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REVIEW ARTICLE

Obstetrics

A snapshot of the prevalence of endocrine disorders in pregnancies complicated by coronavirus disease 2019: A narrative review with meta-analysis

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Abstract

Background: Some maternal characteristics indicate worse prognosis in pregnant women with coronavirus disease 2019 (COVID-19).

Objective: To describe the prevalence of endocrine disorders in pregnancies involving COVID-19, and its impact on maternal outcomes.

Search strategy: Search terms were "pregnancy" and "COVID-19".

Selection: PubMed, Embase, medRxiv, and Cochrane worksheet from February to July 2020 were searched.

Data collection and analysis: Articles describing endocrine disorders in pregnancies with and without COVID-19 involvement were considered. We performed meta-analyses of prevalence using random-effect models and estimated relative risk and 95% confidence intervals (CI) of maternal outcomes relative to presence of endocrine disorders.

Main results: Articles included (n = 141) were divided into three data sets: individual (119 articles, 356 women), case series (17 articles, 1064 women), and national registries (7 articles, 10 178 women). Prevalence of obesity ranged from 16% to 46% and hyperglycemia in pregnancy (HIP) ranged from 8% to 12%. In data set 1, HIP and obesity were risk factors for severe disease in crude and age-adjusted models, although not for intensive care unit admission. In data from two national registries, risk of dying was 5.62 (95% CI 0.30–105.95) in women with diabetes and 2.26 (95% CI 1.03–4.96) in those with obesity.

Conclusion: Obesity and HIP were prevalent in pregnant women with severe COVID-19.

KEYWORDS
COVID-19, endocrine disorders, pregnancy

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was described for the first time in China in December 2019. The disease can complicate around 10% (95% confidence interval [CI] 7–14) of pregnancies worldwide, depending on the type of screening, whether universal (~7%) or based on symptoms (~18%).[1]

According to Thornton,[2] the first report of pregnancies complicated by COVID-19 was the *Study 1. The original Lancet nine*, which

described outcomes of nine pregnancies in Chinese women; they were in the third trimester and the authors focused on the possible vertical transmission of COVID-19 during labor. Cases occurred from January 20, 2020 onward in Zhongnan Hospital of Wuhan University.[3] Since then, a myriad of articles have appeared in the literature, most of them as case reports or case series. After the spread of the disease to other continents, more consistent reports became available.[1]

As described for non-pregnant adults,[4] some features seem to behave as risk factors for more severe forms of COVID-19 and worse pregnancy outcomes; among them, obesity, chronic hypertension, diabetes (pre-gestational or gestational diabetes), and smoking were described.[1]

In this narrative review with meta-analysis, we investigate the prevalence of endocrine disorders in pregnant women positive for COVID-19 and the burden that these disorders impose on pregnancy outcomes.

2 | MATERIALS AND METHODS

Our review was registered in PROSPERO on June 22, 2020, CRD42020192063.[5] The study was approved on August 18, 2020 by the ethics committee of Hospital de Clínicas de Porto Alegre (CAAE 35017020600005327), project 2020-0382.

We performed a systematic search for articles describing the presence of endocrine disorders in pregnant women positive for COVID-19, irrespective of study design or primary outcome and severity of infection, at any gestational age and either outpatients or inpatients, pre-delivery or post-delivery.

We searched PubMed, Embase, medRxiv, and the Cochrane EXCEL sheet "Perinatal outcomes in COVID-19 infection" available from the Cochrane Gynaecology and Fertility site.[6] No restriction for language was applied, except for manuscripts written exclusively in Chinese that could not be electronically translated. Case series/case reports and cohort studies from the first published report (February 2020) until July 3, 2020 for PubMed and Embase and until July 15, 2020 for medRxiv and the Cochrane EXCEL worksheet, were inserted in the database.

A broad search strategy was used in PubMed, Embase, and medRxiv: (pregnancy) and (COVID-19), because of the paucity of studies at the time of the search (see Appendix S1).

AJR, MLRO, and VKG screened article titles and abstracts. All articles listed in the Cochrane worksheet were eligible, after obtaining the permission of Dr Madelon van Wely. Studies were screened for relevance and eligibility. We extracted information on location of the study (country, city, and setting), study design, maternal age, ethnicity, gestational age (or trimester) at diagnosis, body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters), categorization of BMI, diabetes (pre-gestational or gestational or other), thyroid disorders (hypothyroidism or hyperthyroidism), diagnostic tool for COVID-19, severity of disease, maternal and pregnancy outcomes, frequency of endocrine disorders in non-COVID-19 and COVID-19 cases, and frequency according to disease severity.

COVID-19 was deemed positive if the reverse-transcriptase polymerase chain reaction test detected SARS-CoV-2 or if lung images by computed tomography were those typically found in the disease.[7] We did not include studies reporting women with serologic diagnostic tests, except for one woman.[8] If severity of disease was not described, we used the World Health Organization recommendation of a four-level classification: asymptomatic disease, mild disease, moderate (presence of pneumonia/hospital admission) disease, and severe/critical disease.[7]

Endocrine disorders were extracted as reported by the authors: normal BMI, overweight, obesity, diabetes, pre-gestational diabetes (PGDM), gestational diabetes (GDM), hypothyroidism, hyperthyroidism, and any other. We considered BMI as normal when clearly reported, or if authors stated that women had no comorbidities, were deemed as fit or pregnancy was classified as uneventful. BMI was considered as pre-gestational if stated or when reported with other pre-pregnancy morbidities; and as calculated in pregnancy if authors reported so. Hyperglycemia in pregnancy (HIP) refers to any kind of diabetes in pregnancy.[9] The main outcome was prevalence of endocrine disorders. Intensive care unit (ICU) admission and death were the outcomes for risk estimation.

AJR and VKG extracted data in an SPSS sheet. After extraction, AJR, VKG, and MLRO, in pairs, confirmed and corrected the data. Discordances were discussed with MLRO or VNH. Several authors were contacted to provide additional data on participants or to clarify information.

Studies were evaluated by the Quality Assessment Tool for Case Series (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools; accessed February 17, 2021). The tool encompasses nine queries: study objective, case definition, consecutiveness, comparability, intervention, outcome definition, length of follow up, statistical methods, and results well described. Intervention did not apply here; consecutiveness and comparability did not apply to case reports. Therefore, the maximum score was 5 for individual reports and 8 for case series. Studies were ranked as good (score 4 to 5, individual reports; 6 to 8, case series), fair (score 3, individual reports; 4 to 5, case series) or poor (score 1 to 2, individual reports; 1 to 3, case series).

During data extraction, we realized that some cases could be duplicated because authors focused on different disease aspects of the same pregnancy, reporting them in independent articles. Cases considered similar were further scrutinized for hospital of origin, dates of admission or delivery, maternal age, gestational age, and data on the neonate.

Due to evidence of duplicated reports, we decided to perform analyses combining articles into three groups. Individual data could be extracted from 119 articles, some originally reported as case series (see Appendix S2, data set 1; Supplementary references 1–119); case series were reported in 17 articles (see Appendix S3, data set 2; Supplementary references 120–136); and seven articles provided data from five national registries,[10–14] a national COVID-19 reference hospital[15] and a national study group of obstetricians and gynecologists,[16] comprising the third data set.

We calculated prevalence and 95% CI of each endocrine disorder. Meta-analysis of prevalence was performed using random-effect models in data sets 2 and 3. Cochrane χ^2 and I^2 tests were used to evaluate heterogeneity among studies, and an α value of 0.10 was considered significant. Publication bias was assessed using a funnel plot of study's effect size against standard error. Funnel plot asymmetry was evaluated by Begg and Egger tests. Due to the small number of studies in each data set, trim and fill and sensitivity analyses were not performed.

Relative risks and 95% CI were calculated for maternal outcomes using Poisson regression with robust estimation of variance. Evaluable outcomes were disease severity and admission to ICU in data set 1, and cure or death in data set 3.

SPSS version 18 (IBM Corp., Armonk, NY, USA), R and WIN-PEPI programs were used to perform analyses.

We wrote the article following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[17] References were updated to the most recent version.

3 | RESULTS

We identified 1227 titles/abstracts, of which 234 were eligible. After exclusions, many during the extraction process, 141 articles remained for final synthesis (PRISMA diagram, see Figure S1).

In Figure 1, we present number of cases described in 62 studies, after excluding probable duplicates (n = 10 717 women), grouped by continent of the original publication. No cases were reported in Oceania and only a few in Africa; reports from Asia totaled 512 cases, from Latin America, 293, and from Europe, 1380. The largest series was from the USA, a report from the Centers of Disease Control involving 8207 women[11]; reports from North America contributed with more than 8500 cases.

The analyses within each data set are described below.

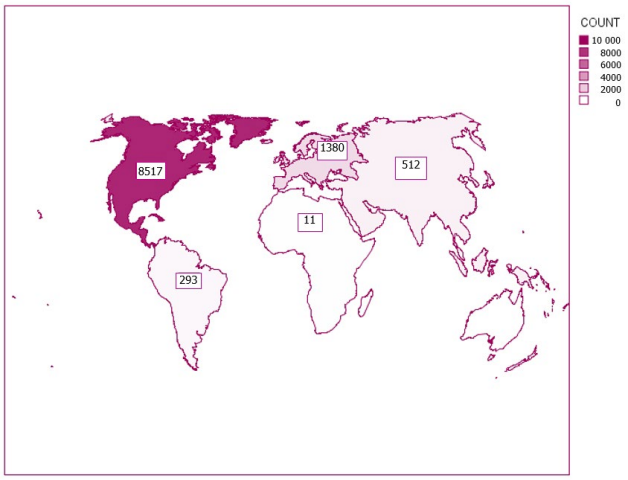

FIGURE 1 Number of women described in case series according to continent of study

3.1 | Data set 1 (individual cases)

One hundred and nineteen articles provided individual information about 356 women with COVID-19. Individual cases were described in 70 papers (19.7%) and the other 286 (80.3%) were extracted from papers describing series of cases. More than half of reports were from university hospitals; 114 (32.0%) women were from China, 102 (28.7%) were from Europe; 86 (24.2%) from the USA and the others were from Latin America, Africa, and other Asian countries. Table S1, Panel A, shows the quality assessment of studies: all except one were graded as good.

Mean maternal age was 31 (±5.8) years, mean pregnancy length at diagnosis was 32.7 (±7.4) weeks and median gestation at delivery was 37.0 weeks (interquartile range 23.4–41.2 weeks) (n = 258 women). Characteristics of women and prevalence of endocrine disorders are presented in Table 1. Information about prenatal period was available for 354 women (99%; 95% CI 98–100): it was uneventful in 203 pregnancies, 151 women had morbidities and in two cases only information on BMI was available.

Data about BMI were available for 143 women (40%; 95% CI 35–45). In 66 women (46.2%) pre-pregnancy BMI was known; in 17 (11.9%) it was calculated during pregnancy, and in 60 (42.0%) it was not specified.

Risk of having severe COVID-19 disease if a morbidity was present is exhibited in Table 2. Obesity and HIP were risk factors in both crude and age-adjusted models. Obesity heightened the risk of severe disease in crude and adjusted models, but HIP was not significant when adjusted for obesity.

Risk of admission to ICU was two times higher in women with obesity and in those with PGDM (Table 2). Obesity was significant in the age-adjusted model, but not in a model adjusted by maternal age and hyperglycemia; after adjustments for maternal age and obesity, risk attributed to PGDM did not remain significant.

Due to the low prevalence of other endocrine disorders, no risk analyses were performed.

3.2 | Data set 2 (case series)

In this section, we included 17 articles. Eight papers were from the USA, two from each of China, Spain, and the UK, and one from each of India, Italy, and Sweden. Quality of studies was good (see Table S1, Panel B, left side).

COVID-19 was diagnosed in 1064 women; five articles compared characteristics of women with COVID-19 (n = 298) with those without COVID-19 (n = 5659).

Details of the diagnostic tool for SARS-CoV-2, clinical presentation of the disease, and presence of morbidities before or during pregnancy were available in 16 papers.

Information on BMI could be extracted from nine articles (52.9%), mainly as frequency of obesity; overweight or normal BMI were described in three articles. BMI was labeled as pre-gestational in five

TABLE 1 Dataset 1: characteristics and prevalence of endocrine disorders in 356 pregnant women with COVID-19[a]

Characteristic	Total *N* (%)	
Maternal age (years)	356 (100)	31 ± 5.8
Ethnicity/skin color	209 (58.7)	
White		38 (18.2)
Non-white		12 (5.7)
Asian		148 (70.8)
Other		11 (5.3)
BMI	143 (40.2)	
Normal		56 (39.2)
Overweight		21 (14.7)
Obese		66 (46.2)
Diagnostic tool	356 (100)	
RT-PCR		341 (95.8)
Tomography		14 (3.9)
Other		1 (0.3)
Trimester of diagnosis	356 (100)	
First		10 (2.8)
Second		53 (14.9)
Third		293 (82.3)
COVID-19 severity	356 (100)	
Asymptomatic		53 (14.9)
Mild		129 (36.2)
Moderate		90 (25.3)
ICU admission		84 (23.6)
Maternal outcome	324 (91.0)	
Cure		291 (89.8)
Death		15 (4.6)
Inpatient		18 (5.6)
Pregnancy outcome	346 (97.2)	
Miscarriage		10 (2.9)
Termination		2 (0.6)
Vaginal delivery		66 (19.1)
Cesarean section		197 (56.9)
Continuing		60 (17.3)
Other[b]		11 (3.2)
Pregnancy duration	284 (79.8)	
<22 weeks		12 (4.2)
Term		156 (54.9)
Preterm		116 (40.8)

Endocrine disorder	N(%)	Prevalence	95% CI
Overweight	143 (40.0)	21 (15.0)	9.0–22.0
Obese	143 (40.0)	66 (46.0)	38.0–55.0
GDM	354 (99.0)	29 (8.0)	6.0–12.0
PGDM	354 (99.0)	15 (4.0)	2.0–7.0
HIP	354 (99.0)	44 (12.0)	9.0–16.0
Hypothyroidism[c]	354 (99.0)	18 (5.0)	3.0–8.0

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); GDM, gestational diabetes; HIP, hyperglycaemia in pregnancy; ICU, intensive care unit; PGDM, pregestational diabetes; RT-PCR, reverse transcriptase polymerase chain reaction.

[a]Values are given as mean ± standard deviation or as number (percentage).

[b]"Other" includes nine non specified deliveries and two intrauterine deaths in dead mothers.

[c]Includes one case of subclinical hypothyroidism.

articles (55.6%), probably calculated in pregnancy in three (33.3%), and not specified in one (11.1%). Figure 1 shows prevalence of obesity in the nine series (n = 599); obesity was present in one-third of cases, with high heterogeneity among studies (prevalence 33%; 95% CI 23–45), I^2 84%, P < 0.01).

Information on the presence of diabetes was provided in 16 articles: in two papers, there were no cases of diabetes; in the other 14, diabetes was described as pre-existing or GDM in 10 articles, and generically as diabetes in the other four. In one paper, cases of diabetes were under the umbrella of comorbidities.[18] Prevalence of hyperglycemia in pregnancy (14 articles, 1022 women) was 9% (95% CI 6–12). Gestational diabetes was described in seven papers (653 women) with a prevalence of 8% (95% CI 6–12). Pregestational diabetes was described in six studies (502 women) with a prevalence of 5% (95% CI 3–7); and diabetes was reported in five studies (280 women) with a prevalence of 7% (95% CI 3–15) (Figure 1).

Thyroid diseases were reported in 16 papers: there were nine cases of hypothyroidism and one case of hyperthyroidism described in four articles.[19–22] Meta-analysis was not conducted.

We could not group studies to calculate the risk of adverse pregnancy outcomes because of the low number of risk factors or outcomes. No other endocrine disorders were reported.

3.3 | Data set 3 (national data)

Among the seven articles in this section, one was from Kuwait, three were from Europe (France, Italy, and the UK) and three were from the Americas (Brazil, Mexico, and the USA). All studies were of good quality (see Table S1, Panel B, right side).

The studies provided data on 10 178 pregnancies in women with confirmed COVID-19. In 503 women (4.9%; 95% CI 4.5–5.4) ICU treatment was required; 157 pregnancies were in progress at the time of the reports; and 65 women died (0.64%; 95% CI 0.49–0.81). Five studies reported gestation at diagnosis, with most in the third trimester.

Maternal BMI was provided in five studies (71.4%), mainly as number of women with obesity (n = 363): in two studies, prepregnancy, in two, not specified and in one, probably calculated during pregnancy.

TABLE 2 Risk of adverse outcomes in pregnancies with endocrine disorders (articles with individual data)

Disorder	*N*	Crude RR (95% CI)	*P*	*N*	Adjusted RR (95% CI)	*P*
Severe COVID-19						
HIP	151	1.16 (1.05–1.28)	0.003	147[a]	1.17 (1.06–1.29)	0.003
				71[b]	1.07 (0.95–1.22)	0.271
				70[c]	1.08 (0.95–1.23)	0.214
Obesity	143	1.23 (1.12–1.35)	<0.001	141[a]	1.23 (1.12–1.36)	<0.001
				71[d]	1.16 (1.001–1.346)	0.049
				70[e]	1.16 (1.01–1.35)	0.042
ICU admission						
PGDM	151	2.09 (1.28–3.42)	0.003	147[a]	1.86 (1.11–3.11)	0.019
				71[b]	1.48 (0.90–2.42)	0.120
				70[c]	1.37 (0.85–2.23)	0.198
Obesity	143	2.40 (1.49–3.87)	<0.001	141[a]	2.39 (1.49–3.83)	<0.001
				71[d]	1.68 (0.89–3.18)	0.108
				70[e]	1.63 (0.87–3.06)	0.127

Abbreviations: COVID-19, coronavirus disease 2019; HIP, hyperglycemia in pregnancy; ICU, intensive care unit; PGDM, pre-gestational diabetes mellitus; RR, relative risk.

[a]Adjusted for age.

[b]Adjusted for obesity.

[c]Adjusted for age and obesity.

[d]Adjusted for hyperglycemia in pregnancy.

[e]Adjusted for age and hyperglycemia in pregnancy.

GDM (*n* = 140) and PGDM (*n* = 28) were reported in three studies; only one provided data about the severity of COVID-19 in women with diabetes[16]; four studies reported number of women with diabetes (*n* = 346) but did not specify whether gestational or pre-gestational; five studies reported data on the presence of thyroid disorders, mainly hypothyroidism (10 cases). No cases of hyperthyroidism were reported. Mode of delivery was reported in four studies.

Prevalence of endocrine disorders in data set 3 is shown in Figure 2b; obesity and GDM were the most frequent disorders, with prevalence higher than 10%. Prevalence of individual endocrine conditions was: obesity 16% (95% CI 9–27, I^2 96%, $P < 0.01$); GDM 11% (95% CI 10–13, I^2 0%, $P = 0.87$); PGDM 2% (95% CI 2–3, I^2 0%, $P = 0.22$); diabetes 6% (95% CI 3-9), I^2*90%, P < 0.01;* HIP 8% (95% CI 5–12, I^2 95%, $P < 0.01$); and hypothyroidism 2% (95% CI 1–5, I^2 46%, $P = 0.06$).

Two papers,[10,13] involving 596 women, could be compared because they used similar definitions: obesity (not classified as pre-gestational or in pregnancy) and diabetes (not specified) as risk factors, and cure or death as maternal outcomes (see Figure S2). Risk of dying was 2.26 (95% CI 1.03–4.96) for women with obesity and 5.62 (95% CI 0.30–105.95) for those with diabetes.

Publication bias was not significant in either data set 2 or data set 3, except for HIP in data set 2, case series ($P = 0.028$). Funnel plot analyses are shown in the Figure S3.

4 | DISCUSSION

In the three settings, obesity was the most prevalent endocrine disorder in pregnant women with COVID-19, with rates from 16% to 46%. Hyperglycemia in pregnancy ranged from 6% to 12%. The presence of these morbidities was associated with unfavorable maternal outcomes. Other endocrine disorders were rare.

A state of inflammation is associated with obesity and diabetes. This is, probably, the hallmark aspect by which these disorders behave as risk factors for SARS-CoV-2 infection and, moreover, as predictors of severe forms of the disease with worse outcomes. Adipose tissue is vulnerable to hyperplasia and hypertrophy and these alterations, mediated by tissue hypoxia, provoke increased release of inflammatory elements. The misbalance between increased inflammatory cytokine release and diminished action of the anti-inflammatory immune system results in chronic and diffuse inflammation.[23] Other mechanisms, such as an increased pro-thrombotic profile, can further contribute to the severity of COVID-19.[24] Conversely, pregnancy is a state of active and complex immune changes that lead to maternal tolerance for successful implantation of the trophoblast/blastocyst unit.[25] These alterations may potentially increase the susceptibility of pregnant women to SARS-CoV-2 infection. In a meta-analysis, prevalence of severe COVID-19 was 7% (95% CI 4–10) if universal screening of women arriving for delivery was performed, and 18% (95% CI 10–28) in symptomatic women.[1]

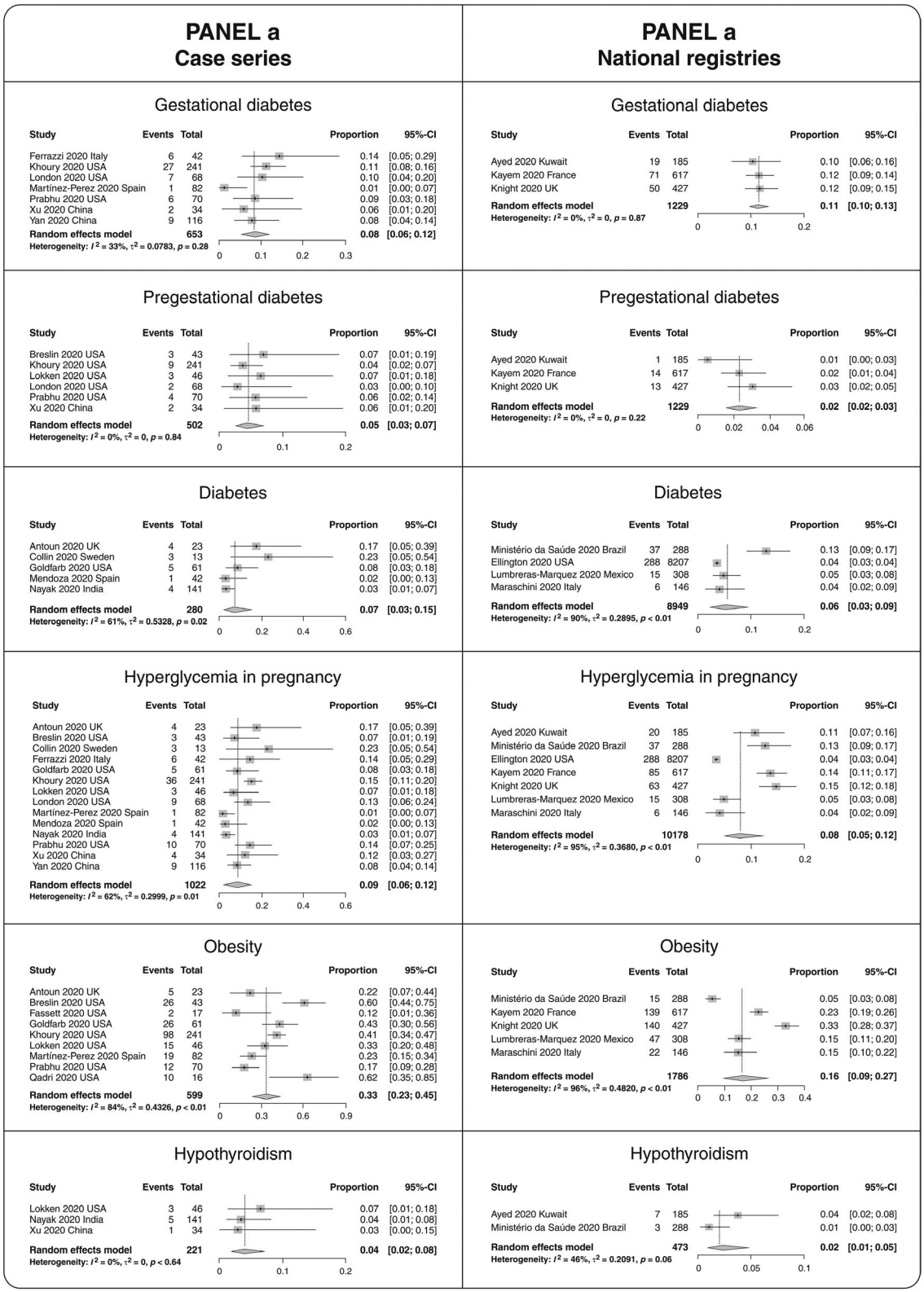

FIGURE 2 Prevalence of endocrine disorders in pregnant women with coronavirus disease 2019. Panel a: case series. Panel b: national registries

Pregnant women are being infected with SARS-CoV-2, but present different grades of severity and there is a possibility that endocrine disorders can behave as risk factors.

Prevalence of obesity ranged from 16% to 46% in the three distinct settings of our study. Prevalence of obesity was 10.5% in a large cohort of British non-pregnant adults with COVID-19 (n ~ 16 000),

but mean age of the participants was approximately 74 years old, which limits comparisons with our data.[26] In a large Mexican large cohort, obesity was present in 20.7% of more than 51 000 patients with COVID-19, compared with 14.2% in those who tested negative; in that study, participants were also older.[27] The presence of obesity doubled the risk of severe disease in pregnant women in a living meta-analysis[1] and in an Italian study[28]; in the present study, we found an increased risk for severe infection in the data set with individual data; nevertheless, risk was not so high (23% higher), but remained significant when adjusted for age and hyperglycemia; the association was lost for the risk of ICU admission. Risk of dying was 2.26-fold higher if obesity was present in the analyses performed using the national registry data set; the latter included 596 women, contrasting with the approximately 140 women in the individual data set. In case series, prevalence of obesity was 33%, intermediate between the two other data set estimates. Of note, amid nine studies including 599 women, all but two were from the USA, and prevalence reached 60% or more in some studies, probably mirroring the high burden of obesity in that country. High heterogeneity was found in those analyses.

Regarding diabetes, the prevalence of GDM varied from 8% to 11% in the three data sets, prevalence of PGDM vaired from 2% to 5% and of diabetes from 7% in the case series and 6% in the national registry samples. The composite of these three labels, hyperglycemia in pregnancy, varied from 8% to 12%. Higher estimates were found in the data set with individual information, probably because of the highly selected cases included. In case series, estimates reflected those described in several studies in pregnancies without COVID-19, both for GDM, which accounts for approximately 84% of cases of HIP, and for PGDM, which accounts for less than 8% of the cases of HIP; estimates were lower than the prevalence of HIP reported in the 2019 International Diabetes Federation Diabetes Atlas, 15.8% in women aged 20–49 years.[29] Concerning COVID-19 cases in non-pregnant women, 19.3% of women in the British cohort had diabetes without complications and 6.2% had diabetes with complications, but the women were considerably older than in the present study.[26] In the Mexican study, 18.3% of those with COVID-19 presented with diabetes, compared with 10.7% in those negative for SARS-CoV-2.[27] There was an increased frequency of adverse outcomes in individuals with diabetes and aged less than 40 years in the latter study, which may suggest that early diabetes, perhaps undiagnosed until childbearing age, poses a risk of adverse outcomes when occurring in pregnancy. HIP posed a five-fold risk of dying in women with COVID-19 in the sole analysis we could perform using data set 3. For comparison, chronic hypertension was associated with a risk of 2.77 (95% CI 1.30–5.93) of dying. In the meta-analysis of Allotey et al.[1], both increased age and presence of PGDM posed higher risk of having severe forms of COVID-19 in pregnancy, whereas the risk of GDM was not significant, in consonance with the findings of an Italian study y.[28]

Our study has strengths. We evaluated the prevalence of endocrine disorders, which are potential risk factors associated with COVID-19 adverse outcomes in pregnancy, showing that obesity is frequent, followed by hyperglycemia. Analyses included individuals and case series, with the largest containing information of national data sets from different countries. However, limitations outweighed strengths. Either in individual or case series studies, although considered of good quality, there was a lack of information on BMI and HIP, to such an extent that among the eligible studies, around 10% did not provide that information and were excluded. Few studies could be included and we had to break data into three data sets to better extract information and avoid duplications. Samples were not large enough to perform several risk estimations. This impacted on the precision of estimates, as corroborated by the large CI found in some analyses. BMI was inconsistently reported; when reported, it was frequently not clear if pre-gestational measures were used or if it was calculated during pregnancy, and this may have influenced estimates of prevalence and risk. Hyperglycemia was classified generically as diabetes in several studies, precluding more exact evaluation of GDM and PGDM as risk factors. We could speculate that GDM, although more frequent, may not be associated with increased risk of severe forms of COVID-19 and consequences for both mother and fetus, unlike PGDM, because of the lower levels of and shorter exposure to hyperglycemia seen in GDM. The imprecision of definitions of diabetes may have had an impact on the high heterogeneity found; studies including women from several ethnic backgrounds could also have contributed. There is a high risk of bias in the data set of individual data because it is probable that severe and selected cases were published, leaving milder cases unpublished. Conversely, data from large national registries may encompass incomplete information or use broader definitions of several parameters, such as for diabetes, without specifying if GDM or type 1/type 2 PGDM were present; case series may provide more accurate data on this. Finally, the possibility of duplicated cases precluded inclusion of several studies. We are convinced that these limitations are mostly explained by the rush to publish information about this new, dangerous, and multifaceted disease that rapidly spread worldwide, in such way that a pandemic had to be declared.

In conclusion, among pregnant women with COVID-19, obesity was a prevalent risk factor, followed by hyperglycemia, similar to what is described outside pregnancy. Due to the scarce and sometimes confusing data available, more studies are deemed necessary to elucidate the role of endocrine disorders in the outcomes of pregnancies complicated by COVID-19.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

AJR was responsible for conception of the study; all authors contributed to planning and carrying out the study. All authors were

responsible for data analyses and writing of the manuscript and all endorsed the final version of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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