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Predisposing risk factors for the development of Gestational Diabetes

Fatores de risco predisponentes para o desenvolvimento de Diabetes Gestacional

Factores de riesgo predisponentes para el desarrollo de Diabetes Gestacional

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ABSTRACT

Introduction: Gestational diabetes mellitus (GDM) is one of the main public health problems around the world. The present study aimed to determine the prevalence and risk factors of GDM. **Objective:** To carry out a systematic review through the analysis of scientific articles in relation to the predisposing risk factors for the development of Gestational Diabetes. **Methodology:** A systematic review of the studies focused on the predisposing risk factors for the development of Gestational Diabetes was carried out. The bibliographic search was carried out through Pubmed, Scielo, Elsevier and a total of 20 articles are included. **Results:** Adequate glycemic control is the most important goal in the treatment of gestational diabetes, and theoretically this optimal control can reduce maternal and fetal morbidity and mortality to levels similar to those of pregnant women without diabetes. **Conclusions:** It is important to know the risk factors for the detection and diagnosis of GD and thus be able to start the treatment and multidisciplinary care of pregnant women to reduce maternal and perinatal morbidity and mortality.

Keywords: Gestational diabetes, risk factors, systematic review, Prevalence.

RESUMO

Introdução: A diabetes mellitus gestacional (DMG) é um dos principais problemas de saúde pública em todo o mundo. O presente estudo teve como objetivo determinar a prevalência e os fatores de risco do DMG. **Objetivo**: Realizar uma revisão sistemática por meio da análise de artigos científicos em relação aos fatores de risco predisponentes para o desenvolvimento do Diabetes Gestacional. **Metodologia**: Foi realizada uma revisão sistemática dos estudos focados nos fatores de risco predisponentes para o desenvolvimento do Diabetes Gestacional. A busca bibliográfica foi realizada através do Pubmed, Scielo, Elseiver e um total de 20 artigos estão incluídos. **Resultados**: O controle glicêmico adequado é o objetivo mais importante no tratamento do diabetes gestacional e, teoricamente, esse controle ideal pode reduzir a morbimortalidade materna e fetal a níveis semelhantes aos de gestantes sem diabetes **Conclusões**: É importante conhecer os fatores de risco para a detecção e o diagnóstico da DG e, assim, poder iniciar o tratamento e o atendimento multidisciplinar das gestantes para reduzir a morbimortalidade materna e perinatal.

Palabras clave: Diabetes gestacional, fatores de risco, revisão sistemática, Prevalência.

RESUMEN

Introducción: La diabetes mellitus gestacional (DMG) es uno de los principales problemas de salud pública alrededor del mundo. El presente estudio tenía como objetivo determinar la prevalencia y los factores de riesgo de la DMG. **Objetivo:** Realizar una revisión sistemática mediante el análisis de artículos científicos en relación a los factores de riesgo predisponentes para el desarrollo de Diabetes Gestacional. **Metodología:** Se realizó una revisión sistemática de los estudios centrados en los factores de riesgo predisponentes para el desarrollo de Diabetes Gestacional. La búsqueda bibliográfica se realizó a través de Pubmed, Scielo, Elsevier y se incluyen un total de 20 artículos. **Resultados:** El control glucémico adecuado es el objetivo más importante en el tratamiento de la diabetes gestacional, y teóricamente este control óptimo puede reducir la morbilidad y la mortalidad materna y fetal a niveles similares a los de las mujeres embarazadas sin diabetes **Conclusiones:** Es importante conocer los factores de riesgo para la detección y el diagnóstico de la EG y así poder iniciar el tratamiento y la atención multidisciplinar de las embarazadas para reducir la morbilidad y la mortalidad materna y perinatal.

Palavras-chave: Diabetes gestacional, factores de riesgo, revisión sistemática, Prevalencia.

INTRODUCTION

Diabetes is a systemic disease that occurs frequently in pregnancy and 90% of diabetes cases detected during pregnancy are diagnosed as gestational diabetes mellitus (GDM) and 10% as pregestational diabetes mellitus (PMDM). (Tuesca Molina et al., 2019).

GDM is defined as glucose intolerance of varying degrees that first appears during pregnancy. This GDM negatively affects the mother's health in the form of preeclampsia, cesarean delivery, and an increased risk of developing type 2 diabetes later in life. Babies born to mothers with GDM are at increased risk of macrosomia and developing childhood obesity, prediabetes and type 2 diabetes. (Carvajal Andrade et al., 2019).

Also, gestational diabetes mellitus is a non-communicable disease affecting pregnant women and worldwide, estimates of GDM range from 6 to 13%. In North America, recent estimates show that up to 9% of all pregnancies are complicated by GDM. On the other hand, in Central and South America, the recent overall prevalence of GDM is estimated at 11%. (Quintero-Medrano et al., 2018).

Well-established evidence shows that women with GDM are at risk for preeclampsia, preterm delivery, increased risk of cesarean section, and subsequent development of type 2 diabetes. GDM is also associated with an increased risk of perinatal complications, such as malformations, shoulder dystocia, neonatal hypoglycemia, and perinatal mortality. Shortly after delivery, glucose homeostasis is restored to pre-pregnancy levels, but affected women remain at high risk of developing type 2 diabetes mellitus later in life. (Bougherara et al., 2018).

For any population and ethnic group, the risk of gestational diabetes indicates the underlying frequency of type 2 diabetes. The incidence of gestational diabetes and type 2 diabetes is increasing worldwide, with enormous health and economic costs. Diabetes predisposes people to cardiovascular, renal and retinal disease, costing between $1 billion and $8 billion per year (Maryuri Madeleine Párraga-Moreira et al., 2021).

Women who have had gestational diabetes are advised to have their glucose tolerance assessed 6 weeks after delivery. However, low attendance rates at the 6-week follow-up suggest that health care professionals, women with gestational diabetes, or both, do not realize the importance of this condition as an early warning sign of susceptibility to developing type 2 diabetes in the future; thus, an opportunity to promote health and prevent disease is missed. In addition, there is no consensus on how and whether mothers should continue to be monitored after this period. (García-de Lucas, 2019).

However, the association between gestational diabetes and type 2 diabetes mellitus has implications for the elucidation of the causes of these disorders, and for the prediction and possible prevention or delay of the development of type 2 diabetes in women.

On the other hand, some of the complications are preterm delivery, excessive birth weight, respiratory distress syndrome, hypoglycemia (due to excessive levels of insulin in the baby), and the risk of developing type 2 diabetes mellitus (T2DM) later in life. (Chávez-García et al., 2019).

Nor is the mother spared from the devastating effects of this disease. She can develop a number of associated complications, such as high blood pressure, preeclampsia and future diabetes. All these well-established risks require a relevant solution for early detection and prevention of the disease.

Likewise, obesity and family history of diabetes have been consistently identified as major risk factors for GDM in previous studies. Other risk factors for GDM include advanced maternal age, non-white race, previous unexplained stillbirth, and obesity. (Fernández et al., 2020).

In addition to an increased risk of GDM, maternal obesity increases the risk of multiple adverse maternal health outcomes, such as thrombosis, gestational hypertension, preeclampsia, preterm delivery, and cesarean section. Notably, important neonatal complications have been associated with obesity and GDM.

These include congenital anomalies, macrosomia, and birth injury. Increasing evidence implicates unipolar major depressive disorder as a major risk factor and coexisting condition for GDM, although the evidence is inconsistent. (Zuccolotto et al., 2019).

Consequently, the prevalence of GDM varies according to the test and diagnostic criteria used and also according to social characteristics. In the analysis conducted by the Centers for Disease Control and Prevention, a prevalence of 9.2% for GDM was reported. In studies conducted in various parts of the world, they note that the prevalence of GDM varies between 2.6% and 27.9%.

However, the pathogenesis of GDM encompasses insulin resistance and impaired insulin secretion. GDM is often

associated with maternal obesity and increased white fat tissue, as well as placental inflammation.

International studies reveal that there are numerous risk factors associated with GDM. Family history of diabetes, overweight, ethnicity, advanced maternal age, polycystic ovarian disease, corticosteroid use, hypertension, history of GDM, history of delivery of a macrosomic baby and glycosuria are described as risk factors (María Isabel Peña-Cano et al., 2022).

GDM can lead to adverse short- and long-term outcomes for both mother and child. These increase the risk of maternal preeclampsia, infections and cesarean deliveries and can lead to congenital malformations in the fetus, as well as stillbirth, macrosomia and growth retardation, hypocalcemia in the newborn, polycythemia, respiratory distress syndrome, hypomagnesemia, and hyperbilirubinemia (Bougherara et al., 2018).

In addition, long-term adverse effects of GDM in children include obesity, attention deficit, hyperactivity and motor function disorders. In addition, the mother is at increased risk of developing type 2 diabetes in the future and should be screened for this reason every 1-3 years.

Because of the high prevalence of GDM and the short- and long-term adverse effects it has on the health of mother and child, early diagnosis and treatment are crucial. Symptoms such as excessive thirst and excess urination, dry mouth and tiredness in a pregnant woman may be signs of hyperglycemia. Blood tests are the best method for diagnosing GDM. (María Isabel Peña-Cano et al., 2022).

Two different approaches are adopted in screening for GDM: the one-step and the two-step approach. While many international associations recommend the two-step method, the World Health Organization (WHO) recommends the one-step method. The WHO defines the criteria for the diagnosis of GDM at any stage of pregnancy as a fasting plasma glucose reading equal to or greater than 126 mg/dl, oral glucose tolerance test (OGTT) readings of 75 g of a plasma glucose reading greater than 180 mg/dl after one hour and 200 mg/dl after two hours (Fernández et al., 2020).

The Ministry of Health has set out detailed information on the diagnosis and treatment of gestational diabetes in its Guideline for the Management of At-Risk Pregnancies. This guideline emphasizes that all pregnant women should undergo a routine OGTT at 24-28 weeks of their pregnancy (Zuccolotto et al., 2019).

It details how women who are at risk of developing GDM have a good chance of protecting themselves against it by adopting lifestyle changes, such as exercise and healthy eating habits before and during pregnancy.

On the other hand, when GDM does develop, proper treatment of the disease can reduce complications for both mother and baby to some extent. Health personnel working in obstetrics clinics and family and public health centers have important obligations (Chávez-García et al., 2019).

These healthcare personnel can attend training courses to learn more about healthy lifestyle behavior for women, monitoring of blood glucose levels, acceptable fasting and postprandial blood glucose levels in pregnancy, insulin administration, and symptoms of hypoglycemia and hyperglycemia.

Thus, GDM is an issue that needs to be carefully addressed, not only in terms of maternal and child health, but to protect and improve the health of future generations and public health. It is an issue that needs more scientific research. There is a need to broaden the knowledge landscape on the prevalence of GDM and related risk factors that may be of interest to interdisciplinary and international researchers, as well as to family physicians, obstetricians, midwives, nurses and other health professionals (Collantes-Gutiérrez et al., 2020).

When reviewing the studies conducted in recent years, it is observed that research has been carried out on the prevalence of GDM, its diagnosis and treatment, risk factors, its impact on maternal and child health, and related issues. However, there is a need for comprehensive evaluations through meta-analyses to investigate aspects related to GDM.

For this reason, we conducted this systematic review based on studies on GDM in an effort to determine the prevalence of GDM and related risk factors. It is hoped that the data obtained at the national and international level will make a contribution to current and future international and local scientific research on the subject. The objective of this study is to identify the prevalence and risk factors related to GDM, based on studies on this disease.

METHODS

This study was conducted as a qualitative systematic review based on a compilation of information of interest based on scientific evidence, case analysis, literature review, among others.

Research design

To reduce the risk of bias in this meta-analysis, the process of literature exploration, article selection, data extraction, and article quality assessment was performed by the research group and each step was checked by an investigator-in-charge.

Differences of opinion among the researchers were resolved by discussion. In addition, in order to ensure that the whole process was carried out properly and with high quality, the group of researchers participated in a session in which the archival search on the study topic (diabetes mellitus) was performed and the steps of scanning, article selection, data extraction of five research articles, and article quality assessment were discussed, and differences of opinion were eliminated through discussion.

Determination, selection, and extraction of study data

To identify research for this study, a search was performed in Pubmed, Scielo, Elseiver databases during the period of 2018-2022. In addition, use was made of Boolean operators (AND, OR, NOT) and key terms to elevate the search level.

International databases were accessed using the keywords "gestational diabetes" AND "Risk factors". In addition, databases were explored using the word groups, "gestational diabetes", "diabetes in pregnancy", "pregnancy and diabetes" and "diabetes in pregnancy".

Table 1 Bibliographic search strategies

Use of key terms	(Gestational Diabetes) OR (Diabetes in Pregnancy) AND (Risk) OR (Factors)
Language	English, Spanish,
Use of Boolean operators	AND, OR,
Publications of the last 5 years	2018-2022

Note: Prepared by authors with research data

Likewise, searches were made with modified variables that are related to the original study variables.

Table 2 Original variables and modifications made

Original variables	Variables with contradiction, implication or modification
Gestational diabetes	Definition Diabetes in pregnancy
Risk Factors	Importance

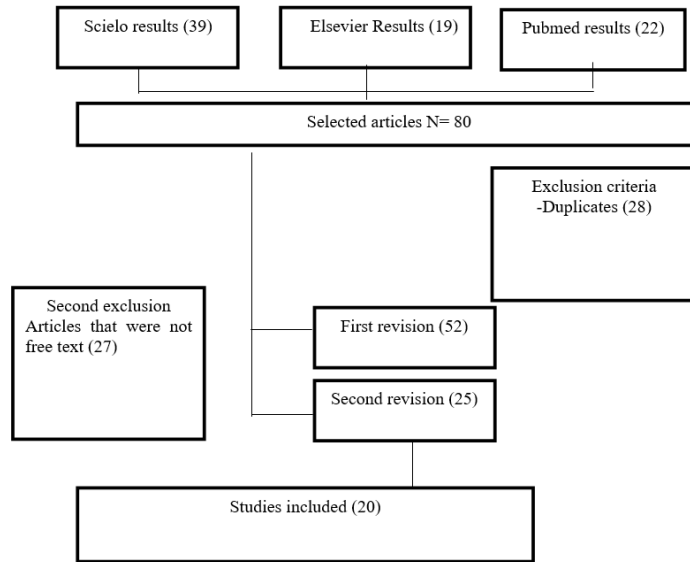Note: Prepared by authors with research data

Information selection criteria

Descriptive and cross-sectional literature studies conducted at any time in the general population of pregnant women and reporting prevalence and/or risk factors for GDM were included in the study. Twenty articles were analyzed in the investigation. The article selection process is shown in Figure 1.

Studies conducted with special groups, such as adolescents, obese, elderly, and pregnant women in the hospital, as well as research in which the diagnostic test was not reported, were excluded from the review.

A data extraction instrument devised by the investigators was used to access the research data. The data extraction tool was used to obtain data from the studies included in the systematic review on the method, sample size, outcomes, number of cases, year in which data were collected, prevalence of GDM, and possible risk factors.

Figure 1 Selection of studies

Note: Prepared by authors with research data

RESULTS

This section may be divided by subheadings. It should provide a concise and precise description of the results, their interpretation, as well as the experimental conclusions that can be drawn. Present textual and / or visual (illustrations and / or tables) research results:

	Title of article, author, year of publication	Participants	Study design	Results	Authors' interpretation	Categories
1	Vitamin D concentrations in pregnant women and their relationship with gestational diabetes.	25 patients with gestational diabetes and 25 without this disease.	Prospective case study	There is no association between gestational diabetes and vitamin D deficiency.	The risk factors are similar, i.e., family history of diabetes, increased body mass index, increasing age, and Asian and black ethnicity.	Gestational diabetes AND Risk factors
2	Maternal-fetal outcome in patients with early or late diagnosis of gestational diabetes.	459 pregnant women	Observational, retrospective and analytical study.	Maternal and fetal outcome of patients with gestational diabetes changes according to weeks of pregnancy	The frequency of some alleles associated with increased risk of developing type 2 diabetes increased in women who had gestational diabetes	Gestational diabetes AND Risk factors
3	Improvement of the gestational diabetes screening protocol: diagnostic validation study.	2007 pregnant women	Prospective study	The risk of type 2 diabetes appears to be maintained over several years, it is important to consider whether some form of ongoing screening would lead to health benefits.	Women who have had gestational diabetes also have increased lipid concentrations and blood pressure, and it is estimated that type 2 diabetes confers an equivalent risk of aging of 15 years.	Gestational diabetes AND Risk factors
4	Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: systematic review and meta-analysis.	106 pregnant women	Prospective study	Gestational diabetes mellitus (GDM), gestational hypertension (GH) and preeclampsia (PE) are associated with short- and long-term health 5problems for mother and child.	Smoking, obesity and family history of diabetes are high risk factors for gestational diabetes.	Gestational diabetes AND Risk factors
5	Implication of gestational diabetes treatment on maternal weight gain and neonatal low birth weight: large retrospective cohort study.	1,765 pregnant women with gestational diabetes	Retrospective study	Dietary treatment for gestational diabetes may lead to lower maternal weight gain and in turn induce an impact on neonatal weight.	Subjects with GDM had had macrosomic/large for gestational age (LGA) babies, resulting in more cesarean sections.	Gestational diabetes AND Risk factors
6	Gestational diabetes Maternal programming	472 pregnant women	Retrospective study	There is sufficient clinical evidence linking gestational diabetes to the subsequent development of type 2 diabetes mellitus, chronic arterial hypertension, and chronic hypertension.	Socially disadvantaged women with GDM are less likely to seek perinatal care and thus to have more pregnancy complications.	Diabetes gestacional AND Factores de riesgo
7	Validity of fasting blood glucose as a diagnostic test for gestational diabetes during the first trimester of pregnancy.	204 pregnant women	Observational, retrospective, case study.	No ethical issues related to gestational diabetes.	Regardless of ethnicity, all women are at risk for GDM and should be screened promptly.	Gestational diabetes AND Risk factors
8	A Pragmatic, Randomized Clinical Trial of Gestational Diabetes Screening	23792 women	Observational, retrospective study.	Most cases of GDM received medical nutrition therapy (MNT) or dietary management as a treatment option.	Monitoring of glucose control, HbA1C is also used to detect GDM and identify the high risk of fetomaternal complications associated with it.	Gestational diabetes AND Risk factors
9	Conditions of newborns born to mothers with gestational diabetes at the Enrique C. Sotomayor Obstetric Gynecological Hospital in September 2015 - August 2016.	64 newborns	Retrospective, descriptive study	HbA1c levels at 28 weeks gestation can help identify women who need careful and regular glycemic index monitoring.	Measurement of HbA1c could be used both as a means of diagnosing and monitoring a subject's diabetic status.	Gestational diabetes AND Risk factors
10	Prospective study of perinatal factors associated with early hypoglycemia in the late preterm and term neonate.	59 newborns	Prospective analytical study	GDM was associated with an increased rate of cesarean delivery, preeclampsia, polyhydramnios, neonatal hypoglycemia, and smoking cessation behavior.	GDM was associated with an increased rate of cesarean delivery, preeclampsia, polyhydramnios, neonatal hypoglycemia, and smoking cessation behavior.	Gestational diabetes AND Risk factors
11	Gestational diabetes and the risk of late stillbirth: a case–control study from England, UK	291 pregnant women	Retrospective descriptive study	Women with previous GDM and PCOS may form a distinct subgroup from women with normal ovaries and previous GDM.	Increased tendency to develop insulin resistance syndrome traits	Gestational diabetes AND Risk factors
12	Gestational diabetes: the need for preconceptional genetic counseling in Matanzas	186 pregnant women with gestational diabetes	Retrospective descriptive study	Not all pregnant women with a family history of diabetes mellitus may have diabetes mellitus.	The traditional and most frequently reported risk factors for GDM are high maternal age, weight and parity.	Gestational diabetes AND Risk factors
13	Gestational diabetes and the risk of late stillbirth: a case–control study from England, UK	291 pregnant women	Retrospective descriptive study	Women with previous GDM and PCOS may form a distinct subgroup from women with normal ovaries and previous GDM	Increased tendency to develop insulin resistance syndrome traits	Gestational diabetes AND Risk factors

14	Changes in nutritional status, anemia and diabetes in pregnant women in a semirural area of Honduras.	98 pregnant women	The study was retrospective and cross-sectional	Number of fetuses in multifetal pregnancies may influence the incidence of GDM	The impact of fetal reduction (selective feticide of one or more fetuses in high-order multiple pregnancies) on the incidence of GDM may also support this theory.	Gestational diabetes AND Risk factors
15	Clinical profile of patients with gestational diabetes and incidence of neonatal complications in a Colombian maternal-fetal referral center.	197 mothers and 203 newborns	Descriptive study of a retrospective cohort.	The rate of GDM was significantly higher in the triplet group.	GDM is a frequent indication for induction of labor and indication for cesarean section.	Gestational diabetes AND Risk factors
16	Neonatal macrosomia and gestational diabetes	544 patients and 41 newborns	Descriptive study of a retrospective cohort.	GDM was significantly more frequent in twin deliveries.	Risk Factors, Body Mass Index, Gestational Age at diagnosis, Type of delivery and Newborn complications.	Gestational diabetes AND Risk factors
17	Prediction of insulin therapy in patients with gestational diabetes mellitus.	133 women with gestational diabetes	Observational, prospective, case-control, prospective study	Upon diagnosis of gestational diabetes, it is possible to select a group of pregnant women at higher risk of requiring medical treatment.	Controlling for other risk factors such as advanced age, parity, maternal history of diabetes, and the woman's own birth weight, it does not associate an elevated risk of GDM.	Gestational diabetes AND Risk factors
18	Anthropometric evaluation and follow-up of children born to mothers with gestational diabetes.	51 children of mothers with gestational diabetes	Prospective descriptive longitudinal study	The clinically optimal blood glucose level during pregnancy should be as close to normal as possible.	The proportion of infants admitted to special care in relation to glucose tolerance range, and they found an association between blood glucose and both outcomes	Gestational diabetes AND Risk factors
19	Gestational diabetes: opportunities for improving maternal and child health	-	Bibliographic review	Gestational diabetes, the most common medical condition in pregnancy, is defined as glucose intolerance resulting in hyperglycemia that begins or is first diagnosed during pregnancy.	Hypertension and labor induction were only marginally associated with glucose levels.	Gestational diabetes AND Risk factors
20	Women's experiences of a diagnosis of gestational diabetes mellitus: a systematic review	-	Systematic review	Gestational diabetes mellitus (GDM), a transient form of pregnancy-induced diabetes, has potentially significant short- and long-term health consequences for both mother and baby.	Insulin resistance in the pathogenesis of hypertensive disorders of pregnancy, as they found that women with GDM had a higher relative risk of preeclampsia and all hypertensive disorders.	Gestational diabetes AND Risk factors

Note: Prepared by authors with research data

DISCUSSION AND FINAL CONSIDERATIONS

The strength of the association between gestational diabetes and type 2 diabetes, and the knowledge that many of the risk factors are the same (i.e., family history of diabetes, increased body mass index, increasing age, and Asian and black ethnicity), suggest that the two disorders may have overlapping causation (Collantes-Gutiérrez et al., 2020).

The results of the studies analyzed support this hypothesis and show that the frequency of some alleles associated with increased risk of developing type 2 diabetes increased in women who had gestational diabetes. (Villota-Burbano et al., 2019). Regardless of the precise biological link between these two disorders, the development of gestational diabetes could help identify women at high risk of developing type 2 diabetes.

Moreover, although women who have had gestational diabetes are recommended to undergo a glucose tolerance test at 6 weeks after delivery, most do not attend. The increased risk of type 2 diabetes reported in this meta-analysis could help motivate mothers to attend screening programs, and health care professionals to increase participation in these programs, or perhaps to suggest the best time for rescreening. Given that the risk of type 2 diabetes appears to be maintained over several years, it is important to consider whether some form of ongoing screening would lead to health benefits. Women who have had gestational diabetes also have increased lipid concentrations and blood pressure, and it is estimated that type 2 diabetes confers an equivalent risk of aging of 15 years.

Early identification and treatment of these factors could also help to reduce premature cardiovascular and renal disease in this group of individuals. In addition, Davenport et al., report that smoking, obesity and family history of diabetes are high risk factors for gestational diabetes, along with older age, parity and history of gestational diabetes. Of these factors, pre-pregnancy maternal obesity and excessive weight gain during pregnancy are independent and potentially modifiable risk factors that often occur together with GDM or hyperglycemia in pregnancy. BMI measurement alone is not a true indicator of obesity in our population because of the different cut-off points used to define obesity.

On the other hand, Civantos Modino et al., observed a low percentage of the women have a previous history of GDM, while the majority developed GDM in recent pregnancy. When analyzing the history of complications, i.e., macrosomia and GDM-related cesarean deliveries. That is, subjects with GDM had had macrosomic/large for gestational age (LBW) babies, resulting in more cesarean sections compared to healthy controls (p<0.01). Given this, Vigo y Silvares, formulate that socially disadvantaged women with GDM are less likely to seek perinatal care and, therefore, to have more pregnancy complications. With this in mind, we studied additional variables representing the socioeconomic status of these subjects and observed that the majority belonged to a high socioeconomic class.

Previous studies have reported conflicting results due to the different definitions used for economic status depending on the region of investigation. However, the prevalence of GDM has a weak but significant relationship with socioeconomic status, including educational level, ethnicity, parity, maternal age, smoking, nutrition, history of GDM, and family history of diabetes. Regarding the effect of physical activity, most subjects reported a sedentary lifestyle; therefore, we could not find an association of lifestyle pattern with GDM.

On the other hand, in the study of Font-López et al., When stratified by ethnicity, 61.5% of the women in the GDM

group were of different ethnicities. Despite this, there are no articles that find any association between GDM and different ethnicities. Therefore, it is suggested that regardless of ethnicity, all women are at risk for GDM and should undergo timely screening.

However, within the study of Hillier et al., most cases of GDM received medical nutrition therapy (MNT) or diet control as a treatment option, while 47% required the use of metformin, insulin or combination therapy for glycemic control. Glycemic status was identified by measuring the HbA1c values of subjects with GDM. It was observed that both treatment options could provide a satisfactory level of glucose control for most patients. In addition to monitoring glucose control, HbA1C is also used to detect GDM and to identify the high risk of fetomaternal complications associated with GDM (Hillier et al., 2021).

However, recent research has revealed that HbA1C values are not affected by hemoglobin levels and can be used as a reliable tool in pregnant women affected by anemia. This new development is especially beneficial for the population, as research reports that almost 51% of pregnant women suffer from anemia. In connection with Yépez et al., who mentions that HbA1c levels at 28 weeks of gestation can help identify women who need careful and regular glycemic index control. Therefore, we suggest that HbA1c measurement could be used both as a means of diagnosing and monitoring a subject's diabetic status.

Within this systematic review, risk factors associated with GDM were found to be, above all, advanced maternal age, overweight before pregnancy and weight gain during pregnancy, diabetes in the family, history of GDM or birth of a large baby, gestational week, number of pregnancies, deliveries and abortions, and history of stillbirths. In other studies on this topic, the risk of GDM has been similarly reported to increase with advancing age, increasing BMI, diabetes in the family, history of GDM, large and stillbirth, abortion, number of pregnancies, and gestational week.

In a study conducted by Ruiz et al., has reported that GDM was associated with an increased rate of cesarean delivery, preeclampsia, polyhydramnios, neonatal hypoglycemia, and smoking cessation behavior. In some studies in other countries, GDM has been similarly reported to be associated with increased risk of cesarean delivery, chronic hypertension, dietary habits, regular physical exercise, and history of infertility.

Under the story line of Ceballos et al., the traditional and most frequently reported risk factors for GDM are maternal age, high weight and parity, previous delivery of a macrosomic baby, and family history of diabetes. On the other hand, polycystic ovary syndrome (PCOS) is a heterogeneous disorder that affects 5-10% of women of reproductive age. It is characterized by chronic anovulation with oligo/amenorrhea, infertility, typical ultrasound appearance of the ovaries, and clinical or biochemical hyperandrogenism; insulin resistance is present in 40-50% of patients, especially in obese women. (Trujillo Saínz et al., 2019).

Other studies reported a higher rate of ultrasonographic, clinical and endocrine signs of PCOS in 291 women who had had GDM 3-5 years earlier, compared with 36 matched controls with uncomplicated pregnancies. They concluded that women with previous GDM and PCOS may form a distinct subgroup from women with normal ovaries and previous GDM, characterized by an increased tendency to develop features of insulin resistance syndrome. Similar results were reported by many other investigators (Stacey et al., 2019). As mentioned in Hernández et al., the number of fetuses in multifetal pregnancies may influence the incidence of GDM due to the increased placental mass and thus increased hormones. However, reports are somewhat contradictory, probably due to the heterogeneity of the populations studied.

Nevertheless, the impact of fetal reduction (selective feticide of one or more fetuses in high-order multiple pregnancies) on the incidence of GDM may also support this theory. Preciado et al., found that the rate of GDM was significantly higher in the triplet group than in the reduction group (22.3% vs. 5.8%). Similar results were reported by (León et al.,) which showed that GDM was significantly more frequent in twin deliveries (7.7% vs. 4.1%, P < 0.05). However, insulin requirements were not different, suggesting a minor clinical impact. In contrast, using data derived from the study of Méndez et al., controlling for other risk factors such as advanced age, parity, maternal history of diabetes, and the woman's own birth weight, they found no elevated risk of GDM among 9271 multifetal pregnancies. Others have also failed to demonstrate an increased prevalence of GDM in multiple pregnancies.

On the contrary, (Pérez et al., suggested that the clinically optimal blood glucose level during pregnancy should be as close to normal as possible. They studied the proportion of assisted deliveries and the proportion of babies admitted to special care in relation to the range of glucose tolerance, and found an association between blood glucose and both outcomes. Other authors also reported conflicting results stipulating that women with gestational diabetes were older and more obese, and had higher parity, and heavier babies than pregnant women with normal screening plasma glucose, and found no significant difference in the incidence of prenatal complications between mothers with normal and impaired glucose tolerance

The risk of hypertensive disease and cesarean section for fetal distress/ meconium-stained thick amniotic fluid was

also higher in the ATG group, but the differences were not statistically significant when maternal age and obesity were excluded.

In another recent study the following outcomes increased significantly with increasing glucose values on SOG: shoulder dystocia, macrosomia, emergency cesarean section, assisted delivery, hypertension, and induction of labor. However, when other risk factors were corrected for, hypertension and labor induction were only marginally associated with glucose levels. These findings may also be associated with a possible increased risk of cardiovascular complications. Craig et al., provided further support for the role of insulin resistance in the pathogenesis of hypertensive disorders of pregnancy, finding that women with GDM were at increased relative risk for preeclampsia and all hypertensive disorders.

CONCLUSIONS

Because insulin resistance is an early risk factor for diabetes, it is well known that women with gestational diabetes mellitus are at high risk of developing type 2 diabetes. Recent studies have shown that decreasing insulin resistance through diet, exercise or metformin can reduce the development of diabetes in high-risk individuals.

Adequate glycemic control is the most important goal in the treatment of gestational diabetes, and theoretically this optimal control can reduce maternal and fetal morbidity and mortality to levels similar to those of pregnant women without diabetes. Gestational diabetes is a disease that causes symptoms in the mother that put the fetus and newborn at high risk. Therefore, it is important to know the risk factors for detection and diagnosis of GD so that treatment and multidisciplinary care of pregnant women can be initiated to reduce maternal and perinatal morbidity and mortality. Postnatal screening is important to ensure follow-up of these patients, as a certain percentage of women are more likely to develop gestational diabetes in the next pregnancy and are prone to type II diabetes in the future.

One of the main limitations of this systematic literature review was the lack of gray literature studies, which may be discussed in future articles. On the other hand, new studies are suggested that would address other types of determinants of GDM, such as the socioeconomic context, public health guidelines, etc.

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