysiology of GDM are not yet fully understood, the gestational period is considered a diabetogenic phase, due to hormonal imbalance, evidenced by insulin sensitivity and pancreatic beta cell dysfunction (Alejandro et al., 2020; Edu et al., 2016).

Increased villous immaturity, corangiosis, ischemia, clinical hyperglycemia, hyperlipidemia, hyperinsulinemia and placental endothelial dysfunction are associated with GDM, which can lead to fetal morbidity and stillbirth (Ramírez-Emiliano et al., 2017; Kadivar et al., 2020).

In the literature, it is widely described about GDM generating structural changes in the placenta such as increased placental weight (Table 1), leading to complicated pregnancies, influenced by decreased fetal oxygenation and increased lactate concentration (Pooransari et al., 2020; Bianchi et al., 2021).

Table 1. Morphological changes.

Study type	Sample size (n)	Findings	Ref.
Prospective study	Total (n=222) GDM (n=117) Control group (n=105)	**Placental weight (grams):** GDM (587,89) and Control group (606,14). **Placental diameter (cms):** GDM (16,14) and Control group (16,21).	Kadivar et al., 2020
Prospective study	Total (n=60) GDM (n=30) GH (n=30)	**Placental weight (grams):** GDM (684.66±44.21 female / 700.5±47.79 male) and GH (499.25±49.04 female / 549.78±101.27 male).	Istrate-Ofiteru et al., 2020
Prospective study	Total (n=80) GDM (n=40) Control group (n=40)	**Placental weight (%):** >500grams – GDM (92.5%) and Control group (5%). ≤500grams – GDM (7.5%) and Control group (95%). **Placental diameter (cms):** GDM (21.37) and Control group (13.51). **Mean number cotyledons:** GDM (21.08) and Control group (13.73).	Malathi and Ashok, 2019
Observational study	Total (n=80) GDM (n=40) Control group (n=40)	**Placental weight (grams):** GDM (426.25 ± 48.02) and Control group (397.50 ± 42.29). **Placental diameter (cms):** GDM (16.33 ± 1.14) and Control group (15.40 ± 1.34). **Number of cotyledons:** GDM (18.38 ± 2.27) and Control group (16.93 ± 2.49).	Saini et al., 2015

Legend: GDM – Gestational diabetes mellitus; GH - Gestational hypertension. Source: Authors (2022).

However, when diabetes is diagnosed early and treated with optimal glycemic control, the changes are smaller compared to pregnant women without diabetes, as observed in Table 1, in which the measurements of placental weight and diameter were not significantly different. (Kadivar et al., 2020). Therefore, it is understood that the spectrum of morphological changes will directly depend on glycemic control, metabolic control and other maternal-fetal conditions that are associated (Berceanu et al., 2018).

4. Conclusion

The development of the fetus depends on the placental structure and vascularization, requiring investigations regarding morphophysiological changes resulting from pathological conditions. We show, in table format, the studies carried out between 2015 and 2020 with the main placental morphological changes that reflect the condition of pregnant women with diabetes mellitus, the most considered in the literature, increase in placental weight and thickness. It was evident that there are still few studies on placental changes, requiring the encouragement of scientific productions on the approach.

In conclusion, understanding the mechanism of placental development allows the assessment of changes when pregnant women are diagnosed with GDM, taking into account therapeutic strategies that can intervene in glycemic and metabolic control, in order to ensure maternal-fetal health.

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