A portrait of gestational diabetes mellitus in Brazil: A systematic review and meta-analysis

Betine Pinto Moehlecke Iser[1]
https://orcid.org/0000-0001-6061-2541

Caroline Stein[2]
https://orcid.org/0000-0003-4777-1630

Luisia Feichas Alves[3]
https://orcid.org/0000-0002-8400-6148

Morgana Lourenço de Souza Carvalho[2]
https://orcid.org/0000-0001-8171-503X

Sergio Angelo Rojas Espinoza[2]
https://orcid.org/0000-0001-7664-2948

Maria Inês Schmidt[2]
https://orcid.org/0000-0002-3837-0731

[1] Universidade do Sul de Santa Catarina, Programa de Pós-graduação em Ciências da Saúde, Tubarão, SC, Brasil
[2] Universidade Federal do Rio Grande do Sul (UFRGS), Faculdade de Medicina, Porto Alegre, RS, Brasil
[3] Universidade Federal do Rio Grande do Sul (UFRGS), Biblioteca Central, Porto Alegre, RS, Brasil

ABSTRACT

The diagnostic criteria for gestational diabetes mellitus (GDM), a transient hyperglycemic state during pregnancy, has varied remarkably over time, resulting in a diversity of prevalence rates. The aim of this systematic literature review was to provide estimates of prevalence rates of GDM in Brazil according to different diagnostic criteria. We identified, reviewed, and extracted data from the scientific literature on studies estimating the prevalence of diabetes in pregnant women living in Brazil. The databases searched were PubMed, LILACS, SciELO, Embase, Web of Science, and Cochrane Library. We grouped studies by the source of information assessing GDM, patients' age, and criteria used to diagnose GDM. When three or more studies were available in a group, we calculated the pooled prevalence. The Joanna Briggs Institute (JBI) appraisal tool was used to assess the risk of bias. The data were reported according to the 2020 PRISMA recommendations. The study protocol was registered in PROSPERO. We identified 1,328 records and selected 21 studies involving 122,635 pregnant women. Studies in adults only, with primary data and laboratory measurements, and using the IADPSG criteria (n = 3) had a GDM prevalence of 18.0% (95% confidence interval [CI]: 16.0-20.1%) and included 6,243 participants. Estimates of self-reported GDM (n = 3; 10,136 participants of all ages) had a pooled GDM prevalence of 2.1% (95% CI: 1.5-5.2%), with high heterogeneity (I^2 = 85.0%, p < 0.01). Studies including adolescents had consistently low prevalences. The prevalence of GDM in Brazil varied, was greater when the IADPSG criteria were applied, and depended on the methods used to obtain the GDM information and the age structure of the sample.

Keywords
Gestational diabetes; Brazil; prevalence; epidemiology

Correspondence to:
Betine Pinto Moehlecke Iser
Universidade do Sul de Santa Catarina, Programa de Pós-graduação em Ciências da Saúde
Av. José Acácio Moreira, 787, Bairro Dehon
88704-900 – Tubarão, SC, Brasil
betinee@gmail.com

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INTRODUCTION

Gestational diabetes mellitus (GDM), a transient hyperglycemic state diagnosed in pregnancy, is associated with adverse maternal and fetal outcomes (1). Although the concept of GDM is generally consensual, the diagnostic criteria for GDM have experienced marked heterogeneity over time, resulting in diverse prevalence rates, as attested by systematic reviews across different countries, regions, and even globally (2-4).

In Brazil, routine detection of GDM was incipient before the implementation of the national health unified system (*Sistema Único de Saúde* [SUS]). Screening for GDM was generally restricted to university centers and usually followed the guidelines of the American Diabetes Association (ADA) based on pregnancy-specific criteria. These guidelines were derived from a series of studies conducted methodically by O'Sullivan's group (5). The ADA position was reiterated in 1979 by the National Diabetes Data Group (NDDG), when the diagnostic criteria for diabetes and other categories of glucose intolerance were defined (6). The recommended diagnostic procedure for GDM was

based on a two-stage screening in which the patients initially underwent a 50-g glucose challenge, and those with a positive result underwent a 100-g oral glucose tolerance test (OGTT) with samples collected at fasting and at 1, 2, and 3 hours. The diagnosis of GDM was defined as the presence of at least two abnormal plasma glucose results. While agreeing with most NDDG recommendations, a World Health Organization (WHO) panel in 1980 defined GDM using the same criteria applied outside pregnancy for impaired glucose tolerance (7), without specifying a cutoff value for fasting glucose levels.

Confronted with this diagnostic controversy, the Brazilian Ministry of Health conducted a national study – the Brazilian Study of Gestational Diabetes (8). In the study, the protocol for GDM diagnosis involved a 2-hour 75-g OGTT, with samples collected at fasting and at 1 and 2 hours. During a workshop, the panel recommended adopting a two-stage screening, in which the patient would first undergo measurement of fasting plasma glucose level and, if elevated, a 2-hour 75-g OGTT, defining GDM according to the same criteria established for impaired glucose tolerance outside pregnancy (9). While adopting the same criteria established for impaired fasting glucose outside pregnancy (≥100 mg/dL or 110 mg/dL) (10), the panel also considered including this category in the definition of GDM (9).

In 2008, new data on GDM emerged with the publication of the study Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) (11), which involved more than 23,000 women across nine countries. The study's results compelled a committee of experts – The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) – to develop and validate the diagnostic criteria for GDM based on adverse pregnancy outcomes. The procedures and criteria proposed were agreed upon during international meetings and were published in 2010 (12). The main recommendation from the committee was to adopt universal screening with a 2-hour 75-g OGTT (fasting and 1 and 2 hours) and consider the diagnosis of GDM when one or more values were abnormal. These criteria have been increasingly adopted (13-15), but the controversy around them persists.

In 2014 in the United Kingdom, the National Institute for Health and Care Excellence (NICE) (16) proposed a two-stage screening for women at high risk for GDM based on a 2-hour 75-g OGTT. Although their definition of GDM included the cutoff value considered for impaired glucose tolerance outside pregnancy (as recommended by the 1979 WHO panel), the NICE recommendations also incorporated the cutoff value of 100 mg/dL for fasting plasma glucose.

In the United States, a consensus from a 2012 National Institutes of Health (NIH) conference recommended maintaining the two-stage screening procedure based on O'Sullivan's criteria (with Carpenter and Coustan corrections) (5). The ADA maintained this recommendation but also included the option of universal screening based on IADPSG procedures and criteria (17).

The debate continues. A comparison of these two screening criteria – IADPSG and Carpenter-Coustan – showed a substantial increase in GDM prevalence with the IADPSG criteria but did not detect improvement in pregnancy outcomes (5,6).

In Brazil, a 2016 consensus panel proposed two strategies for GDM screening and diagnosis, to be chosen according to the financial viability and technical resources in different regions of the country (18).

Given the diversity of diagnostic criteria that emerged over the last decades and the long experience in GDM screening in Brazil, we aimed to conduct a systematic review of the pertinent literature on the prevalence of GDM in the country, establishing no limit for the year of publication.

MATERIALS AND METHODS

The study protocol was registered in PROSPERO (February 14, 2022) under the title "Prevalence of gestational diabetes in Brazil: a systematic review" and can be accessed online using the record ID CRD42022300767 (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=300767).

We used the following search strategy to conduct the systematic literature review of original studies on the prevalence of GDM in pregnant women in Brazil. First, we searched the PubMed database (US National Library of Medicine, NIH). Then, we replicated the search in other databases, specifically, LILACS (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*), SciELO, Embase, Web of Science, and Cochrane Library. For the search, we included free text words and indexed vocabulary (DeCS Health Science Descriptors) for articles published in Portuguese and used Medical

Subject Headings (MeSH) terms for the Medline/PubMed search. The initial terms were: (prevalence OR prevalence [MeSH Terms] OR survey OR epidemiology OR incidence) AND (diabetes mellitus [MeSH Terms] OR diabetes OR hyperglycemia) AND (pregnant* OR gestation* OR gravid*) AND (brasil OR brazil). The complete PubMed search strategy is available in the Supplementary Material.

Selection of studies

The search was limited to studies in humans, without restriction of publication language or year, from the oldest records available until November 2021. A library with all the records found in the search was created by the researcher LFA using the software Zotero (https://www.zotero.org/). After removing duplicates, we uploaded the file into the software Rayyan to organize the references and share the file among the researchers for study selection and data extraction.

Using the list of references, two researchers (MLSC, SARE) independently screened the studies by reading the titles and abstracts using the following inclusion criteria (PICO framework): (A) Population: general population of pregnant women living in Brazil, regardless of gestational age, sample size, or study setting; (B) I: diagnostic methods applied, including fasting plasma glucose (FPG), OGTT, glycated hemoglobin (HbA1c), previous self-reported diagnosis of GDM, or direct evaluation of medical record; (C) Outcome measure: prevalence of GDM diagnosed according to screening methods; (D) Study design: observational study estimating prevalence data. Since our study aimed to describe the population's GDM prevalence, we did not include the "C" (comparison or control) from the PICO acronym. We excluded studies conducted on groups with specific pathologies, review articles, editorials, case-control studies, and studies with incomplete data estimating prevalence. In cases of disagreement, we consulted the full-text papers with the help of a third researcher experienced in the field (BPMI). In doubtful cases, the record was considered eligible for full-text reading.

After the initial screening, the full text was read independently by two researchers (MLSC, SARE) and later revised by two other researchers (BPMI, CS). During the full-text reading, we excluded studies that did not meet all the eligibility criteria or those that selected women at high risk for GDM (due to lifestyle and medical factors) or from high-risk prenatal centers, as detailed in Figure 1.

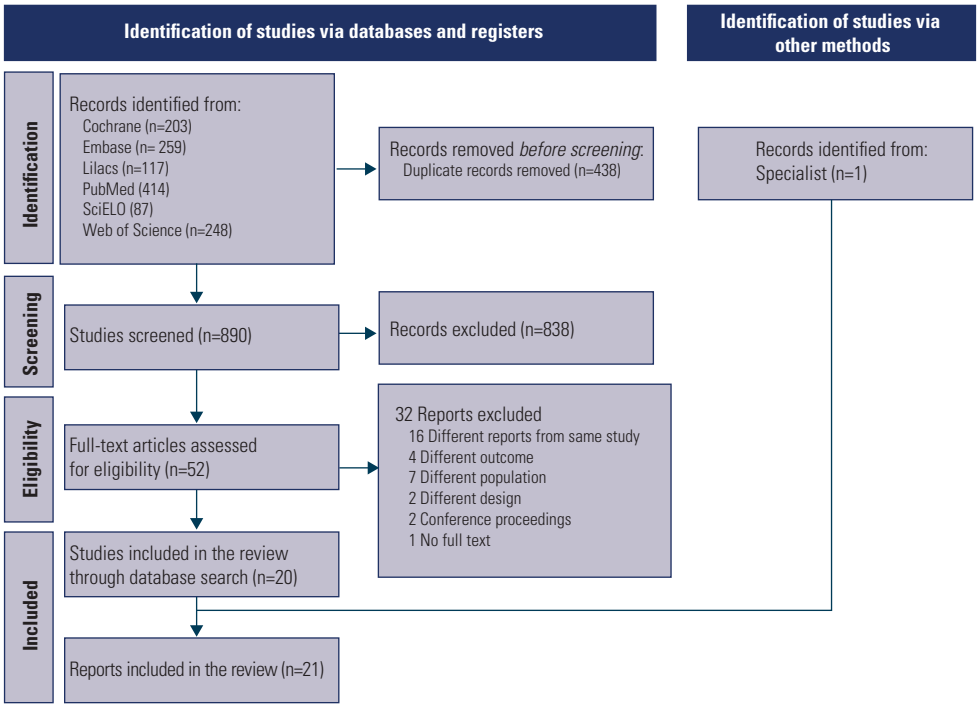


Figure 1. PRISMA flow diagram.

Data extraction

The primary outcome for analysis was the prevalence of GDM in pregnant women living in Brazil, regardless of gestational age. We extracted the data using a standard form built into a Google Spreadsheet containing items of interest to the review for use by the reviewers after initial training (BPMI, MLSC, SARE). The data, compiled for each study, included the following: first author, year of publication, study or cohort name (when available), location (city, state, region), year of data collection, method used for sample selection, study design, sample size, method used to define the outcome (self-reporting, medical record, or primary laboratory data), diagnostic criteria used to analyze the medical record or laboratory data, number of cases diagnosed with GDM, and prevalence rate reported in each study. If more than one study used the same database or population, we included only the study with the largest sample size or complete information. In case of disagreement, we consulted a senior researcher (MIS).

The data were reported according to the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) recommendations. The inclusion/exclusion process is described in Figure 1.

Methodological quality appraisal

The researchers BPMI, MLSC, and SARE assessed the studies' quality and risk of bias using the Joanna Briggs Institute (JBI) appraisal tool checklist for prevalence studies. For the evaluation, we considered the appropriateness of the sample frame and recruitment of participants, adequacy of the sample size, description of the subjects and settings, validity of the identification method, standardization of the condition measured, adequacy of the statistical analysis, and rate of responses. We adapted the evaluation of these parameters for the specific setting of our GDM question, considering also scales used in similar systematic reviews, such as those used by Hoy and cols. (19) and Muche and cols. (4). We adapted the criteria of representativeness to the setting of studies of GDM, usually conducted within the health services. We considered a sample to be drawn from the general population of pregnant women when the source covered the majority of the population, such as population registries, general practice registries, or registries of clinics for pregnant women.

We considered the sample size adequate when it was calculated *a priori*. We considered the description of the subjects and settings adequate if the participants' mean age and body mass index (BMI) were available. We considered having a low risk of bias those studies that used methods to identify GDM based on a laboratory test (*e.g.*, OGTT, FPG, HbA1c) or laboratory data from medical records. We considered other methods (such as those from medical records with no specification of the test used or self-reported GDM) as having a high or uncertain risk of bias. The identification method was considered standardized when it used the same approach for data collection for all patients (a unique criterion) and training of the researchers on data extraction for each study. We considered the response rate adequate when ≥75% (4,19), considering the study's total target population when described. We considered the statistical analysis adequate when the study provided values for the total sample size (denominator) and total number of GDM cases (numerator) to allow for the estimation of prevalence. When the information provided was insufficient, we agreed to grade that item as unclear (uncertain).

Analysis

We initially grouped the studies according to the methods they used to identify GDM into (A) primary data and laboratory measurements, (B) medical records, and (C) self-reporting. If individual studies reported multiple prevalence rates based on different diagnostic criteria, we included each specific finding for the initial grouping. Then, based on the number of events and sample size obtained for each study, we calculated the pooled prevalence using a random effects model for each subgroup whenever three or more studies were available. We chose the random effects model to combine studies due to the nature of observational studies and the certainty of heterogeneity among them, even between studies with the same diagnostic criteria. We built forest plots to visualize the extent of the heterogeneity between studies. We considered the presence of heterogeneity when I^2 was ≥50% and the Cochran's Q test and its respective p value was < 0.05. We conducted analyses using R language in RStudio (RStudio PBC, Boston, MA, USA) and the packages meta and metafor.

RESULTS

Description of the studies included in the review

The database search identified 1,328 records from January 1, 1965 (when the first document was available) to November 30, 2021. After removal of duplicates (n = 438) and exclusions by title and abstract (n = 838), 52 studies were considered eligible for full-text reading. Of these, 29 were excluded as they duplicated reports of studies already included (n = 16) or had a different outcome (n = 4), population (n = 7), or study design (n = 2). We also excluded records based on conference proceedings (n = 2) and those without full text accessible online (n = 1). One study published recently was added by an expert (BPMI) due to its potential relevance. Altogether, we extracted results from 21 studies. The PRISMA flowchart of study identification is presented in Figure 1.

We evaluated the 21 studies according to the method they used to assess the occurrence of GDM, *i.e.*, primary data with laboratory measurements (FPG, OGTT, or a combination of both; n = 10) (8,20-28), self-reported GDM diagnosis (n = 3) (29-31), self-reported diabetes during pregnancy without specifying the type of diabetes (n = 1) (32), medical records with previous diagnostic tests (such as a medical chart or prenatal card; n = 6) (31,33-37), and data collected using other systems (including the International Classification of Diseases [ICD]), for which specific criteria could not be identified (n = 2) (38,39). We considered the studies using the two latter methods as having poorly defined criteria. Two studies (31,34) compared different criteria and provided data for both. The characteristics of the included studies and the methods they used to identify GDM are shown in Table 1.

Of the 10 studies based on primary data and measurement of laboratory tests, nine used a universal approach to identify GDM, and one used a two-step approach for this purpose. In the universal approach, the diagnostic test is applied to all study participants, while in the two-step approach, the diagnostic test is applied only to those with a positive result in the first test. Among the studies using the universal approach, most (six) used the IADPSG criteria, two used the 1999 WHO criteria, and one used Carpenter-Coustan values. Studies adopting a two-step approach used FPG or a 50-g glucose challenge as the first test. Finally, we included one study that used the 1999 WHO criteria and the presence of impaired FPG.

Although the report of GDM prevalence was not the primary aim of most studies, they all provided the values (numerators and denominators) required for the calculation of prevalence. The sample size varied widely, from 120 to 79,368 participants, with a median of 792, resulting in the inclusion of 122,635 women in the systematic review. Two studies were conducted at a national level (32,33), while two were conducted in six capitals (8,21) and one in five capitals (20). Ten studies originated in the South and Southeast regions of Brazil.

Quality of the studies

Table 2 summarizes the risk of bias in each study. We categorized the studies according to their overall risk of bias, considering six studies as having a low risk, 13 as having a moderate risk, and two as having a high risk. We considered a high risk of bias when the method used to identify GDM was invalid or when three or more items in the study were considered potentially biased.

Forest plots

The meta-analysis included 16,379 pregnant women. We grouped the studies according to the diagnostic criteria they used to identify GDM and the participants' age (*i.e.*, whether the study included pregnant women of all ages or just adults aged ≥ 18 years). Studies with primary data and laboratory measurements including only adult women and adopting the IADPSG criteria (n = 3) had a pooled GDM prevalence of 18.0% (95% CI: 16.0-20.1%) and 6,243 participants (Figure 2). This estimate was not heterogenous (I^2 = 0%, p = 0.62) and was comparable to that found in studies using the IADPSG criteria based on medical records (18.3%).

For studies based on medical records (n = 5) and using other diagnostic criteria, the overall estimates were 4.3-9.1%, depending on the age of the participants and diagnostic criteria used. Estimates of prevalences in studies using self-reported GDM (n = 3), which included 10,136 participants of all ages, were even lower, with a pooled prevalence of 2.1% (95% CI: 1.5-5.2%). For this pooled estimate, we found significant heterogeneity (I^2 = 85.0%, p < 0.01) when we summarized the GDM prevalence. As expected, studies that included women of all ages had a lower prevalence of GDM due to the lower prevalence of this condition among adolescents.

Table 1. Summary and characteristics of the studies included in the systematic review

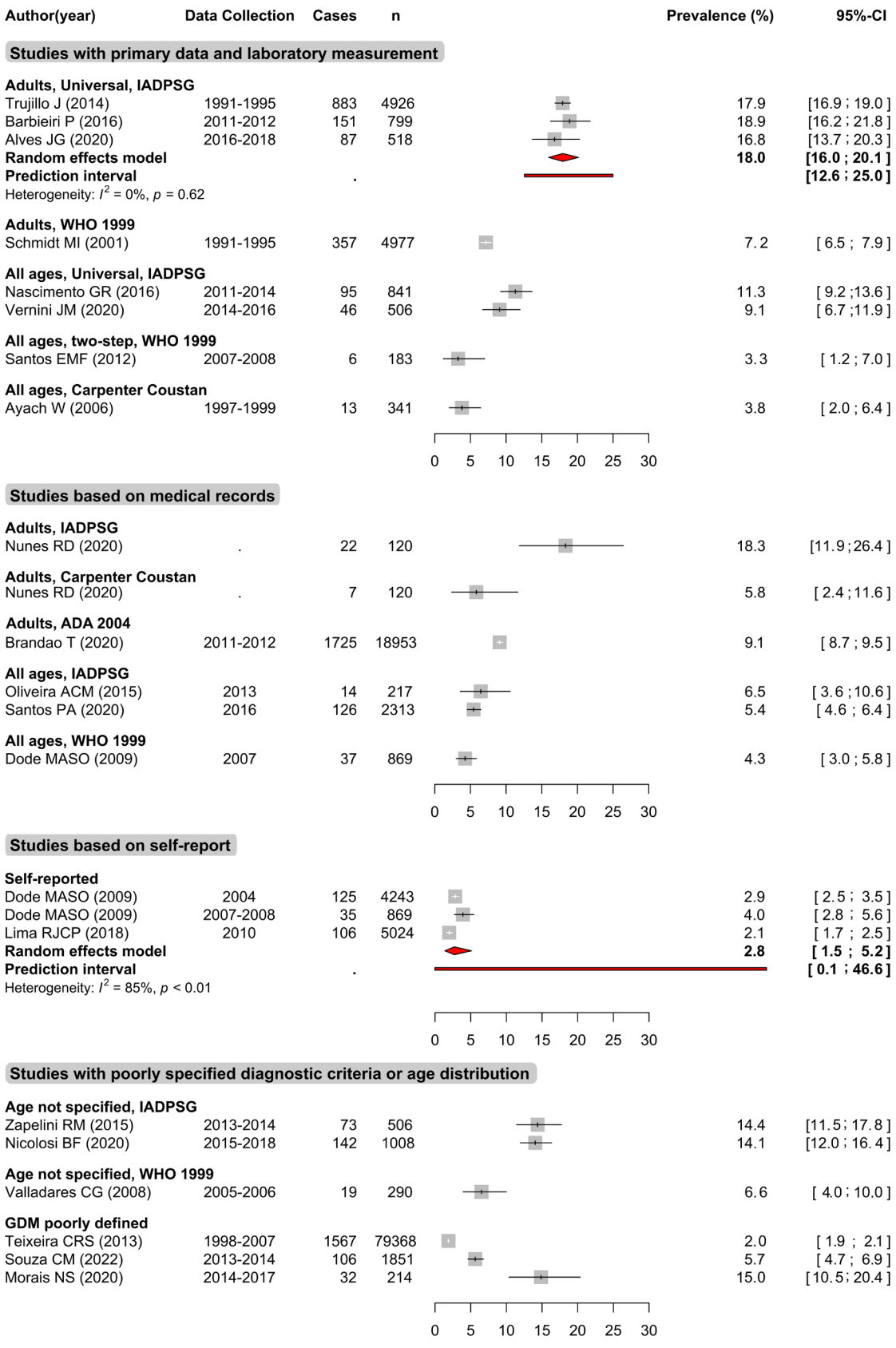
Diagnostic criteria	Author and year	Location	Data collection	Setting	Age (years) mean (SD) or age groups	Sample selection	Universal/two steps	Sample	Cases	%
Primary data with laboratory measurements										
IADPSG[§]	Alves JG, 2020	Recife – PE	2016-2018	Hospital	26.1(5.8)	Convenience	Universal	518	87	16.8
IADPSG	Barbieiri P, 2016	Ribeirão Preto – SP	2011-2012	Primary Health Care	≥20	Convenience	Universal	799	151	18.9
IADPSG	Nascimento GR, 2016	Recife – PE	2011-2014	Prenatal Clinics	26.2 (5.8); 18-40	Convenience	Universal	841	95	11.3
IADPSG	Nicolosi BF, 2020 (SAMBA)	Five Brazilian cities*	2015-2018	Primary Health Care and Prenatal Clinics	Information not available	Convenience	Universal	1,008	142	14.1
IADPSG	Trujillo J, 2014 (EBDG)	Six Brazilian capitals[‡]	1991-1995	Prenatal Clinics	27.8 (5.4); ≥20	Census	Universal	4,926	883	17.9
IADPSG	Vernini JM, 2020	Botucatu – SP	2014-2016	Primary Health Care and Prenatal Clinics	All ages	Convenience	Universal	506	46	9.1
WHO 1999[≈]	Schmidt MI, 2001 (EBDG)	Six Brazilian capitals[‡]	1991-1995	Prenatal Clinics	≥20	Census	Universal	4,977	357	7.2
WHO 1999 (with IFG)[¶]	Santos EMF, 2012	Salvador – BA	2007-2008	Hospital	26(6.4); All ages (13-42)	Convenience	Two-steps	183	6	3.3
WHO 1999 (with IFG)	Valladares CG, 2008	Brasília – DF	2005-2006	Primary Health Care	Information not available	Convenience	Universal	290	19	6.6
Carpenter-Coustan**	Ayach W, 2006	Campo Grande – MS	1997-1999	Prenatal Clinics	All ages	Census	Universal	341	13	3.8
Medical record										
ADA 2004[††]	Brandao T, 2020 (*Nascer no Brasil*)	Brasil	2011-2012	Hospital	≥20	Convenience		18,953	1 725	9.1
WHO 1999	Dode MASO, 2009	Pelotas - RS	2007-2008	Hospital	26.7; All ages (13-49)	Census		869	37	4.3
IADPSG	Nunes RD, 2020	Palhoça – SC	2019	Hospital and Prenatal Clinics	27.3 (7.0)	Convenience		120	22	18.3
Carpenter-Coustan								120	7	5.8
GDM not defined	Morais NS, 2020	Rio de Janeiro – RJ	2014-2017	Primary Health Care	18-35	Convenience		214	32	15.0
IADPSG	Oliveira ACM, 2015	Maceió – AL	2013	Hospital	24.5 (7.69); All ages	Convenience		217	14	6.5
IADPSG	Santos PA, 2020	Caxias do Sul – RS	2016	Primary Health Care	Information not available	Census		2,313	126	5.4
GDM not defined	Teixeira CRS, 2013	Ribeirão Preto – SP	1998-2007	Hospital	All ages	Census		79,368	1 567	2.0
IADPSG	Zapelini RM, 2015	Tubarão – SC	2013-2014	Hospital	Information not available	Census		506	73	14.4
Self-report										
	Dode MASO, 2009	Pelotas – RS	2004	Hospital	All ages	Census		4,243	125	2.9
	Dode MASO, 2009	Pelotas – RS	2007-2008	Hospital	26.7; All ages (13-49)	Census		869	35	4.0
	Lima RJCP, 2018 (BRISA)	São Luís – MA	2010	Hospital	25.1(6)	Stratified		5,024	106	2.1
	Souza CM, 2022 (Brazilian National Health Survey 2013)	Brazil	2013-2014	Domestic	18-49	Cluster		1,851	106	5.7

Abbreviations: ADA, American Diabetes Association; AL, Alagoas; AM, Amazonas; BA, Bahia; BRISA, Brazilian Ribeirão Preto and São Luís Birth Cohort Studies; CE, Ceará; DF, Distrito Federal; EBDG, *Estudo Brasileiro de Diabetes Gestacional*; MA, Maranhão; OGTT, oral glucose tolerance test; PE, Pernambuco; RJ, Rio de Janeiro; RS, Rio Grande do Sul; SC, Santa Catarina; SD, standard deviation; SP, São Paulo; WHO, World Health Organization. *Fortaleza – CE, Recife – PE, Porto Alegre – RS, Botucatu – SP, Campinas – SP. [‡]Porto Alegre – RS, São Paulo – SP, Rio de Janeiro – RJ, Salvador – BA, Fortaleza – CE, and Manaus – AM. [§] The International Association of the Diabetes and Pregnancy Study Groups (IADPSG): 75-g OGTT: fasting ≥92 mg/dL, 1 hour ≥180 mg/dL, 2 hours ≥153 mg/dL. [≈] WHO 1999: 75-g OGTT: fasting ≥126 mg/dL or 2 hours ≥140 mg/dL. [¶]WHO 1999 (including impaired fasting plasma glucose): 75-g OGTT: fasting ≥110 mg/dL or 2 hours ≥140 mg/dL. ** Carpenter-Coustan: 100-g OGTT: fasting ≥95 mg/dL, 1 hour ≥180 mg/dL, 2 hours ≥155 mg/dL, 3 hours ≥140 mg/dL. [††]ADA 2004: 100-g OGTT: fasting ≥95 mg/dL, 1 hour ≥180 mg/dL, 2 hours ≥155 mg/dL.

Table 2. Summary of risk of bias evaluated using the JBI adapted scale

Study	Sample frame	Study participants	Sample size	Study subjects description	Data analysis coverage	Valid methods of identification*	Measurement standardized	Appropriate statistical analysis	Adequate response rate	Overall risk of bias
Primary data with laboratory data										
Alves JG (2020)	U	Y	U	Y	Y	Y	Y	Y	Y	Low
Barbieiri P (2016)	N	U	Y	Y	Y	Y	Y	Y	Y	Moderate
Nascimento GR (2016)	Y	N	U	Y	N	Y	Y	Y	Y	Moderate
Nicolosi BF (2020)	U	U	Y	N	Y	Y	U	Y	Y	Moderate
Trujillo J (2014)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Low
Vernini JM (2020)	U	U	Y	Y	Y	Y	Y	Y	Y	Low
Schmidt MI (2001)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Low
Santos EMF (2012)	N	U	U	Y	U	Y	Y	Y	Y	Moderate
Valladares CG (2008)	Y	Y	U	N	Y	Y	Y	Y	Y	Moderate
Ayach W (2006)	U	U	Y	N	Y	Y	Y	Y	Y	Moderate
Medical record										
Brandao T (2020)	Y	Y	Y	Y	Y	Y	U	Y	Y	Low
Dode MASO (2009)*	Y	U	U	Y	Y	U	N	Y	Y	Moderate
Nunes RD (2020)	N	U	U	Y	U	Y	Y	U	U	Moderate
Morais NS (2020)	U	Y	N	Y	U	U	U	Y	Y	Moderate
Oliveira ACM (2015)	U	Y	Y	Y	Y	Y	U	Y	Y	Low
Santos PA (2020)	Y	Y	Y	Y	U	Y	U	U	N	Moderate
Teixeira CRS (2013)	Y	Y	Y	U	Y	N	U	U	U	High
Zapelini RM (2015)	Y	U	U	N	U	Y	U	Y	N	Moderate
Self-report										
Dode MASO (2009)†	Y	Y	Y	Y	Y	U	U	N	Y	Moderate
Lima RJCP (2018)	Y	U	Y	Y	Y	U	N	Y	Y	Moderate
Souza CM (2022)	Y	Y	U	Y	U	N	U	Y	Y	High

Abbreviations: Y, yes; N, no; U, uncertain; N/A, not applicable *Data collected in 2007. †Data collected in 2004. *Gestational diabetes mellitus not clearly specified, possibly including other types of diabetes in pregnancy; or diagnostic criteria not fitting in any conventional form.



Abbreviations: ADA, American Diabetes Association; 95% CI, 95% confidence interval; FIGO, The International Federation of Gynecology and Obstetrics; GDM, gestational diabetes mellitus; IADPSG, The International Association of the Diabetes and Pregnancy Study Groups; IFG, impaired fasting glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization.

Figure 2. Forest plot of the studies included and meta-analysis.

DISCUSSION

The prevalence of GDM in Brazil varied widely according to the diagnostic criteria adopted in the study, with the highest prevalence found in studies using the IADPSG criteria (18.0%, 95% CI: 16.0-20.1%). Because of the heterogeneity across studies, we were unable to provide a pooled estimated prevalence of GDM in Brazil, except in studies using the IADPSG criteria and in those based on self-report. The multitude of diagnostic criteria that we described illustrates the lack of consensus in establishing the diagnosis of this condition over time. Notably, most studies originated in the Southeast and South regions of the country, which have easier access to health care facilities and more research centers.

To the best of our knowledge, this is the first study determining the prevalence of GDM in Brazil using a systematic review and meta-analysis. The variation in prevalence rates is similar to that seen in the literature, with the IADPSG criteria accounting for an almost two times higher proportion of diabetes in pregnancy (40,41). Of note, the IADPSG criteria have been adopted more recently in Brazilian studies, so the higher prevalence associated with its use can be influenced or inflated by the increasing occurrence and diagnosis of GDM in Brazil, following the increasing trend of overall diabetes in the country, as seen worldwide (42,43). However, when we considered only studies using the IADPSG criteria, we could not find a trend of increasing GDM prevalence over the years.

Our findings are consistent with results from systematic reviews conducted in other countries, which showed that the highest prevalence of GDM occurred in studies using the IADPSG criteria (44). According to data from the International Diabetes Federation, the global prevalence of hyperglycemia in pregnancy is 16.7%, of which 80.7% is due to GDM, with similar results in Central and South Latin America, where one out of six live births are affected by hyperglycemia in pregnancy. In our systematic review of Brazilian studies, the prevalence was similar (14.5%) when we analyzed studies using universal screening based on IADPSG thresholds. A global systematic review (2) evaluating the impact of diagnostic criteria on the prevalence of GDM had shown that, regardless of the type of screening criteria, the overall prevalence was 4.4% and increased to 10.6% when the IADPSG criteria were used.

Variations in prevalence rates depending on the criteria used for diagnosis of GDM have been previously reported (40,44,45). For example, in Europe, an overall 5.4% (95% CI: 3.8-7.8%) prevalence of GDM has been reported, ranging from 6.4% (95% CI: 3.8-10.4%) to 4.7% (95% CI: 2.7-8.1%) when using, respectively, one-step or two-step screening (3). Another European study (46) that analyzed the prevalence of GDM between 2014 and 2019 across 24 European countries reported an overall weighted prevalence of 10.9% (95% CI: 10.0-11.8%, I^2 = 100%).

In the Eastern Mediterranean region (47), the prevalence of GDM has been estimated at 11.7% (95% CI: 10.7-12.6%; I^2 = 99.6%) and varied widely depending on the five adopted criteria, suggesting little agreement between the IADPSG (28.2%), Carpenter-Coustan (6.2%), WHO (15.2%), ADA (10.3%), and NDDG (8.1%) criteria. In studies from Africa published from 2013 to 2018 (4), the random effect pooled prevalence estimate of GDM was 13.6% (95% CI: 10.9-16.2%; I^2 = 96.1%), with variations across subregions.

Additional considerations regarding the findings on GDM prevalence in Brazil are worth mentioning. First, we found the lowest prevalence in studies based on a prior self-reported diagnosis of GDM. This result was not surprising since a self-report diagnosis depends on the women's perception of their health status and related factors (48,49), including the degree of use of health care services. For example, the 2013 National Health Survey data reported a low (59%) sensitivity for self-reported diabetes, indicating a high proportion of false-negative results and a likely underestimation in prevalence rates based on self-reporting (50). Interestingly, self-reported GDM in the immediate postpartum has great sensitivity (>70%) (31), with a reported prevalence of 4.1% (95% CI: 3.0-5.5%) compared with 4.3% (95% CI: 3.2-5.7%) for diagnoses based on prenatal cards. Second, the prevalence of GDM based on prenatal care data, even considering possible quality issues, is likely to represent proper population estimates, given the high coverage of prenatal care in Brazil (98.5%) and the fact that more than 80% of the women reportedly undergo at least one measurement of blood glucose level, according to the Birth in Brazil study (51).

We must consider a few limitations in our study. First, we could not describe the prevalence rates according to some characteristics of the participants, like race or nutritional status (higher BMI), which are known to affect the prevalence of GDM in Brazil

(45) and worldwide (3,4,47). Most studies did not report maternal age or BMI, limiting the possibility of adjusted analysis. Additionally, we were unable to perform subgroup analysis by Brazilian macro-regions since most of the included studies were specific to one center or region. Finally, the different settings across studies limited our ability to provide a pooled prevalence estimate. However, the heterogeneity between studies reflecting the status of GDM in Brazil over time is, by itself, an important finding of our study.

In conclusion, the diagnostic criteria of GDM varied substantially, which is the main reason for discrepancies in this condition's prevalence. The pooled prevalence was greater when we considered studies adopting the IADPSG criteria based on primary laboratory data (18.0%, 95% CI: 16.0-20.1%), followed by the use of medical records (range 4.3-9.1%) and self-reported data (2.1%, 95% CI: 1.5-5.2%). Other factors also contributed to the variation in GDM prevalence. For example, reports that included only adult women had higher prevalences than those that also included adolescents. In addition, referral centers, by having higher proportions of high-risk pregnancies, had a higher prevalence of GDM. Although global uniform criteria for GDM screening and diagnosis have been desired for a long time and will allow simplification of the guidelines and more adequate international comparisons, we have not reached this stage yet. New studies in the field may help reach this goal.

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Availability of data and materials: all data pertaining to this study are contained and presented in this document. Additional data may be available upon request.

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SUPPLEMENTARY

Supplementary Table 1. Diagnostic criteria in the studies used to estimate the prevalence rates of gestational diabetes mellitus

Criteria	OGTT (g)	Fasting (mg/dL)	1 hour (mg/dL)	2 hours (mg/dL)	3 hours (mg/dL)
Carpenter-Coustan	100	95	180	155	140
ADA 2004	100	95	180	155	-
WHO 1999 (with IFG)	75	110	-	140	-
WHO 1999	75	126	-	140	-
IADPSG	75	92	180	153	-
FIGO	75	92	180	153	-

Abbreviations: ADA, American Diabetes Association; FIGO, The International Federation of Gynecology and Obstetrics; IADPSG, The International Association of the Diabetes and Pregnancy Study Groups; IFG, impaired fasting glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization.

Supplementary Table 2. Search strategy used in the final search on November 30, 2021

Database	Search strategy	Items found
Cochrane	#1 MeSH descriptor: [Prevalence] explode all trees #2 MeSH descriptor: [Epidemiology] explode all trees #3 MeSH descriptor: [Surveys and Questionnaires] explode all trees #4 MeSH descriptor: [Incidence] explode all trees #5 prevalence OR epidemiology OR survey OR incidence #6 MeSH descriptor: [Diabetes Mellitus] explode all trees #7 MeSH descriptor: [Hyperglycemia] explode all trees #8 MeSH descriptor: [Glucose Intolerance] explode all trees #9 MeSH descriptor: [Diabetes, Gestational] explode all trees #10 diabetes OR diabetic OR hyperglycemia OR "glucose intolerance" #11 MeSH descriptor: [Pregnancy] explode all trees #12 pregnan* OR gestation* #13 MeSH descriptor: [Brazil] explode all trees #14 brasil* OR brazil* OR brasil OR brazil #15 #1 OR #2 OR #3 OR #4 OR #5 #16 #6 OR #7 OR #8 OR #9 OR #10 #17 #11 OR #12 #18 #13 OR #14 #19 #15 AND #16 AND #17 AND #18	203
Embase	#1 'diabetes mellitus'/exp OR 'diabetes':ti,ab,kw OR 'diabetes mellitus':ti,ab,kw OR 'diabetic':ti,ab,kw OR 'pregnancy diabetes mellitus'/exp OR 'diabetes mellitus gravidarum':ti,ab,kw OR 'diabetes, gestational':ti,ab,kw OR 'diabetes, pregnancy':ti,ab,kw OR 'gestational diabetes':ti,ab,kw OR 'gestational diabetes mellitus':ti,ab,kw OR 'pregnancy diabetes':ti,ab,kw OR 'pregnancy diabetes mellitus':ti,ab,kw OR 'pregnancy in diabetics':ti,ab,kw OR diabetes:ti,ab OR diabetic:ti,ab #2 'prevalence'/exp OR 'prevalence' OR 'prevalence study' OR 'questionnaire'/exp OR 'questionnaire' OR 'questionnaires' OR 'surveys and questionnaires' OR 'survey'/exp OR 'epidemiology'/exp OR 'incidence'/exp OR 'incidence' OR 'incidence rate' OR 'rate, incidence' #3 'pregnancy'/exp OR 'gestation':ti,ab,kw OR 'pregnancy':ti,ab,kw OR 'gravidity':ti,ab,kw OR gestational:ti,ab OR pregnancy:ti,ab OR gravidez:ti,ab #4 'brazil'/exp OR 'brazil':ti,ab,kw OR 'federative republic of brazil':ti,ab,kw OR 'united states of brazil':ti,ab,kw OR brasil*:ti,ab OR brazil*:ti,ab #5 #1 AND #2 AND #3 AND #4	259
LILACS	(prevalencia OR prevalence OR epidemiologia OR epidemiology OR survey OR inquérito OR incidência OR incidence) AND (pregnancy OR gestational OR gravidez) AND (diabetes OR diabete OR diabético OR diabeticos) AND (brasil OR Brazil OR brasil* OR brazil*)	117
PubMed	#1 "prevalencia"[All Fields] OR "prevalencias"[All Fields] OR "epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalencia"[All Fields] OR "prevalencias"[All Fields] OR "epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields] OR "survey"[All Fields] OR "surveys"[All Fields] OR "surveys and questionnaires"[MeSH Terms] OR "incidence"[All Fields] OR "incidence"[MeSH Terms] #2 "diabetes, gestational"[MeSH Terms] OR "diabetes mellitus"[MeSH Terms] OR "diabete"[All Fields] OR "diabetes mellitus"[All Fields] OR "diabetes"[All Fields] OR "diabetic"[All Fields] OR "diabetics"[All Fields] OR "diabets"[All Fields] OR "diabete"[All Fields] OR "glucose intolerance"[All Fields] OR "glucose intolerance"[MeSH Terms] OR "hyperglycemia"[MeSH Terms] OR "hyperglycaemia"[All Fields] OR "hyperglycemia"[MeSH Terms] OR "hyperglycemia"[All Fields] OR "hyperglycaemias"[All Fields] OR "hyperglycemias"[All Fields] OR "hyperglycemia s"[All Fields] #3 "pregnan*"[All Fields] OR "gestation*"[All Fields] OR "gravidez"[All Fields] OR "pregnancy"[MeSH Terms] #4 "brazil"[MeSH Terms] OR brasil[All Fields] OR brazil[All Fields] OR "brasil*"[All Fields] OR "brazil*"[All Fields] #5 #1 AND #2 AND #3 AND #4	414
SciELO	(prevalencia OR prevalence OR epidemiologia OR epidemiology OR survey OR inquérito OR incidência OR incidence) AND (pregnancy OR gestational OR gravidez) AND (diabetes OR diabete OR diabético OR diabeticos) AND (brasil OR Brazil OR brasil* OR brazil*)	87
Web of Science	#1 TS=(prevalencia OR prevalence OR epidemiologia OR epidemiology OR survey OR inquérito OR incidência OR incidence) #2 TS=(pregnancy OR gestational OR gravidez) #3 TS=(diabetes OR diabete OR diabético OR diabeticos) #4 TS=(brasil OR Brazil OR brasil* OR brazil*) #5 #1 AND #2 AND #3 AND #4	248