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Obstetric-Neonatal Complications of Gestational Diabetes: A Systematic Review

Complicaciones obstétrico-neonatales de la diabetes gestacional: revisión sistemática

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Abstract:

The analysis of evidence provided regarding neonatal and obstetric complications derived from gestational diabetes were realized. A systematic search of the scientific literature, PUBMED, ScienceDirect was carried out with various search strategies guaranteeing the completeness and reproducibility of the phases of the PRISMA guide. Thirteen studies were included, 10 simultaneously evaluated obstetric and neonatal complications, and the other three evaluated only neonatal complications. The prevalence of GDM (gestational diabetes mellitus) was 12.5% (65,852 of 527,351) Obstetric complications include emergency caesarean or C-section (OR 1.1 to 2.37), preeclampsia with an OR range of 1.1 to 2.96, and prematurity (OR 1.1 to 2.3). The most frequent neonatal complications are macrosomia with an OR range of 1.2 to 5.2, with a prevalence of 10.3%; while hypoglycaemia is the one with the highest risk (OR 3.19-11.97), other complications include greater height for gestational age OR 1.3 to 3.43; perinatal asphyxia (OR 1.2-3.4); shoulder dystocia (OR 1.3-2.56); respiratory distress (OR 1.3-2) and hyperbilirubinemia (OR 1.02-1.39). No increased risk of perinatal death was found, the reported OR range is 0.7-0.8. Both obstetric and neonatal gestational diabetes complications are very prevalent and may require intensive care, being a highly relevant public health problem. Although an efficient screen for the early detection of gestational diabetes has been established, greater efforts are required to comply with it and to avoid these complications.

Keywords:

Gestational diabetes, obstetric complications, neonatal complications, review

Resumen:

Se analizaron las evidencias aportadas referentes a las complicaciones neonatales y obstétricas derivadas de la diabetes gestacional mediante una búsqueda sistemática de la literatura científica, PUBMED, ScienceDirect con varias estrategias de búsqueda garantizando la exhaustividad y reproducibilidad de las fases de la guía PRISMA. Se incluyeron 13 estudios, 10 evaluaron simultáneamente complicaciones obstétricas y neonatales, el resto (3) evaluaron solo complicaciones neonatales. La prevalencia de DMG (diabetes mellitus gestacional) fue de 12.5% (65,852 de 527,351). Las complicaciones obstétricas incluyen: cesárea de urgencia (OR 1.1 a 2.37), preeclampsia con un rango de OR de 1.1 hasta 2.96 y prematuridad (OR 1.1 a 2.3). Las complicaciones neonatales más frecuentes son: macrosomía con un rango de OR de 1.2 hasta 5.2, con prevalencia de 10.3%; mientras que la hipoglicemia es la que presenta un riesgo mayor (OR 3.19-11.97), otras complicaciones incluyen talla mayor para la edad gestacional OR de 1.3 hasta 3.43; asfixia perinatal (OR 1.2-3.4); distocia de hombros (OR 1.3-2.56); distrés respiratorio (OR 1.3-2) e hiperbilirrubinemia (OR 1.02-1.39). No se encontró mayor riesgo de presentar muerte perinatal, el rango de OR reportado es de 0.7-0.8. Las complicaciones de la diabetes gestacional tanto obstétricas como neonatales son muy prevalentes y pueden llegar a requerir cuidados intensivos, siendo un problema de salud pública de gran relevancia. Aunque se ha establecido un tamiz eficiente para la detección temprana de diabetes gestacional se requieren mayores esfuerzos por parte de los médicos de primer contacto, gineco-obstetras y personal de salud, así como educar a las pacientes sobre la importancia de las revisiones, con el objetivo de evitar estas complicaciones.

Palabras Clave:

Diabetes gestacional, complicaciones obstétricas, complicaciones neonatales, revisión

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INTRODUCTION

Gestational diabetes (GDM) is the most frequent metabolic disorder in pregnancy, defining itself as intolerance to carbohydrates of variable severity, which is diagnosed for the first-time during pregnancy and may or may not persist after delivery.[1]

The Center for Disease Control and Prevention (CDC) estimates that the incidence in the United States can reach 10%, annually,[2] Mexico is within this data since the prevalence of GDM is reported between 8.7 to 17.7%, annually.[3]

Studies have detected several risk factors of GDM including overweight, obesity, advanced maternal age and family history of diabetes.[4,5] Pregnancy generates a state of insulin resistance and hyperinsulinism, both aspects are physiological and reversible, this situation may be the result of the combination of increased maternal adiposity and the anti-insulin effect of hormones produced by the placenta (progesterone, prolactin, lactogenic placental hormone cortisol, and leptin); these appear at the beginning of the second trimester of pregnancy and are accentuated in the third.[6,7] Therefore, GDM is the result of a mismatch between endogenous insulin secretion and tissue needs, in addition to the factors already mentioned, it has been shown that in pregnant women with this condition the reserve of cells of pancreatic beta cells is reduced.[8] It must be differentiated from type 2 diabetes, since hyperglycemia is present in the organogenesis stage, the pathophysiology and complications differ.[9]

To make the diagnosis of this disease many guidelines have been published; the screening is carried out between weeks 24 to 28 through two procedures or methods, either, in one step (with 75g of glucose) or in 2 steps (initial screening with 50g of glucose and confirmation with 100g), it is necessary to obtain both values out the range (the screening and the confirmation) for GDM diagnosis; both tests have the same sensitivity.[6-8]

This early detection is necessary to avoid complications, GMD is closely associated with different adverse pregnancy outcomes both in the fetus (brachial plexus palsy, macrosomia, shoulder dystocia, hypoglycemia) and the mother (caesarean section, preeclampsia, increased risk of developing type 2 diabetes, abortions, etc.),[8,10,11] and is also associated with newborns delayed brain maturity and neurobehavioral abnormalities including comparatively lower intelligence than normal babies, language impairments, poor attention and impulsivity.[12]

The treatment consists of improving the hygienic-dietary measures, prescription of physical activity, continuous monitoring of glucose accompanied or without insulin.[3,8,13,14]

This study aims at characterizing and summarizing maternal and neonatal complications that occur in the short term because of gestational diabetes.

METHODS

Methodological search:

A systematic review of the literature was carried out in September 2021 on PubMed and ScienceDirect, following the next methodological scheme. The combination of terms that yielded the best results in the 2 bases was the following:

PubMed: ((diabetes, gestational [Title / Abstract] OR gestational diabetes mellitus [Title / Abstract]) AND (outcomes [Title / Abstract] OR complications [Title / Abstract])) NOT (management [Title / Abstract] OR treatment [Title / Abstract] OR Therapeutics [Title / Abstract])

Science direct: (gestational diabetes mellitus OR gestational diabetes) AND (outcomes OR complications) NOT (covid-19 OR SARS-COv-2) NOT (treatment OR care OR diagnosis)

The PRISMA method (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) was used.

The following filters were used to search strategies: words in title or abstract, 10 years old, original or research articles. 129 results were obtained in PubMed and 549 in ScienceDirect. (Table 1)

When comparing both databases, it was detected that there were 5 duplicate articles. For the selection of articles, the following criteria were determined:

Inclusion criteria: Original or empirical works, no more than 10 years old, that the search term is included in the title or abstract, talk about maternal and fetal complications secondary to diabetes.

Exclusion criteria: Studies in which maternal or fetal complications were secondary to type 1, type 2, LADA (Latent Autoimmune Diabetes of the Adult), or diabetes insipidus, make it a single case report or letter to the editor, that they do not meet methodological quality according to the Newcastle-Ottawa scale.

With these criteria and only considering the titles, 34 articles were selected to verify eligibility. After reading the summary of each one and considering the results, 13 articles were chosen for the systematic review. The characterization is described in table 2.

Reproducibility and evaluation of the methodological quality of the studies.

For the evaluation of the quality of the publications, the criteria of MMAT (Mixed methods appraisal tool) were applied[10]. Reproducibility in the search and selection of publications was guaranteed by applying the search protocol on three different occasions with an interval of 5 days, and an Excel database was designed, which was completed on two different occasions to verify the concordance of the extracted data.

Table 1. Absolute frequency of studies identified with the application of three search strategies in the consulted databases

	Search strategy		
Database	1	2	3
PubMed			
Without filters	14 873	14 780	1213
Search restriction (Title, abstract)	5195	3 793	609
Search restriction (year, original article, humans)	249	214	129
Science Direct			
Without filters	54 764	54899	5 409
Search restriction (Title, abstract, year)	2564	2526	1 383
Search restriction (year, original article, topic)	1,067	1 053	549

Source: Own elaboration from the data obtained in the methodological search

RESULTS

The amount of 6622 articles (5409 on ScienceDirect and 1213 on PubMed) were found, then, when applying the rest of the filters, (year, word included in title or abstract, full text available and original article) the number was reduced to 678 (129 on ScienceDirect and 540 on PubMed). Subsequently, the inclusion and exclusion criteria reduced the number to 34 and with the reading of the abstract, 13 articles were chosen for inclusion, this process summarized in Figure 1.

Only one of the 13 studies rated as low quality (MMAT 25%), eight studies were rated as average quality (MMAT 50%), four studies were rated as high quality (MMAT 75%), none study was rated as very poor quality (MMAT 0%) or the highest quality (MMAT 100%).

The articles were published between 2011 and 2021; 84.6%% of the studies are observational,[15-25] while 15.4% are clinical trials.[26,27] 76.9% of the articles report the results in Odds Ratio with 95% CI, determining both maternal and fetal complications. The rest of the articles (23.1%) present their results in percentage.

The prevalence of GDM was 12.5% (65,852 of 527,351). Women with a pre-existing diagnosis of diabetes mellitus (DM) were excluded (0.7%). The obstetric complications[15,16,18-20,22-26] were (Table 3): emergency cesarean section[15,16,18-20,22,23,25,26] (OR 1.1 to 2.37), in Malaysia a high prevalence was obtained (31.1%); preeclampsia [15,16,18-20,22-26] with an OR range of 1.1 to 2.96, the prevalence was reported around 7%; prematurity[15,16,18-20,23-25] (OR 1.1 to 2.3) with a prevalence of 8.9% and 12.6%.

The neonatal complications [15-27] were (Table 4): 10 of the 13 studies (76.9%) reported macrosomia [15-20,22,23,25,26] with an OR range of 1.2 to 5.2, with a prevalence of 10.3%; while hypoglycemia [15,19-21,24,25] is the one with the highest risk (OR 3.19-11.97); other complications included greater height for gestational age [15-17,19,26] OR 1.3 to 3.43; perinatal asphyxia (OR 1.2-3.4); shoulder dystocia [16,19,22,23] (OR 1.3-2.56); respiratory distress[15,16,20,21,23,24,27] (OR 1.3-2) and hyperbilirubinemia [18,19,21,27] (OR 1.02-1.39). No increased risk of perinatal death was found, four of the 13 studies (30.8%) [12,15,17,19] evaluated this complication reporting an OR range of 0.7-0.8.

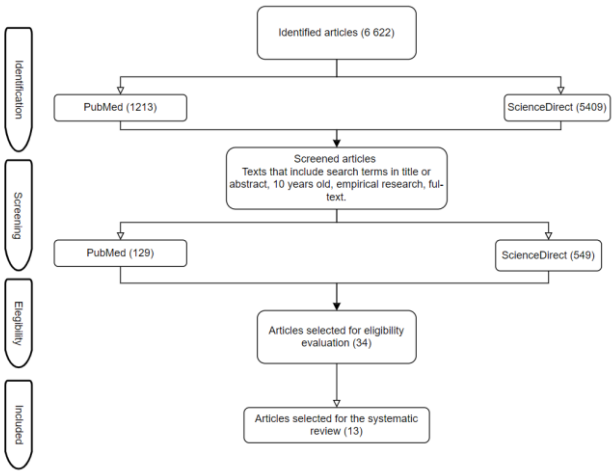

Figure 1. Flowchart of the search and methodological selection. Source: own elaboration.

DISCUSSION

This systematic review aimed at collecting information on maternal and fetal complications of DMG. The prevalence of DMG changes according to the diagnostic criteria used, if they used one-step screening methods the prevalence of GDM was 14.7%, while the prevalence of GDM two-step screening method (7.2%) was half that of the one-step method.[28] For 2016, the WHO-PAHO (World Health Organization - Pan American Health Organization) reports that GDM affects between 1% and 35% of pregnant women,[29] what was found in this work is within that range (12.5%).

Complications of GDM can be short-term and long-term, this article approaches the short-term consequences, which can be subdivided into obstetric and neonatal. The obstetric complication more commonly found in this review was preeclampsia, associated with an overexpression of pro inflammatory molecules can cause maternal and fetal complications[9] that increased the possibility of premature termination of pregnancy and the indiscriminate use of a cesarean section, being an important cause of obstetric and perinatal morbidity and mortality.[16,18] Maternal mortality due to this disease is high, ranging from 1.5% to 2.9%, as it can trigger postpartum hemorrhage, placental abruption, coagulopathy, renal failure, hypertensive encephalopathy, intracerebral hemorrhage, Hellp syndrome, and rupture of the hepatic hematoma.[30] Cesarean section is an indirect complication of fetal macrosomia, if the baby is atypically large, vaginal birth will be more complicated, so, an instrumental delivery (with forceps or vacuum) may be needed, or emergency cesarean section,[31] in this review it was found that the risk can increase up to 2.37 times (OR 2.37, 95% CI 1.30-4.44).

Among the fetal complications it was found: macrosomia, this being the most prevalent complication,[17,20] the main reason for this weight gain is the mother's insulin resistance, because more glucose passes through the placenta to reach the fetal circulation[31] and consequently, the extra glucose is stored as body fat in the fetus causing macrosomia[32]. It was also found large size compared to the age, neonatal hypoglycemia due to hyperinsulinism,[33] hyperbilirubinemia, stillbirths, the leading causes related to this are abnormalities of placenta, congenital malformations and intrauterine growth retardation,[34] suffocation, and respiratory distress.

GDM is an entity that occurs in the second trimester so there are no effects on organogenesis as in pregestational diabetes,[35] a condition for which cardiac and Central Nervous System malformations have a low risk, OR 1.2 and 0.8, respectively.

Since this review highlights the relevance of GDM in increasing the prevalence of both maternal and fetal complications, it is important that the competent authorities in formulating Health strategies further emphasize preventive measures and timely sieve in all pregnant women in order to decrease both GDM and complications that may occur.

Although the results presented are relevant, it is important to be careful in the interpretation of them, since the quality of 8 of the 13 included studies was of average quality and 1 presented low quality. In addition, there was significant heterogeneity between the selected studies in terms of age, BMI, study design, diagnostic methods and presentation of results, and may have affected the reliability and validity of the findings.

CONCLUSIONS

In general, in the findings of this systematic review, a positive association is shown, since both maternal and fetal complications increase with the presence of GDM and decrease in its absence.

In those patients in whom prevention was not possible, it is imperative to make lifestyle modifications, provide a treatment scheme if necessary, and perform laboratory studies to detect changes in a timely manner. All of this must be managed by a multidisciplinary group (doctors, nutritionists, nurses, psychologists), to provide a better quality of life and to avoid complications in the short and long term.

Although the information collected is not in the Mexican population, the results provide relevant information for health authorities to carry out efficient initiatives to address the issue, being able to improve the care of patients with GDM from screening to the prevention of complications. Likewise, it is important to carry out longitudinal studies in Mexican populations to have a better overview of the current situation in our country.

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Table 2. Characterization of the included studies, according to year, country, population and type of study.

Year	Country	Population	Type of study	Results	Author
2011	Ireland	680	Prospective cohort	OR (95% CI)	O'Sullivan et al. [15]
2011	Swiss	10 525	Retrospective cohort	OR (95% CI)	Fadl et al.[16]
2011	Taste	262	Prospective cohort	n (%)	Bener et al.[18]
2012	Canada	558	Retrospective observational	OR (95% CI)	Bodmer-Roy et al.[19]
2012	India	286	Cases and controls	OR (95% CI)	Bhat et al.[20]
2012	Saudi Arabia	419	Retrospective cases and controls	OR (95% CI)	AlFaleh et al.[21]
2015	Denmark	9014	Prospective cohort	OR (95% CI)	Ovesen et al.[22]
2016	EEUA	841	Randomized clinical trial	OR (95% CI)	Blackwell et al.[26]
2017	France	57 629	Cross	OR (95% CI)	Billionnet et al.[23]
2017	India	139	Prospective observational	n (%)	Thiruvikrama et al.[24]
2018	Malaysia	193	Randomized prospective cohort	n (%)	Basri et al.[25]
2019	EEUA	306	Randomized clinical trial	RR (95% CI)	Werner et al.[27]
2020	Ethiopia	684 neonates	Prospective cohort	RR (95% CI)	Muche et al.[17]

Source: own elaboration from the articles found in the methodological search. OR: odds ratio RR: relative risk CI: confidence interval

Table 3. Obstetric complications of GDM

Year	Results	Cesarean section	Preeclampsia	Prematurity	Author
2011	OR (95% CI)	1.3 (1.0–1.6)	1.1 (0.7–1.8)	1.7 (1.1–2.6)	O'Sullivan et al. [15]
2011	OR (95% CI)	1.46 (1.38–1.54)	1.81 (1.64–2.00)	1.71 (1.58–1.86)	Fadl et al.[16]
2011	n (%)	23 (8.8%)	19 (7.3%)	33 (12.6%)	Bener et al.[18]
2012	OR (95% CI)	1.45 (0.89–2.39)	2.40 (0.92–6.27)	1.10 (0.53–2.27)	Bodmer-Roy et al.[19]
2012	OR (95% CI)	1.18 (0.85–1.64)	1.81 (1.23–2.65)	2.30 (1.24–4.27)	Bhat et al.[20]
2014	OR (95% CI)	1.11 (1.04-1.18)	1.30 (1.20-1.41)	-	Ovesen et al.[22]
2016	OR (95% CI)	2.37 (1.30-4.44)	2.96 (1.35-7.03)	-	Blackwell et al.[26]
2017	OR (95% CI)	1.4 (1.4, 1.5)	1.6 (1.5, 1.7)	1.2 (1.2, 1.3)	Billionnet et al.[23]
2017	n (%)	-	12 (9)	14 (11)	Thiruvikrama et al.[24]
2018	n (%)	60 (31.1%)	15 (7.72%)	16 (8.9%)	Basri et al.[25]

Source: own elaboration from the articles found in the methodological search. OR: odds ratio RR: relative risk CI: confidence interval

Table 4. Neonatal complications of GDM

Results	Macrosomia	Size> GA	Hypoglycemia	Hyperbiliru binemia	Perinatal death	Suffocation	Shoulder dystocia	Respiratory Distress	Author
OR (95% CI)	1.2 (0.7–2.1)	1.3 (1.0–1.7)	3.4 (1.3–9.0)	-	-	-	-	2.0 (1.1–3.7)	O'Sullivan et al. [15]
OR (95% CI)	1.63 (1.50–1.78)	3.43 (3.21–3.67)	-	-	0.80 (0.58–1.10)	0.94 (0.85–1.03)	2.56 (1.96–3.32)	0.94 (0.85–1.03)	Fadl et al.[16]
n (%)	27 (10.3%)	-	-	33 (12.6%)	-	-	-	-	Bener et al.[18]
OR (95% CI)	1.28 (0.71–2.31)	1.58 (0.79–3.13)	0.49 (0.16–1.48)	1.08 (0.55–2.13)	-	-	0.66 (0.13–3.32)	-	Bodmer-Roy et al.[19]
OR (95% CI)	5.2 (1.13–23.99)	-	11.97 (2.79–51.38)	-	0.67 (0.19–2.40)	-	-	0.94 (0.53–1.64)	Bhat et al.[20]
OR (95% CI)	-	-	3.19 (1.05,9.71)	1.02 (0.95–1.10)	-	3.4 (0.66-20.9)	-	0.55 (0.13-2.2)	AlFaleh et al.[21]
OR (95% CI)	1.40 (1.23-1.59)	-	-	-	0.73 (0.48-1.13)	-	1.72 (1.40-2.11)	-	Ovesen et al.[22]
OR (95% CI)	2.56 (1.54-4.40)	2.94 (1.81-4.93)	-	-	-	-	-	-	Blackwell et al.[26]
OR (95% CI)	1.8 (1.7, 1.8)	-	-	-	0.7 (0.6, 0.8)	1.2 (1.1-1.3)	1.3 (1.1- 1.5)	1.3 (1.2-1.3)	Billionnet et al.[23]
n (%)	-	-	6 (4.5)	-	-	-	-	15 (11)	Thiruvikrama et al.[24]
n (%)	7 (3.6%)	-	5 (2.5%)	-	-	-	-	-	Basri et al.[25]
RR (95% CI)	-	-	-	1.39 (1.03–1.88)	-	-	-	0.84 (0.61–1.17)	Werner et al.[27]
RR (95% CI)	3.81 (1.95, 7.45)	2.38 (1.41, 4.03)	-	-	-	-	-	-	Muche et al.[17]

Source: own elaboration from the articles found in the methodological search. OR: odds ratio RR: relative risk CI: confidence interval EG: gestational age