Adverse pregnancy and perinatal outcomes in Latin America and the Caribbean: systematic review and meta-analysis

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ABSTRACT
Objective. To estimate the point prevalence and likely ranges of pregnancy-induced hypertension, pre-eclampsia, gestational diabetes, low birth weight and preterm delivery in Latin America and the Caribbean, and evaluate the heterogeneity of the estimates.
Methods. We conducted a systematic review and meta-analysis of observational studies reporting the prevalence of maternal and perinatal adverse outcomes in populations in Latin American and the Caribbean published between 2000 and 2019 in English, Spanish, or Portuguese. We searched PubMed, Embase, and LILACS. We estimated the point prevalence and evaluated overall heterogeneity and, in sub-group analyses, heterogeneity by study design and level of bias.
Results. Of 1087 records retrieved, 50 articles were included in the review: two on hypertensive disorders of pregnancy, 14 on pre-eclampsia, six on gestational diabetes, nine on low birth weight and 19 on preterm birth. No meta-analysis for hypertensive disorders of pregnancy could be done because of the small number of studies. Point prevalence estimates and 95% confidence intervals (CIs) for pre-eclampsia, gestational diabetes, low birth weight, and preterm birth were: 6.6% (95% CI: 4.9%, 8.6%), 8.5% (95% CI: 3.9%, 14.7%), 8.5% (95% CI: 7.2%, 9.8%), and 10.0% (95% CI: 8.0%, 12.0%), respectively. We observed substantial heterogeneity overall and by study design. No major differences in estimates were observed by level of bias.
Conclusions. The results of this study provide updated estimates of some of the most prevalent adverse pregnancy and perinatal outcomes in Latin America and the Caribbean. They highlight that important heterogeneity exists in prevalence estimates, which may reflect the diversity of populations in the region.

Keywords
Hypertension, pregnancy-induced; pre-eclampsia; diabetes, gestational; infant, low birth weight; premature birth; Latin America; Caribbean Region.

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Worldwide, maternal and perinatal health has improved markedly in the last half century. While maternal mortality has decreased substantially (1), maternal morbidity has remained high. Common adverse pregnancy outcomes include: pregnancy-induced hypertension (systolic blood pressure (SBP) > 140 mmHg and diastolic blood pressure (DBP) > 90 mmHg), pre-eclampsia (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg after 20 weeks’ gestation in an individual with previously normal blood pressure, and proteinuria ≥ 0.3 g), gestational diabetes (abnormal oral glucose tolerance test), low birth weight (< 2500 g), and preterm birth (birth before 37 weeks’ gestation).

In Latin America and the Caribbean, morbidity as a result of adverse pregnancy and birth outcomes is a major burden and long-term surveillance of the prevalence of these outcomes is important. For example, up to 26% of maternal deaths are estimated to be related to pre-eclampsia, compared with 9% of maternal deaths in Africa and Asia (2). The prevalence of this condition in the region is important to monitor. Gestational diabetes has risks for both mother and infant. Furthermore, many women who are diagnosed with gestational diabetes may actually have undiagnosed diabetes before pregnancy, which poses greater risks. While it is well known that the prevalence of diabetes has been increasing in Latin America and the Caribbean, estimating the prevalence of gestational diabetes for the region is particularly important, as few estimates exist due to the lack of a unified definition for screening and diagnosis of the condition (3). With respect to birth outcomes, low birth weight is an important predictor of prenatal and adult mortality and puts an infant at higher risk for late chronic disease (4). Indeed, preterm birth is the most common cause of neonatal death and, when infants survive, is associated with high hospitalization costs and long-term sequelae (5). In high-income settings, as medical technology has advanced, babies under 25 weeks’ gestation have a high chance of survival compared with low-income settings where half of babies born at 32 weeks still die (5). Thus, in Latin America and the Caribbean, which has a mix of high-, middle- and low-income countries, monitoring the prevalence of preterm birth over time is very important in order to improve survival and short- and long-term health outcomes for infants. The prevalence of each of these adverse maternal and perinatal outcomes varies both within and between countries, and identifying point estimates, or likely ranges of prevalence, for each is challenging.

Improving the health of women of childbearing age and pregnancy outcomes is a priority of national governments as well as multinational agencies in this region of the world, as improvements directly affect the health and long-term well-being of current and future generations. Although a number of published studies exist that provide prevalence estimates of adverse pregnancy outcomes for individual countries in Latin America and the Caribbean, no attempt has been made to consolidate prevalence estimates of several maternal and perinatal outcomes for the region. Furthermore, because of the large cultural, economic, and demographic variability in the region, understanding the likely ranges of prevalence values would be informative for understanding differences in maternal and child health outcomes. Thus, the aim of the current study was to estimate point prevalence and likely ranges of five maternal and perinatal outcomes (pregnancy-induced hypertension, pre-eclampsia, gestational diabetes, low birth weight, and preterm birth) in Latin America and the Caribbean and to evaluate the heterogeneity of the prevalence estimates.

METHODS

We conducted a systematic review and meta-analysis of observational studies reporting the prevalence of maternal and perinatal outcomes in Latin American and the Caribbean. Our protocol was registered on 25 January, 2021 with PROSPERO – the International Prospective Register of Scientific Reviews maintained by the United Kingdom of Great Britain and Northern Ireland’s National Institute for Health Research (CRD 42017078786).

Eligibility criteria

We included observational studies (cross-sectional, prevalence, nested case–control, and cohort studies) which reported prevalence within the general population for at least one of the following outcomes: pregnancy-induced hypertension, pre-eclampsia, gestational diabetes, low birth weight, or preterm birth. We chose a long study entrance criterion (19 years) given the changes in socioeconomic conditions that have occurred in many of the countries since 2000 and that there would likely be few articles from the smaller countries of the region. Therefore, studies published between 2000 and 31 August 2019 in either English, Spanish, or Portuguese, which reported the prevalence of one of the outcomes of interest in one or more of the countries of Latin America or the Caribbean, as defined by the World Bank (6), were included in the systematic review (Table S1, supplementary material). While the review focused on observational studies, experimental studies that met all our criteria were evaluated individually to determine if they could be included.

Information sources and search

PubMed, Embase, and LILACS were systematically searched using the following search structure: (“pregnancy outcomes” OR “low birth weight” OR “gestational diabetes” OR “premature delivery” OR “pre-eclampsia” OR “pregnancy-induced hypertension”) AND (“cross sectional study” OR “cohort study” OR “prevalence study” OR “case control study”) AND (“all countries in the World Bank Latin American and Caribbean region”). A comprehensive list of search terms and an example of the final PubMed search strategy for pre-eclampsia are given in the supplementary material (Table S1 and Table S2). Additional manual searching of the reference lists of included papers was undertaken during the data extraction phase.

Study selection and data collection

The titles and keywords of search results were screened for each of the three categories (prevalence reported, published between 2000 and 2019, and from a Latin American or Caribbean country), followed by abstract screening. Justification of exclusion was recorded on a pre-prepared form with guidance provided on the first section of the data extraction form. The full texts of papers that were not excluded in the initial screening were reviewed, which included papers for which abstracts did not provide enough information to determine exclusion. Data were extracted at the same time as the full paper review; data extraction was only stopped when eligibility criteria were no longer met.
The data extraction form, based on the Cochrane data extraction form, was designed to retrieve the following information: study design, outcomes, timeframe of prevalence estimate, prevalence estimate (stratified by age if applicable), sample source of the population, participants, and country (7). All stages of the selection process and data extraction were undertaken by two independent reviewers. Disagreements in quality assessment between reviewers were resolved through discussion with a third reviewer.

Risk of bias assessment

To assess study quality and risk of bias we used the AXIS tool for observational studies (8). Both independent reviewers assessed specific elements (for example, “Were the aims/objectives of the study clear?”) and then assigned an overall level of bias (high, moderate, low).

Summary measures

The primary outcome of the systematic review was the prevalence of each of the five pregnancy and perinatal outcomes within countries of Latin America and the Caribbean, with no prioritization of outcomes.

Synthesis of results

For each study, we provided a brief description (for example, country, publication date, dates of data collection), listed the pregnancy or perinatal outcome and prevalence reported (or calculated), and assessed the risk of bias. Due to clinical and methodological heterogeneity within the included studies, a random effects meta-analysis was undertaken for each outcome where the number of studies was sufficient. Analyses were conducted in R Studio (9) using the “meta” and “metafor” package which uses the metaprop function to estimate results for a proportion (10). The results of the meta-analysis were presented in a forest plot, which included the combined prevalence reported as a percentage and the 95% confidence interval (95% CI), variance between studies (tau), heterogeneity in the analysis (I²), and statistical testing of heterogeneity (chi-square test). The alpha value was set at < 0.05.

Additional analyses

We conducted two additional analyses. First, we stratified by level of bias. Second, for outcomes with more than one article within each of the study designs, a subgroup analysis by study design was performed to determine whether any significant differences in estimates of point prevalence existed.

RESULTS

Study selection

A total of 1087 records were retrieved from the three electronic databases (Figure 1). After removing 172 duplicates, 915 articles were screened based on titles and abstracts, followed by a full text screening of 242 papers. Ultimately, 50 papers were included in the review: two for hypertensive disorders of pregnancy, 14 for pre-eclampsia, six for gestational diabetes, nine for low birth weight, and 19 for preterm birth. Articles included were: 27 studies in Brazil; seven studies in Peru; six studies each in Argentina and Mexico; three studies each in Chile, Ecuador, and Guadeloupe; two studies each in Colombia, Paraguay, Puerto Rico, and Uruguay; and one study each in Bolivia, Dominican Republic, Guatemala, Haiti, Honduras, Nicaragua, Panama, Trinidad and Tobago, and Venezuela. The reasons for excluding papers at the full text stage are listed in Table 1. All included studies were hospital based. Further detailed information on the studies can be found in the supplementary material (Table S3).

In the following sections, we synthesize results related to each specified outcome, namely: point prevalence and 95% CI; presence of heterogeneity (overall and by study design); and estimates by risk of bias.

Hypertensive disorders of pregnancy

Two studies reported the prevalence of hypertensive disorders of pregnancy (Table 2). One was a prospective cohort from Brazil within a maternity hospital unit and included 550 participants. The overall prevalence of hypertensive disorders was 9.1% (95% CI: 6.7%, 11.5%), and the age of women with these disorders was higher than women without these disorders, 30.6 years versus 24.2 years (11). The second study was a prospective cohort study from three maternal units in Chile with 627 participants. The prevalence of hypertensive disorders was 10.4% (95% CI: 8.0%, 12.8%) with no observed differences by age (12). These studies had high (11) and medium (12) risk of bias. The main weakness was that the samples included may not have been representative of the general population. No meta-analysis was performed because of the small number of studies included.

Pre-eclampsia

A total of 14 studies were included: six studies from Brazil (13–18); two from Argentina (19, 20); two from Mexico (21, 22); and one each from Chile (12), Haiti (23), Peru (24), and Trinidad and Tobago (25). Seven of the studies were prospective cohort studies (12, 14, 15, 18, 19, 21, 25), four were cross-sectional studies (16, 17, 20, 24), two were nested case-control studies (13, 22), and one was a retrospective cohort study (23). The minimum and maximum sample size was 156 (25) and 549 681 (24) participants, respectively. The prevalence of pre-eclampsia was between 2.1% in Argentina (19) and 12.5% in Mexico (22). Of the 14 studies, three were rated as having low risk of bias, eight as medium risk, and three as high risk of bias, mainly due to greater or lesser degree of representativeness of the general population and the presence or absence of study protocols, or standardized measurements (Table 2).

In the meta-analysis of all 14 studies, we estimated an overall prevalence of 6.6% (95% CI: 4.9%, 8.6%) for pre-eclampsia (Figure 2, panel a). We observed substantial heterogeneity between the studies and also found evidence of significant heterogeneity by study design (Figure S1, supplementary material). Overall prevalence estimates and 95% CI were similar to those stratified by level of bias (Table S4, supplementary material).

Gestational diabetes

We included six studies on gestational diabetes: two from Mexico (26, 27), and one each from Brazil (28), Chile (29), and Colombia (30) respectively.
The prevalence of gestational diabetes ranged from 2.1% (28) to 15.8% (31). Three studies had a low risk of bias (29–31), two had a medium risk (27, 28), and one had a high risk (26) (Table 2). The main reasons for bias were lack of certainty on how the outcome was measured and because the prevalence was not directly reported (we were able to calculate the prevalence based on information reported in the article).

Figure 2 (panel b) shows the results of the meta-analyses conducted using all six studies on gestational diabetes. The estimated prevalence was 8.5% (95% CI: 3.9%, 14.7%). Substantial heterogeneity was observed between the studies and significant heterogeneity by study design (Figure S2, supplementary material). Overall prevalence estimates and 95% CI were similar to those stratified by level of bias (Table S4, supplementary material).

Low birth weight

Eight studies on low birth weight were included from Brazil (32–39) and one study analyzed data from the following countries: Guadeloupe (30), and Peru (31). As regards study design: two were cross-sectional studies (28, 31), two were prospective cohort studies (27, 30), one was a retrospective cohort study (29), and one was an experimental study (26). The sample size varied from 450 (27) to 5024 (28) participants. The prevalence of gestational diabetes ranged from 2.1% (28) to 15.8% (31). Three studies had a low risk of bias (29–31), two had a medium risk (27, 28), and one had a high risk (26) (Table 2). The main reasons for bias were lack of certainty on how the outcome was measured and because the prevalence was not directly reported (we were able to calculate the prevalence based on information reported in the article).

Figure 2 (panel b) shows the results of the meta-analyses conducted using all six studies on gestational diabetes. The estimated prevalence was 8.5% (95% CI: 3.9%, 14.7%). Substantial heterogeneity was observed between the studies and significant heterogeneity by study design (Figure S2, supplementary material). Overall prevalence estimates and 95% CI were similar to those stratified by level of bias (Table S4, supplementary material).
TABLE 2. Summary of articles selected to estimate the prevalence of maternal and perinatal outcomes in Latin America and the Caribbean

| Outcome                                | Reference number | Prevalence (95% CI), % | Risk of biasa |
|----------------------------------------|------------------|------------------------|---------------|
| Hypertensive disorders of pregnancy    |                  |                        |               |
|                                        | 11               | 9.1 (6.7, 11.5)        | +++           |
|                                        | 12               | 10.4 (8.0, 12.8)       | ++            |
| Pre-eclampsia                          |                  |                        |               |
|                                        | 12               | 4.6 (3.0, 6.2)         | ++            |
|                                        | 13               | 7.5 (6.0, 9.0)         | +             |
|                                        | 14               | 7.5 (5.2, 9.8)         | ++            |
|                                        | 15               | 10.3 (6.2, 14.4)       | +++           |
|                                        | 16               | 9.5 (8.6, 10.4)        | ++            |
|                                        | 17               | 7.5 (7.2, 8.0)         | +             |
|                                        | 18               | 4.5 (1.7, 7.3)         | +++           |
|                                        | 19               | 2.1 (2.0, 2.2)         | +             |
|                                        | 20               | 10.0 (8.7, 11.3)       | ++            |
|                                        | 21               | 5.0 (2.6, 7.4)         | +++           |
|                                        | 22               | 12.5 (12.1, 12.9)      | +++           |
|                                        | 23               | 3.2 (2.8, 3.6)         | +             |
|                                        | 24               | 4.4 (4.3, 4.5)         | ++            |
|                                        | 25               | 10.1 (5.4, 14.8)       | +             |
| Gestational diabetes                   |                  |                        |               |
|                                        | 26               | 2.1 (1.7, 2.5)         | ++            |
|                                        | 27               | 6.1 (4.7, 7.5)         | +             |
|                                        | 28               | 9.6 (7.8, 11.4)        | +             |
|                                        | 29               | 10.8 (8.7, 12.9)       | +++           |
|                                        | 30               | 10.0 (7.2, 12.8)       | +             |
|                                        | 31               | 15.8 (13.8, 17.8)      | +             |
| Low birth weight                       |                  |                        |               |
|                                        | 4                | Various                | ++            |
|                                        | 32               | 9.0 & 10.9 (8.1, 9.9) & (10.1, 11.7) | + |
|                                        | 33               | 9.7 (9.6, 9.8)         | ++            |
|                                        | 34               | 5.1 (4.9, 5.3)         | ++            |
|                                        | 35               | 9.1                   | ++            |
|                                        | 36               | 10.0 (7.3, 12.7)       | ++            |
|                                        | 37               | 10.0 (9.1, 10.9)       | +             |
|                                        | 38               | 6.9 (6.5, 7.3)         | ++            |
|                                        | 39               | 8.7 (8.1, 9.3)         | +++           |
| Preterm birth                          |                  |                        |               |
|                                        | 40               | 7.3 (6.9, 7.7)         | +             |
|                                        | 41               | 9.9 (9.4, 10.4)        | +             |
|                                        | 42               | 9.5 (9.4, 9.6)         | ++            |
|                                        | 43               | 6.7 (6.0, 7.4)         | ++            |
|                                        | 44               | 9.7 (8.1, 11.3)        | +             |
|                                        | 45               | 13.7 & 13.8 (12.7, 14.7) & (12.8, 14.8) | + |
|                                        | 46               | 13.7 (12.7, 14.7)      | +             |
|                                        | 47               | 16.2 (14.7, 17.7)      | +             |
|                                        | 48               | 14.3 (14.0, 14.6)      | +             |
|                                        | 49               | 8.1 (8.0, 8.2)         | ++            |
|                                        | 50               | 8.1 (7.8, 8.4)         | ++            |
|                                        | 51               | 5.9 (5.8, 6.0)         | +             |
|                                        | 52               | 14.7 (12.6, 16.8)      | ++            |
|                                        | 53               | 15.8 (13.4, 18.2)      | ++            |
|                                        | 54               | 17.4 (17.3, 17.5)      | +             |
|                                        | 55               | 14.5 (14.4, 14.6)      | +             |
|                                        | 56               | 4.2 (3.8, 4.6)         | +             |
|                                        | 57               | Various                | +             |
|                                        | 58               | 13.3                   | +++           |

CI, confidence interval
a+ = low; ++ = medium; +++ = high risk of bias.
bUsed for both pre-eclampsia and hypertensive disorders of pregnancy.
cCIs not given.
Source: prepared by authors from results.
low birth weight was estimated at 8.5% (95% CI: 7.2%, 9.8%). Substantial heterogeneity was observed and additional analysis showed significant heterogeneity by study design (p < 0.01; see Figure S3, supplementary material). No major differences in estimates and 95% CI were seen by level of bias (Table S4, supplementary material).

Preterm birth

This perinatal outcome included 19 studies: nine from Brazil (40–48), three from Peru (49–51), two each from Guadeloupe (52, 53) and Puerto Rico (54, 55), and one from Argentina (56). The other two studies included samples from different countries (57, 58). Eight studies were cross-sectional studies (42, 43, 48, 54–58), six were prospective cohort studies (44–47, 52, 53), and five were retrospective cohort studies (40, 41, 49–51). The

The lower diamond in the plot represents the overall cumulative estimate. Source: prepared by authors from results.

countries: Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Uruguay, and Venezuela (4). As regards study design, four were cross-sectional studies (4, 33, 35, 39), three were prospective cohort studies (32, 36, 37), and two were retrospective cohort studies (34, 38). The minimum and maximum sample sizes were 474 (36) and 1,342,655 (33), respectively. The prevalence of low birth weight in the individual studies ranged from 5.1% (34) to 14.1% (4) (Table 2). Risk of bias evaluation showed that seven studies had a medium risk of bias (4, 33–38), one a high risk (39), and one a low risk (32). The main reasons for bias were lack of: representativeness of the study sample, a protocol for the study, or standardized measurements (Table 2).

The meta-analysis included the eight individual studies from Brazil and the study with prevalence estimates for several countries (the prevalence for each country represented was entered) (4) (Figure 2, panel c). The point prevalence for low birth weight was estimated at 8.5% (95% CI: 7.2%, 9.8%). Substantial heterogeneity was observed and additional analysis showed significant heterogeneity by study design (p < 0.01; see Figure S3, supplementary material). No major differences in estimates and 95% CI were seen by level of bias (Table S4, supplementary material).
number of maternal units was between 1 and 43 and the sample size ranged from 911 (53) to 1,000,340 (55). The preterm birth prevalence varied from 4.3% (56) to 17.4% (54). As regards bias, 13 studies had a medium risk of bias, four a low risk (40, 47, 48, 51), and two a high risk (42, 58) (Table 2). The main weaknesses were potential selection bias, self-reported outcomes, and lack of a study protocol or standardization.

The meta-analysis included 19 studies, with two studies containing prevalence estimates for several countries which were entered individually (Figure 2, panel d). The overall pooled prevalence of preterm birth was 10.0% (95% CI: 8.0%, 12.0%) Substantial heterogeneity was seen between the studies and significant heterogeneity by study design (Figure S4, supplementary material). No major differences in estimates and 95% CI by level of bias were seen (Table S4, supplementary material).

**DISCUSSION**

We observed prevalence estimates for pre-eclampsia as low as 2.1% in a study conducted in the early 2000s in Argentina (20) and as high as 12.5% in a large nested case–control study in Mexico in 2008 (22). We estimated the prevalence of pre-eclampsia for countries in Latin America and the Caribbean that met the inclusion criteria for our meta-analysis was 6.6% (95% CI: 4.9%, 8.6%), which is higher than that reported in an earlier meta-analysis in Latin America (3.0: 95% uncertainty range: 1.5%, 5.2%) (59). This study estimated the prevalence of eclampsia and pre-eclampsia in the World Health Organization (WHO) regions; thus, while over 36 million women were included, most of the sample came from the United States, which is included in the WHO Americas region in addition to Canada (59). As in our own study, the 2013 analysis included data from Argentina, Brazil, Chile, and Mexico. However, our study also included data from additional countries published in more recent studies, namely: Haiti (23), Peru (24), and Trinidad and Tobago (25). These differences in methodology may, in part, explain the differences in estimates obtained.

For gestational diabetes, we estimated a pooled prevalence of 8.5% (95% CI: 3.9%, 14.7%), which is lower than that recently reported for Europe (60). Interestingly, our estimate and ranges were closest to those reported for northern Europe (8.9%, 95% CI: 7.9%, 10.0%) (60). Comparing results of gestational diabetes across world regions is important; however, the validity of such comparisons is limited by the lack of universally accepted diagnostic criteria. To the best of our knowledge, our analysis is the first meta-analysis to provide estimates of the prevalence of gestational diabetes for the Latin American and the Caribbean region. Thus, our results may be used as a baseline estimate, with hopes that it may be updated as more countries publish results and diagnostic definitions are unified to be consistent across the region.

For low birth weight and preterm birth, our prevalence estimates and ranges were consistent with those reported in other international and regional publications (61–63). A systematic analysis estimated that Latin America had a prevalence of low birth weight of 8.7% in 2015 (61), which is almost identical to our pooled prevalence of 8.5% (95% CI: 7.2%, 9.8%). Our estimates are however lower than the estimated worldwide prevalence of low birth weight of 14.6% (uncertainty interval: 12.4%, 17.1%). This difference likely relates to the very high levels of low birth weight estimated in a few regions (e.g., 26.4% in southern Asia). Our results may be particularly useful for policy-makers working at the regional level to achieve the WHO goal to reduce the number of infants with low birth weight by 30% worldwide by 2025 (64). We estimated the prevalence of preterm birth to range between 8.0% and 12.0% for Latin America and the Caribbean. Using national registries, reproductive health surveys and unpublished data, in addition to published papers, a 2102 study estimated a similar prevalence range for Latin America (6.8–11.4%) and, separately, for the Caribbean (7.8–20.8%) (63). Our ranges were slightly higher than those reported for eastern Asia, but lower than those reported for sub-Saharan Africa and southern Asia. The difference is likely because of differences in the predictors of preterm birth between the regions (e.g., malaria rates in sub-Saharan Africa).

Overall, we observed substantial heterogeneity in the prevalence estimates between studies and therefore ranges of prevalence estimates may be more useful for comparison purposes. Due to the small number of selected studies, some range estimates were large (e.g., 95% CI: 3.9%, 14.7% for gestational diabetes). We also found evidence of methodological diversity or heterogeneity by study design, which may reflect the overall lack of information from the region. We found slightly wider CIs for cross-sectional versus prospective study designs. Taken together, these results may relate to the diversity of experiences in this large world region (e.g., socioeconomic status, maternal characteristics, and pregnancy experiences), which cannot be captured by study design. Future studies should attempt to understand the drivers of this heterogeneity and potential sources of health inequities as an opportunity for the improvement of maternal and child health within the region.

Some study limitations should be considered when interpreting our results. Our review and meta-analysis included articles from 20 of 43 countries of the region, which may mean that the prevalence of maternal and perinatal outcomes may be even more heterogeneous. We focused on results of meta-analyses using all available studies that met our inclusion criteria, regardless of level of bias. While a precedent exists for this approach (59, 65), we understand that the use of estimates only from studies with low or medium levels of bias may be preferred. Estimated point prevalence and CIs by each level of bias are provided in the supplementary material.

In conclusion, the results of our study provide updated estimates of some of the most prevalent adverse pregnancy and perinatal outcomes for Latin America and the Caribbean, and highlight that important heterogeneity exists in prevalence estimates. Our results allow for comparisons between prevalence estimates for individual countries (e.g., is a country- or city-specific prevalence higher or lower than might be expected for the region). They also facilitate comparisons for studies investigating causes for pregnancy and perinatal outcomes in different countries in Latin America and the Caribbean and in other regions of the world. In addition, they are useful for monitoring temporal trends. Combined pre-eclampsia, hypertensive disorders of pregnancy, gestational diabetes, preterm birth, and low birth weight are responsible for an enormous burden of maternal and infant mortality and morbidity. Therefore, identifying regions where the prevalence of these outcomes is high allows specific policies to be developed to target the most disadvantaged and at risk women and infants.
**Author contributions.** All authors reviewed and approved the final version. EB, PRR, and MEQ contributed to the design, collected data, assisted in the analysis, and wrote the paper. MM, LN, ER, XO, KEW, TO, and SEB contributed to data collection and analysis and critically revised the paper. JMD5 and RMH critically revised the paper.

**Conflicts of interests.** None declared.

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**REFERENCES**

1. Maternal mortality: key facts [Internet]. World Health Organization; 2019 [cited 2020 Sep 14]. Available from: https://www.who.int/news-room/fact-sheets/detail/maternal-mortality
2. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. Lancet. 2006;367:e323–33.
3. Avilés-Santa ML, Monroig-Rivera A, Soto-Soto A, Lindberg NM. Current state of diabetes mellitus prevalence, awareness, treatment, and control in Latin America: challenges and innovative solutions to improve health outcomes across the continent. Curr Diab Rep. 2020;20(11):62.
4. Woodhouse C, Lopez Camelo J, Wehby GL. A comparative analysis of prenatal care and fetal growth in eight South American countries. PLoS One. 2014;9:e91292.
5. Born too soon: the global action report on preterm birth [Internet]. World Health Organization; 2012[cited 2021 May 19]. Available from: https://www.who.int/maternal_child_adolescent/documents/born_too_soon/en/
6. Latin America and the Caribbean data [Internet]. The World Bank Group;2019 [cited 2021 May 19]. Available from: https://data.worldbank.org/country/ZJ
7. Higgins JPT, Green S (editors). Cochrane handbook for systematic reviews of interventions, version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011. [cited 2021 May 19]. Available from: https://handbook-5-1.cochrane.org/
8. Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). BMJ Open. 2016;6:e011458.
9. RStudio Team. RStudio: integrated development for R [Internet]. Boston (MA): RStudio; 2020 [cited 2021 May 19]. Available from: http://www.rstudio.com/
10. Schwarzer G, Carpenter JR, Rücker G. An introduction to meta-analysis in R. New York: Springer; 2015.
11. Alves JAG, Miyague AH, De Sousa PCP, Maia SB, Da Silva Costa F, Martins WP. Brachial artery flow mediated dilation in the first trimester to predict the occurrence of hypertensive disorders during pregnancy. Fetal Diagn Ther. 2015;37:216–20.
12. Caradeux J, Serra R, Nien JK, Pérez-Sepulveda A, Schepeler M, Alves JAG, Miyague AH, De Sousa PCP, Maia SB, Da Silva Costa F, Martins WP, Araujo Júnior E, Kane SC, et al. Renal interlobar vein impedance index as a first-trimester marker does not predict hypertensive disorders of pregnancy. J Ultrasound Med. 2016;35:2641–8.
13. Rezende KB de C, Bornia RG, Esteves APV dos S, Cunha AJLA da, Amin Junior J. Preeclampsia: prevalence and perinatal repercussions in a University Hospital in Rio de Janeiro, Brazil. Pregnancy Hypertens. 2016;6:253–5.
14. Souza RT, Cecatti JG, Passini R, Tedesco RP, Lajos CJ, Nomura ML, et al. The burden of provider-initiated preterm birth and associated factors: evidence from the Brazilian multicenter study on preterm birth (EMP1). PLoS One. 2016;11:1–20.
15. Santos EM, de Amorim LP, Costa OLN, Oliveira N, Guimarães AC. Perfil de risco gestacional e metabólico no serviço de pré-natal de maternidade pública do Nordeste do Brasil [Profile of gestational and metabolic risk in the prenatal care service of a public maternity in the Brazilian Northeast]. Rev Bras Ginecol Obstet. 2012;34:102–6.
16. Hauger MS, Gibbons L, Vik T, Belizán JM. Prepregnancy weight status and the risk of adverse pregnancy outcome. Acta Obstet Gynecol Scand. 2008;87:953–9.
17. Castaldí JL, Bertín MS, Giménez F, Lede R. Periodontal disease: is it a risk factor for premature labor, low birth weight or preeclampsia? Rev Panam Salud Publica. 2006;19:253–8.
18. Briones-Garduño AJC, Herrera-Villalobos JE, Anda GFV, Rodríguez-Roldán M, Pardo-Morales DRV, González-Vargas A. Presence of equinocytosis in the preeclampsia–eclampsia syndrome. Is this a subclinical manifestation of the syndrome? Cir Ciruj. 2003;71:455–9.
19. Osorno-Covarrubias L, Rupay Aguirre GE, Rodríguez Chapuz J, Lavadores May AI, Dávila Velázquez J, Echeverría Eguíluz M. Maternal factors associated to prematurity. Ginecol Obstet Mex. 2008;76:526–36.
20. Bridgell M, Handzel E, Hynes M, Jean-Louis R, Fitter D, Hogue C, et al. Hypertensive disorders in pregnancy and maternal and neonatal outcomes in Haiti: the importance of surveillance and data collection. BMC Pregnancy Childbirth. 2019;19:1–11.
21. Tapia V, Betran AP, Gonzales GF. Caesarean section in Peru: analysis of trends using the Robson classification system. PLoS One 2016;11(2):e0148138.
22. Kandimalla BH, Siripurapu A, Nayak BS, Maiya SS. Early antenatal serum lipid levels and the risk of pre-eclampsia in Trinidad and Tobago. Arch Physiol Biochem. 2011;117:215–21.
23. Dueñas-García OF, Ramirez-Torres A, Diaz-Sotomayor M, Rico-Olvera H. Resultados perinatales de pacientes con diabetes gestacional diagnosticada con tres métodos diferentes [Perinatal outcomes of patients with gestational diabetes diagnosed by three different methods]. Ginecol Obstet Mex. 2011;79:411–8.
24. López Caudana AE, López Ridaura R, González Villalpando C et al. Trends and methods of dietary intake in the Mexican population. Rev Nutr. 2018;31(3):165–74.
25. de Belaí A, Scaglia C, Carvalho F, Netto P. Analysis of causes of maternal death: a systematic review. Lancet. 2015;385:1315–21.
26. Alves JAG, Miyague AH, De Sousa PCP, Maia SB, Da Silva Costa F, Martins WP, Araujo Júnior E, Kane SC, et al. Renal interlobar vein impedance index as a first-trimester marker does not predict hypertensive disorders of pregnancy. J Ultrasound Med. 2016;35:2641–8.
29. Huidobro Muñoz A, Torres C D, Paredes F. Diabetes gestacional: asociación con grupo ABO [Gestational diabetes: association with ABO group]. Rev Med Chil. 2017;145:431–5.

30. Saunderson L, Kadhel P, Costet N, Rouget F, Monfort C, Thomé JP, et al. Hypertensive disorders of pregnancy and gestational diabetes mellitus among French Caribbean women chronically exposed to childrenone. Environ Int. 2016;88:171–7.

31. Larrabure-Torrealva GT, Martínez S, Luque-Fernandez MA, Sánchez SE, Mascaro PA, Ingar H, et al. Prevalence and risk factors of gestational diabetes mellitus: findings from a universal screening feasibility program in Lima, Peru. BMC Pregnancy Childbirth. 2018;18:1–9.

32. Sadovsky ADL, Matijasevich A, Santos IS, Barros FC, Miranda AE, Silveira MF, LBW and IUGR temporal trend in 4 population-based birth cohorts: the role of economic inequality. BMC Pediatr. 2016;16:1–8.

33. Mendes CQ de S, Cacella BC de A, Mandetta MA, Balieiro MMFG. Low birth weight in a municipality in the southeast region of Brazil. Rev Bras Enferm. 2015;68:1169–75.

34. Alberto L, Pereira A, Pinheiro PM. Relación entre el bajo peso al nacer y la exposición a partículas inhalables [The relationship between low birth weight and exposure to inhalable particulate matter]. Cad Saude Publica. 2013;29:1101–8.

35. Veloso HJF, Silva AAM da, Barbieri MA, Goldani MZ, Lamy-Filho F, Ferreira Simões VM, et al. Secular trends in the rate of low birth weight in Brazilian State Capitals in the period 1996 to 2010. Cad Saude Publica. 2013;29:91–101.

36. de Menezes LO, Pinheiro RT, Quevedo L de A, de Oliveira SS da, Silva RA, Tavares Pinheiro KA, et al. O impacto do baixo peso ao nacer relacionado à depressão gestacional para o f nanciamento federal da saúde pública: uma análise do Município de Pelotas, Rio Grande do Sul, Brasil [The impact of low birth weight related to gestational depression on Federal funding of public health: a study in Pelotas, Rio Grande do Sul State, Brazil]. Cad Saude Publica. 2012;28:1939–48.

37. Barros FC, Victora CG, Matijasevich A, Santos IS, Horta BL, Silveira MF, et al. Preterm births, low birth weight, and intrauterine growth restriction in three birth cohorts in Southern Brazil: 1982, 1993 and 2004. Cad Saude Publica. 2008;24:390–8.

38. Gaglione MRP, Alves Lamounier J, de Moraes Neto OL. Obstetric delivery and risk of neonatal mortality in Goiânia in 2000. Rev Saude Publica. 2005;39:350–7.

39. Andrade CL de, Szwarzvald CL, Gama SGN da, Leal M do C. Desigualdades sócio-econômicas do baixo peso ao nacer e da mortalidade perinatal em Região Metropolitana do Rio de Janeiro [Socioeconomic inequalities and low birth weight and perinatal mortality in Rio de Janeiro, Brazil]. Cad Saude Publica. 2004;20:544–51.

40. Dombrowski LG, de Souza RM, Silva NRM, Barateiro A, Epifânio S, Gonçalves LA, et al. Malaria during pregnancy and newborn outcome in an unstable transmission area in Brazil: a population-based record linkage study. PLoS One. 2018;13:1–16.

41. Garcia LP, Fernandes CM, Traebert J. Risk factors for neonatal death in the capital city with the lowest infant mortality rate in Brazil. J Pediatr (Rio J). 2019;95:194–200.

42. Raspanini PR, de Miranda MJ, da Silva ZP, Alencar GP, Diniz SG, de Almeida MF. The impact of the type of hospital and delivery on the gestational age in São Paulo city, 2013–2014. Rev Bras Epide- miol. 2016;19:878–82.

43. Rezende Crismam J, Mattos IE, Koifman RJ, Koifman S, Moraes Mello Bocconcelli P, Meyer A. Prevalence of very low birthweight, malformation, and low Apgar score among newborns in Brazil according to maternal urban or rural residence at birth. J Obstet Gynaecol Res. 2016;42:496–504.

44. Shvane M, Grandi C, Brazan M et al. Alcohol consumption during pregnancy and perinatal results: a cohort study. Sao Paulo Med J. 2016;134:146–52.

45. Silveira MF, Victora CG, Horta BL, Da Silva BGC, Matijasevich A, Barros FC. Low birth weight and preterm birth: trends and inequalities in four population-based birth cohorts in Pelotas, Brazil, 1982-2015. Int J Epidemiol. 2019;48:146–53.

46. Silveira MF, Victora CG, Barros AJD, Santos IS, Matijasevich A, Barros FC. Determinants of preterm birth: Pelotas, Rio Grande do Sul State, Brazil, 2004 birth cohort. Cad Saude Publica. 2010;26:185–94.

47. Barros FC, Victora CG, Barros AJD, Santos IS, Albernaz E, Matijasevich A, et al. The challenge of reducing neonatal mortality in middle-income countries: findings from three Brazilian birth cohorts in 1982, 1993, and 2004. Lancet. 2005;365:847–54.

48. Barros FC, Papageorgiou AT, Victora CG, Noble JA, Pang R, Iams J, et al. The distribution of clinical phenotypes of preterm birth syndrome implications for prevention. JAMA Pediatr. 2015;169:220–9.

49. Gonzales GF, Tapia V, Gasco M, Carrillo CE. Maternal hemoglobin concentration and adverse pregnancy outcomes at low and moderate altitudes in Peru. J Matern Neonatal Med. 2012;25:1105–10.

50. Gonzales GF, Steenland K. Maternal hemoglobin level and fetal outcome at low and high altitudes. Am J Physiol Regul Integr Comp Physiol. 2009;297:1477–85.

51. Levine L, Gonzales G, Tapia V, Levine L, Gonzales G, et al. Preterm birth risk at high altitude in Peru. Am J Obstet Gynecol. 2015;217:2399–72.

52. Saunderson L, Guldner L, Costet N, Kadhel P, Rouget F, Monfort C, et al. Effect of a Mediterranean diet during pregnancy on fetal growth and preterm delivery: results from a French Caribbean mother-child cohort study (TIMOUN). Pediatri Perinat Epidemiol. 2014;28:235–44.

53. Rouget F, Lebreton J, Kadhel P, Monfort C, Bodeau-Livinec F, Janky E, et al. Medical and sociodemographic risk factors for preterm birth in a French Caribbean population of African descent. Matern Child Health J. 2013;17:1103–11.

54. Eick SM, Welton M, Cordero JE. Relationship between prepregnancy overweight, obesity, and preterm birth in Puerto Rico. Matern Child Health J. 2019;23:925–35.

55. Xu Y, Feric Z, Cordero JE, Meeker JD, Alshawahbeke A. Potential influence of temperature and precipitation on preterm birth rate in Puerto Rico. Sci Rep. 2018;8:1–9.

56. Weaver EH, Gibbons L, Belizán JM, Altbe F. The increasing trend in preterm birth in public hospitals in northern Argentina. Int J Gynecol Obstet. 2015;130:137–41.

57. Morisaki N, Ganchimeg T, Vogel JP, Zeitlin J, Cecatti JG, Souza JP, et al. Impact of stillbirths on international comparisons of preterm birth rates: a secondary analysis of the WHO multi-country survey of maternal and newborn health. BJOG. 2017;124:1346–54.

58. De Mucio B, Abalos E, Cuesta C et al. Maternal near miss and preterm birth rates: a secondary analysis of the WHO multi-country survey of maternal and newborn health. BJOG. 2016;78:473–9.

59. Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2013;170:1–7.

60. Silva Paulo M, Abdo NM, Bettencourt Silva R, Al-Rifai RH. Gestational diabetes mellitus in Europe: a systematic review and meta-analysis of prevalence studies. Front Endocrinol (Lausanne). 2019;6:91033.

61. Blencowe H, Krasevec J, de Ounes M, Black RE, An X, Stevens GA, et al. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 1990: a systematic analysis. Lancet Global Health. 2017;9:e489–e860.

62. Rodríguez López S, Tumas N, Ortigoza A, de Lima Friche AA, Diez-Roux A V. Urban social environment and low birth weight in 360 Latin American cities. BMC Public Health. 2021;21(1):795.

63. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379:2162–72.

64. Global nutrition targets 2025: low birth weight policy brief. Geneva: World Health Organization; 2014 [cited 2021 May 19]. Available from: https://apps.who.int/iris/handle/10665/149202

65. Harvey LA, Dijkers MP. Should trials that are highly vulnerable to bias be excluded from systematic reviews? Spinal Cord. 2019;57:715–6.

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Reseñas adversas perinatales y del embarazo en América Latina y el Caribe: revisión sistemática y metanálisis

RESUMEN

**Objetivo.** Estimar la prevalencia puntual y los rangos probables de hipertensión provocada por embarazo, preclampsia, diabetes gestacional, peso bajo al nacer y parto prematuro en América Latina y el Caribe, y evaluar la heterogeneidad de las estimaciones.

**Métodos.** Se llevó a cabo una revisión sistemática y metanálisis de los estudios de observación que notificaran la prevalencia de resultados adversos perinatales y maternos en poblaciones de América Latina y el Caribe, publicados entre los años 2000 y 2019 en inglés, español o portugués. Se realizaron búsquedas en PubMed, Embase y LILACS. Se estimó la prevalencia puntual y se evaluó la heterogeneidad general y, en los análisis de subgrupos, la heterogeneidad según el diseño del estudio y nivel de sesgo.

**Resultados.** De 1.087 registros recuperados, se incluyeron 50 artículos en la revisión: 2 sobre los trastornos hipertensivos en el embarazo, 14 sobre preclampsia, 6 sobre la diabetes gestacional, 9 sobre peso bajo al nacer y 19 sobre parto prematuro. No se pudo realizar ningún metanálisis de los trastornos hipertensivos del embarazo debido al número reducido de estudios. Las estimaciones de prevalencia puntual y los intervalos de confianza (IC) del 95% para la preclampsia, la diabetes gestacional, el peso bajo al nacer y el parto prematuro fueron: 6,6% (IC de 95%: 4,9%, 8,6%), 8,5% (IC de 95%: 3,9%, 14,7%), 8,5% (IC de 95%: 7,2%, 9,8%) y 10,0% (IC de 95%: 8,0%, 12,0%), respectivamente. Se observó una heterogeneidad significativa en general, así como según el diseño del estudio. No se advirtieron grandes diferencias en las estimaciones según el nivel del sesgo.

**Conclusiones.** Los resultados de este estudio ofrecen cálculos actualizados de algunos de los resultados adversos perinatales y del embarazo con mayor prevalencia en América Latina y el Caribe. Estos resultados ponen de manifiesto que existe una gran heterogeneidad en las estimaciones de prevalencia, que podría reflejar la diversidad de la población de la región.

**Palabras clave** Hipertensión inducida en el embarazo; preclampsia; diabetes gestacional; recién nacido de bajo peso; nacimiento prematuro; América Latina; Región del Caribe.

Desfechos gestacionales e perinatais adversos na América Latina e no Caribe: revisão sistemática e metanálise

RESUMO

**Objetivo.** Estimar a prevalência pontual e os intervalos prováveis de hipertensão induzida pela gravidez, pré-eclâmpsia, diabetes gestacional, baixo peso ao nascer e parto prematuro na América Latina e no Caribe e avaliar a heterogeneidade das estimativas.

**Métodos.** Realizou-se uma revisão sistemática com metanálise de estudos observacionais que relatam a prevalência de desfechos maternos e perinatais adversos em populações de América Latina e do Caribe, publicados entre 2000 e 2019 em inglês, espanhol ou português. Os bancos de dados PubMed, Embase e LILACS foram pesquisados. Estimou-se a prevalência pontual e avaliou-se a heterogeneidade geral, bem como, em análises de subgrupos, a heterogeneidade por delineamento do estudo e o nível de viés.

**Resultados.** De 1.087 registros encontrados, 50 artigos foram incluídos na revisão: dois sobre distúrbios hipertensivos da gravidez, 14 sobre pré-eclâmpsia, seis sobre diabetes gestacional, nove sobre baixo peso ao nascer e 19 sobre parto prematuro. Não foi possível realizar metanálise para distúrbios hipertensivos da gravidez devido ao pequeno número de estudos. As estimativas de prevalência pontual e intervalos de confiança de 95% (IC) para pré-eclâmpsia, diabetes gestacional, baixo peso ao nascer e parto prematuro foram: 6,6% (IC 95%: 4,9–8,6%), 8,5% (IC 95%: 3,9–14,7%), 8,5% (IC 95%: 7,2–9,8%) e 10,0% (IC 95%: 8,0–12,0%), respectivamente. Observou-se heterogeneidade considerável, tanto em geral como por delineamento de estudo. Não foram observadas diferenças importantes nas estimativas por nível de viés.

**Conclusões.** Os resultados deste estudo fornecem estimativas atualizadas de alguns dos desfechos gestacionales e perinatais adversos mais prevalentes na América Latina e no Caribe. Destacam a existência de uma importante heterogeneidade nas estimativas de prevalência, o que pode refletir a diversidade das populações da região.

**Palavras-chave** Hipertensão induzida pela gravidez; pré-eclâmpsia; diabetes gestacional; recém-nascido de baixo peso; nascimento prematuro; América Latina; Região do Caribe.