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Ultrasound Obstet Gynecol 2022; **59**: 76–82
Published online 17 December 2021 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.24797

Comorbidity, poverty and social vulnerability as risk factors for mortality in pregnant women with confirmed SARS-CoV-2 infection: analysis of 13 062 positive pregnancies including 176 maternal deaths in Mexico

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KEYWORDS: comorbidity; COVID-19; maternal death; poverty; vaccine

CONTRIBUTION

What are the novel findings of this work?
This is one of the largest cohorts to date on coronavirus disease 2019 (COVID-19) in pregnancy. The findings demonstrate that advanced maternal age, pre-existing diabetes, chronic hypertension, obesity, high social vulnerability and low socioeconomic status are risk factors for COVID-19-related maternal mortality.

What are the clinical implications of this work?
The findings of this study should help identify high-risk pregnant women who should observe mask-wearing, social distancing and good hand hygiene and ideally get vaccinated in order to reduce the risk of acquiring severe acute respiratory syndrome coronavirus 2 infection, as well as raise awareness of the possibility of selective vaccination in developing countries in which vaccines and resources are scarce.

ABSTRACT

Objective *Mortality in pregnancy due to coronavirus disease 2019 (COVID-19) is a current health priority in developing countries. Identification of clinical and sociodemographic risk factors related to mortality in pregnant women with COVID-19 could guide public policy and encourage such women to accept vaccination. We aimed to evaluate the association of comorbidities and socioeconomic determinants with COVID-19-related mortality and severe disease in pregnant women in Mexico.*

Methods *This is an ongoing nationwide prospective cohort study that includes all pregnant women with a positive reverse-transcription quantitative polymerase chain reaction result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from the Mexican National Registry of Coronavirus. The primary outcome was maternal death due to COVID-19. The association of comorbidities and socioeconomic characteristics with maternal death was explored using a log-binomial regression model adjusted for possible confounders.*

Results *There were 176 (1.35%) maternal deaths due to COVID-19 among 13 062 consecutive SARS-CoV-2-positive pregnant women. Maternal age, as a continuous (adjusted relative risk (aRR), 1.08 (95% CI, 1.05–1.10)) or categorical variable, was associated with maternal death due to COVID-19; women aged 35–39 years (aRR, 3.16 (95% CI, 2.34–4.26)) or 40 years or older (aRR, 4.07 (95% CI, 2.65–6.25)) had a higher risk for mortality, as compared with those aged < 35 years. Other clinical risk factors associated with maternal mortality were pre-existing diabetes (aRR, 2.66 (95% CI, 1.65–4.27)), chronic hypertension (aRR, 1.75 (95% CI, 1.02–3.00)) and obesity (aRR, 2.15 (95% CI,*

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Accepted: 11 October 2021

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1.46–3.17)). Very high social vulnerability (aRR, 1.88 (95% CI, 1.26–2.80)) and high social vulnerability (aRR, 1.49 (95% CI, 1.04–2.13)) were associated with an increased risk of maternal mortality, while very low social vulnerability was associated with a reduced risk (aRR, 0.47 (95% CI, 0.30–0.73)). Being poor or extremely poor were also risk factors for maternal mortality (aRR, 1.53 (95% CI, 1.09–2.15) and aRR, 1.83 (95% CI, 1.32–2.53), respectively).

Conclusion *This study, which comprises the largest prospective consecutive cohort of pregnant women with COVID-19 to date, has confirmed that advanced maternal age, pre-existing diabetes, chronic hypertension, obesity, high social vulnerability and low socioeconomic status are risk factors for COVID-19-related maternal mortality.* © *2021 International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

In Mexico, coronavirus disease 2019 (COVID-19) is currently the leading cause of death in pregnancy, overtaking obstetric hemorrhage and pre-eclampsia[1]. There are several reasons that could explain the higher rate of mortality among pregnant compared with non-pregnant individuals affected by COVID-19. First, recent studies have demonstrated that pregnancy is an independent risk factor for adverse outcome associated with COVID-19. Studies conducted in developing countries, such as Mexico, have demonstrated that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected pregnant women have higher odds of pneumonia (odds ratio (OR), 1.99 (95% CI, 1.81–2.19)), intensive care unit (ICU) admission (OR, 2.25 (95% CI, 1.86–2.71)) and death (OR, 1.65 (95% CI, 1.30–2.09)), when compared with infected non-pregnant women of the same age[2]. Similar findings have been demonstrated in developed countries, such as the USA, in which Hispanic/Latin-American pregnant women with SARS-CoV-2 infection have experienced a 2.4-times higher risk of death compared with other ethnic groups[3]. Second, in the context of any pandemic, there is a strong influence of ethnicity and socioeconomic status on health-related outcomes among infected individuals[4,5]. The higher rate of COVID-19-related mortality among Latin-American pregnant women raises the questions of why this particular population is more susceptible to developing adverse outcome associated with COVID-19, and which are the clinical and socioeconomic risk factors[6]. It is, therefore, of great importance to unveil all possible prognostic factors associated with COVID-19-related mortality, especially those related to socioeconomic inequality, as the identification of these risk factors could help guide the development of heath policies to protect vulnerable groups, which are defined not only by clinical and demographic criteria but also by socioeconomic indices, such as the poverty and social vulnerability indices.

The objective of this study was to evaluate the association of clinical characteristics and socioeconomic determinants with COVID-19-related mortality and severe morbidity among pregnant women.

METHODS

Study design and participants

This study analyzed data from the Mexican National Registry of Coronavirus[7], which is an ongoing prospective cohort based on information from the Mexican government and is updated weekly with data from 475 monitoring hospitals located across the 32 states of Mexico. Inclusion criteria were all pregnant women with a positive reverse-transcription quantitative polymerase chain reaction (RT-qPCR) test for SARS-CoV-2 in the Mexican National Registry of Coronavirus between 1 April 2020 and 31 July 2021. Maternal deaths due to other causes were excluded from the study population. The study protocol was approved by the General Hospital of Mexico (Dr Eduardo Liceaga), Mexico City, Mexico, under the ethics committee number CE/23020.

Data collection

Data on patients' medical history were collected and transferred from the Mexican National Registry of Coronavirus. Access to the Mexican National Registry is available at each hospital only by institutional approval. The following data were collected for each patient: age; pregestational diabetes mellitus; chronic obstructive pulmonary disease; asthma; immunosuppression; chronic hypertension; cardiovascular disease; obesity (defined as body mass index $\geq 30\,kg/m^2$); chronic renal disease or other non-specified morbidity; smoking; pneumonia; ICU admission; and maternal death. To avoid bias due to missing data, we retrieved and analyzed data from the last update of the Mexican National Registry of Coronavirus, which contains complete information on the outcomes at each update. Socioeconomic determinants included ethnicity (including the proportion of women who were indigenous), access to private health services, social security for public health services, social lag indices or social vulnerability indices and the poverty index for Mexican states. Socioeconomic determinants were calculated based on postal code for every participant; information on postal code, town, state and country is part of the COVID-19 National Database.

Outcomes

The primary outcome was maternal death as a direct result of COVID-19, as labeled by the monitoring hospital. Maternal deaths due to other causes were excluded from the study population. A woman with COVID-19 was defined as any symptomatic patient with a positive RT-qPCR result for SARS-CoV-2. Secondary outcomes were severe pneumonia, ICU admission and intubation. Severe pneumonia due to

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COVID-19 was defined according to the definition of the American Thoracic Society criteria[8], which includes either one major criterion (septic shock with need for vasopressors or respiratory failure requiring mechanical ventilation) or three or more minor criteria (respiratory rate ≥ 30 breaths/min, PaO_2/FiO_2 ratio ≤ 250, multilobar infiltrates, confusion/disorientation, uremia (blood urea nitrogen level ≥ 20 mg/dL), leukopenia (white blood cell count < 4000 cells/μL), thrombocytopenia (platelet count $< 100\,000$/μL), hypothermia (core temperature $< 36°C$) or hypotension requiring aggressive fluid resuscitation). Need for ICU admission was determined using the quick Sequential Organ Failure Assessment (qSOFA) score, with a score of ≥ 2 points indicating need for ICU admission[9]. Viral sepsis was defined according to the Sepsis-3 International Consensus associated with SARS-CoV-2 infection[10,11]. Data for severe pneumonia and ICU admission were missing in some cases; therefore, we included only cases with complete data in the calculation of these outcomes.

Social vulnerability index

The social vulnerability index, also known as the social delay index, allows ranking of the states of Mexico from the highest to the lowest degree of social vulnerability at a given moment in time. Using the Dalenius–Hodges stratification method, the social vulnerability index in Mexico may be divided into five categories: very high vulnerability, high vulnerability, medium vulnerability, low vulnerability and very low vulnerability[12]. It provides a summary of four social deficiencies monitored by the National Council for Evaluation of Social Development Policy[13]: educational lag, access to health services, access to essential services in housing and quality of and space in housing.

Poverty in Mexican states

The poverty index is based on the CONEVAL methodology[14]. It considers the current *per-capita* income, average educational lag in a household, access to healthcare services, access to social security services, quality of and space in housing, access to quality and nutritious food, degree of social cohesion and degree of accessibility to a paved road. The poverty index in Mexico is divided into three categories: not poor, poor and extremely poor. The 2018 poverty report and its methodology were published on 31 July 2019 (MCS-ENIGH 2018 report)[15].

Statistical analysis

Descriptive and inferential statistics were used. Quantitative variables were reported as mean ± SD; categorical variables were summarized as *n* (%). Univariate and multivariate log-binomial regression analyses were performed to establish the association of several clinical, demographic and social risk factors with the primary and secondary outcomes. The treatment effect used for this analysis was relative risk (RR) based on univariate analysis, as well as adjusted RR (aRR) based on multivariate analysis when statistically significant variables were identified on univariate analysis, including maternal age, pre-existing diabetes, obesity, hypertension, renal chronic disease, asthma and ethnicity.

Statistical analyses were performed using Stata version 16 (Stata Corp., College Station, TX, USA). A *P*-value < 0.05 was considered statistically significant.

RESULTS

Description of cohort and characteristics of study population

A total of 13 062 consecutive SARS-CoV-2-positive pregnant women were included in the analysis. Mean age at diagnosis was 28.3 ± 6.0 years. Of those women, 176 (1.35%) died as a direct result of COVID-19, 1191 (9.12%) were diagnosed with severe pneumonia, 322 (2.47%) were admitted to the ICU and 185 (1.42%) were intubated.

On univariate analysis, pregnant women who died due to COVID-19, compared with those who did not die, were older and had higher rates of comorbidities, such as pre-existing diabetes, chronic hypertension, obesity, chronic renal disease and asthma (Table 1). In addition,

Table 1 Characteristics of the study population of 13 062 SARS-CoV-2-positive pregnant women, according to whether maternal death due to COVID-19 occurred

Characteristic	*Maternal survival (n = 12 886)*	*Maternal death (n = 176)*	P
Maternal age (years)	28.3 ± 6.00	31.7 ± 6.63	< 0.001
Maternal age			< 0.001
< 35 years	10 699 (83.03)	106 (60.23)	
35–39 years	1745 (13.54)	47 (26.70)	
≥ 40 years	442 (3.43)	23 (13.07)	
Pre-existing diabetes	391 (3.03)	24 (13.64)	< 0.001
Chronic hypertension	345 (2.68)	19 (10.80)	< 0.001
Obesity	986 (7.65)	30 (17.05)	< 0.001
Chronic renal disease	32 (0.25)	4 (2.27)	< 0.001
Asthma	268 (2.08)	8 (4.55)	0.022
COPD	18 (0.14)	0 (0)	0.623
Immunosuppression	93 (0.72)	2 (1.14)	0.511
Cardiovascular disease	50 (0.39)	1 (0.57)	0.696
Smoker	225 (1.75)	3 (1.70)	0.74
Indigenous ethnicity	330 (2.56)	5 (2.84)	0.815
Type of HS used			0.450
Private	295 (2.29)	4 (2.27)	
Public (SW)	5247 (40.72)	65 (36.93)	
Public (not SW)	7344 (56.99)	107 (60.80)	
Social vulnerability			
Very high	1073 (8.33)	27 (15.34)	0.001
High	2021 (15.68)	37 (21.02)	0.043
Medium	2026 (15.72)	20 (11.36)	0.114
Low	4699 (36.47)	69 (39.20)	0.454
Very low	3067 (23.80)	23 (13.07)	0.001
Poverty			
Not poor	5431 (42.15)	45 (25.57)	0.001
Poor	5226 (40.56)	82 (46.59)	0.042
Extremely poor	2229 (17.30)	49 (27.84)	0.001

Data are given as mean ± SD or *n* (%). COPD, chronic obstructive pulmonary disease; HS, health service; SW, state worker.

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women who died, compared with those who did not die, had a significantly higher rate of very high and high social vulnerability and of poverty and extreme poverty, while the rate of very low social vulnerability was lower in those who died.

Risk factors for maternal death

Risk factors associated with maternal death due to COVID-19 are shown in Table 2. Maternal age, as either a continuous (aRR, 1.08 (95% CI, 1.05–1.10)) or categorical variable, was associated with maternal death; women aged 35–39 years (aRR, 3.16 (95% CI, 2.34–4.26)) or 40 years or older (aRR, 4.07 (95% CI, 2.65–6.25)) had a higher risk for mortality, as compared with those aged < 35 years. Other risk factors associated with maternal mortality were pre-existing diabetes, chronic hypertension and obesity. Chronic renal disease and asthma were not significant on multivariate analysis.

Women with very high social vulnerability had an 88% increased risk of death due to COVID-19 (aRR, 1.88 (95% CI, 1.26–2.80)). Women with high social

Table 2 Risk factors for COVID-19-related maternal death and severe disease among 13 062 SARS-CoV-2-positive pregnant women

	Maternal death (n = *176*)		*Severe pneumonia* (n = *1191*)		*ICU admission* (n = *322*)		*Intubation* (n = *185*)	
Risk factor	*aRR (95% CI)*	P	*aRR (95% CI)*	P	*aRR (95% CI)*	P	*aRR (95% CI)*	P
MA (in years)	1.08 (1.05–1.10)	< 0.001	1.03 (1.02–1.05)	< 0.001	1.02 (1.01–1.04)	0.005	1.06 (1.04–1.09)	< 0.0001
< 35 years	Reference	—	Reference	—	Reference	—	Reference	—
35–39 years	3.16 (2.34–4.26)	< 0.001	1.57 (1.39–1.77)	< 0.001	1.35 (1.07–1.69)	0.012	1.98 (1.49–2.65)	< 0.0001
≥ 40 years	4.07 (2.65–6.25)	< 0.001	1.79 (1.44–2.23)	< 0.001	1.17 (0.74–1.84)	0.505	2.26 (1.43–3.55)	< 0.0001
Pre-existing diabetes	2.66 (1.65–4.27)	< 0.001	1.35 (1.07–1.69)	0.011	1.08 (0.71–1.74)	0.707	0.71 (0.37–1.35)	0.297
Chronic hypertension	1.75 (1.02–3.00)	0.042	1.74 (1.39–2.17)	< 0.001	0.99 (0.62–1.58)	0.973	1.05 (0.58–1.91)	0.880
Obesity	2.15 (1.46–3.17)	< 0.0001	1.35 (1.14–1.59)	< 0.001	1.17 (0.85–1.61)	0.321	1.37 (0.92–2.04)	0.122
Chronic renal disease	1.59 (0.52–4.79)	0.414	1.86 (0.89–3.82)	0.699	0.57 (0.08–3.77)	0.556	1.15 (0.17–7.79)	0.785
Asthma	1.62 (0.74–3.55)	0.228	1.16 (0.82–1.62)	0.400	1.00 (0.52–1.94)	0.998	1.23 (0.56–2.71)	0.600
COPD	1	—	1	—	1	—	1	—
Immunosuppression	1.56 (0.39–6.12)	0.522	1.81 (1.15–2.84)	0.011	2.01 (1.03–3.94)	0.040	2.57 (1.13–5.84)	0.024
Cardiovascular disease	1.42 (0.21–9.83)	0.721	0.86 (0.33–2.19)	0.744	1.73 (0.49–6.13)	0.396	1.62 (0.26–9.94)	0.599
Smoker	0.93 (0.30–2.89)	0.905	0.94 (0.62–1.44)	0.791	1.08 (0.51–2.29)	0.842	1.21 (0.47–3.12)	0.684
Indigenous ethnicity	0.86 (0.35–2.10)	0.740	1.21 (0.91–1.62)	0.192	0.55 (0.25–1.22)	0.144	1.25 (0.59–2.63)	0.559
Using private health services	0.82 (0.30–2.20)	0.695	1.09 (0.78–1.52)	0.608	1.06 (0.62–1.83)	0.825	0.71 (0.30–1.69)	0.447
Using public health services (state worker)	0.82 (0.61–1.12)	0.218	1.04 (0.94–1.17)	0.431	0.78 (0.63–0.96)	0.021	0.91 (0.69–1.21)	0.525
Social vulnerability*								
Very high	1.88 (1.26–2.80)	0.002	3.00 (2.43–3.69)	< 0.001	1.29 (0.89–1.86)	0.165	1.16 (0.70–1.95)	0.342
High	1.49 (1.04–2.13)	0.028	2.62 (2.17–3.18)	< 0.001	0.85 (0.58–1.26)	0.440	1.11 (0.68–1.80)	0.673
Medium	0.76 (0.48–1.20)	0.237	1.03 (0.81–1.32)	0.753	0.92 (0.59–1.42)	0.729	0.98 (0.55–1.76)	0.188
Low	1.07 (0.79–1.45)	0.653	2.13 (1.79–2.54)	< 0.001	1.40 (1.05–1.86)	0.021	1.40 (0.95–2.07)	0.085
Very low	0.47 (0.30–0.73)	0.001	1	—	1	—	1	—
Poverty								
Not poor	Reference	—	Reference	—	Reference	—	Reference	—
Poor	1.53 (1.09–2.15)	0.014	1.66 (1.46–1.88)	< 0.0001	1.17 (0.93–1.47)	0.185	1.08 (0.79–1.47)	0.618
Extremely poor	1.83 (1.32–2.53)	< 0.0001	1.63 (1.44–1.84)	< 0.0001	0.92 (0.71–1.19)	0.511	1.01 (0.72–1.42)	0.939

Adjusted relative risk (aRR) values were calculated using log-binomial regression adjusted for the following confounders: maternal age (MA), pre-existing diabetes, obesity, hypertension, chronic renal disease, asthma and ethnicity. *Each social vulnerability category was treated as a dichotomous variable. COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.

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vulnerability also had a higher risk of death (aRR, 1.49 (95% CI, 1.04–2.13)), while women with very low social vulnerability had a 53% decreased risk (aRR, 0.47 (95% CI, 0.30–0.73)). Being poor (aRR, 1.53 (95% CI, 1.09–2.15)) or extremely poor (aRR, 1.83 (95% CI, 1.32–2.53)) were also significant risk factors for maternal death due to COVID-19.

Risk factors for severe pneumonia, intensive care unit admission and intubation

Risk factors associated with severe pneumonia, ICU admission and intubation are shown in Table 2. Maternal age, as either a continuous or categorical variable, pre-existing diabetes, chronic hypertension, immunosuppression and obesity were risk factors for severe pneumonia. Maternal age and immunosuppression were risk factors for ICU admission and intubation.

Women with very high, high or low social vulnerability had a higher risk of severe pneumonia (aRR, 3.00 (95% CI, 2.43–3.69), 2.62 (95% CI, 2.17–3.18) and 2.13 (95% CI, 1.79–2.54), respectively), which reflects that, overall, the risk of severe pneumonia remained stable across social vulnerability groups. Poor and extremely poor pregnant women had a higher risk for severe pneumonia (aRR, 1.66 (95% CI, 1.46–1.88) and 1.63 (95% CI, 1.44–1.84)). Women with low social vulnerability had a higher risk of ICU admission, while women using public health services had a lower risk of being admitted to the ICU. The relationship between socioeconomic determinants and comorbidities is shown in Table S1.

DISCUSSION

Main findings

The findings of this study in SARS-CoV-2-positive pregnant women demonstrated that: (i) advanced maternal age, pre-existing diabetes, chronic hypertension and obesity were associated with COVID-19-related maternal mortality; (ii) similar to maternal death, risk factors associated with severe pneumonia were advanced maternal age, pre-existing diabetes, chronic hypertension, immunosuppression and obesity; advanced maternal age and immunosuppression were also risk factors for ICU admission and intubation, while women using public health services had a lower risk of being admitted to the ICU; and (iii) women with high social vulnerability had an increased risk of maternal death and severe pneumonia, while very low social vulnerability was associated with a reduced risk of maternal death, but low social vulnerability was associated with higher risks of severe pneumonia and ICU admission. Similarly, being poor and extremely poor were significant risk factors for maternal death and severe pneumonia.

Comparison with existing literature

It has been demonstrated recently that pregnancy *per se* constitutes a risk factor for complications in women with SARS-CoV-2 infection during the reproductive period[16]. Our findings are in agreement with those of previous studies involving non-pregnant and pregnant individuals, in which advanced age, diabetes, chronic hypertension and obesity were found to be risk factors for severe COVID-19 and mortality[2,3,16]. Zambrano *et al.*[3] showed that Latin-American pregnant women living in the USA, who belong to a vulnerable minority group, are at a higher risk of COVID-19-related mortality; therefore, in this study, we explored the interplay between comorbidities and socioeconomic determinants contributing to severe COVID-19 and maternal mortality. Although the possible mechanisms leading to higher maternal mortality related to COVID-19 in developing countries are not clear, some investigators have demonstrated that low socioeconomic status is associated with a higher risk of severe maternal morbidity[17,18]. Previous studies have shown that minority women receive disproportionately delayed or inadequate prenatal care[19], and a systematic review identified strong evidence for the impact of race, ethnicity, insurance and education on maternal mortality and severe morbidity[20].

Measures of socioeconomic disadvantage, such as social vulnerability and poverty indices, are also associated with an increased risk of complications related to SARS-CoV-2 infection[21,22]. The significant association of low social vulnerability with a higher risk of ICU admission may be related to socioeconomic status and access to healthcare, since highly vulnerable women may not have access to adequate healthcare and, therefore, their probability of being admitted to the ICU is lower. On the other hand, women with low social vulnerability, who, by definition, have better access to healthcare, have a higher risk of ICU admission, accompanied by a lower risk of death. During the pandemic, this was observed in the health services; public hospitals were overcrowded, while ICU beds were readily available to people who were able to pay for care at a private hospital. Another explanation for the higher risk of intubation and ICU admission in women with low social vulnerability could be the higher incidence of chronic hypertension in this subgroup; on the other hand, despite the higher incidence of obesity in the very high vulnerability group, multivariate logistic regression analysis showed that high social vulnerability as well as obesity are independent predictors of maternal mortality. Our finding that lower socioeconomic status is associated with a higher incidence of SARS-CoV-2-related severe pneumonia and maternal death supports existing evidence that densely populated communities living in poverty have an increased risk of sustained community transmission of various infectious diseases, including SARS-CoV-2[23,24]. On the other hand, pregnant women with very low social vulnerability had a reduced risk of mortality due to COVID-19. Overall, our findings suggest a possible causal relationship of education, access to health services, basic infrastructure, quality of and space in housing and household assets with mortality in pregnant women with SARS-CoV-2 infection, which could explain why the rate of maternal mortality is higher in developing countries

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and in minority groups in developed countries who have limited access to health services.

In symptomatic pregnant women with COVID-19 in Mexico, the rate of maternal mortality is 1.5%[2]. A recent small cohort of 793 patients from Greece, Turkey, the UK and Austria showed a similar 1.3% incidence of death[25]. However, Zambrano *et al.*[3] described a 0.14% mortality rate in symptomatic pregnant women with SARS-CoV-2 infection in the USA, and Mullins *et al.*[26] found a 0.5% mortality rate in a UK registry and a 0.2% mortality rate in a USA registry, which differ substantially from the rate observed in this study. We speculate that the excess mortality is due to the factors explored in the current study, which are related to lower socioeconomic status, access to healthcare services, housing, education and household assets.

Strengths and limitations

This study reports results based on one of the largest consecutive cohorts of pregnant women with SARS-CoV-2 infection and is the first to demonstrate that comorbidities, including pre-existing diabetes, chronic hypertension, obesity and social determinants, such as poverty and social vulnerability indices, are significant risk factors for COVID-19-related mortality and morbidity during pregnancy. The advantage of a population-based cohort is that it minimizes bias by allowing calculation of real-population estimates in an unselected population. Cohort studies with low numbers or an overselected population tend to overestimate effect size. Our large dataset, including 176 maternal deaths, allowed us to estimate the effect size of each risk factor with a robust CI, thus reducing bias. No other single consecutive cohort of pregnant women with COVID-19 has included such a large number of maternal deaths with sufficient data to calculate robust effect sizes. Another strength of this study is the prospective acquisition of data across the whole country, allowing representative data from a desired population, which is often a limitation of hospital-based cohorts.

A limitation of this study is the amount of missing data on severe pneumonia and ICU admission, which is compensated for by the large number of included participants, allowing us to calculate robust effect sizes for these outcomes. Another limitation is the lack of data on perinatal outcome, such as fetal growth restriction, pre-eclampsia, preterm birth, stillbirth and neonatal death, due to the population-based origin of the information used for the analysis. However, the data included in this study provide sufficient information to allow us to understand the most important risk factors and social determinants associated with the main outcomes related to COVID-19, which are death, severe pneumonia, intubation and ICU admission.

Clinical implications

COVID-19 is now the leading cause of maternal mortality in Mexico[1], and, in most countries, the groups of pregnant women at highest risk of severe complications related to COVID-19 have not been characterized. Furthermore, vaccination against SARS-CoV-2 infection has not been prioritized for pregnant women in most countries, particularly in developing countries, in which the increasing maternal mortality rate related to COVID-19 is alarming. To worsen the situation, there is unequal distribution of the available vaccines, which makes it even more difficult for pregnant women to get vaccinated in a timely manner. The results from this study could help guide decision-making regarding who should be prioritized for vaccination based on their high-risk status, especially in countries in which vaccines are not readily available and resources are scarce. For example, considering the maternal mortality rate of 1.35% in our population and taking into account 90–100% efficacy of the vaccine against severe COVID-19 for normal SARS-CoV-2 variants and 96% efficacy for the Delta variant, we would need to vaccinate 74 pregnant women to avoid one death in a 100% effectiveness scenario for normal variants, 81 in a 90% effectiveness scenario for normal variants and 77 in a scenario of 96% effectiveness against the Delta variant. There is a critical need to identify high-risk pregnant women who should observe mask-wearing, social distancing and good hand hygiene and ideally get vaccinated in order to reduce the risk of acquiring SARS-CoV-2 infection, as well as raise awareness of the possibility of severe COVID-19 so that asymptomatic SARS-CoV-2-infected women or those with mild disease are monitored for clinical deterioration; if they are symptomatic, there should be more proactive management to reduce the risk of deterioration.

Conclusions

The findings of this study, which is one of the largest prospective consecutive cohorts of SARS-CoV-2-positive pregnant women to date, have confirmed that advanced maternal age, pre-existing diabetes, chronic hypertension, obesity, high social vulnerability and low socioeconomic status are risk factors for COVID-19-related maternal mortality. Pregnant women at risk of serious complications of COVID-19 should be identified and prioritized for vaccination and early healthcare, especially in low-resource settings.

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SUPPORTING INFORMATION ON THE INTERNET

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Table S1 Relationship between socioeconomic determinants and comorbidities in 13 062 SARS-CoV-2-positive pregnant women

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Ultrasound Obstet Gynecol 2022; **59**: 76–82
Published online 17 December 2021 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.24797

Enfermedades concomitantes, pobreza y vulnerabilidad social como factores de riesgo de mortalidad en mujeres embarazadas con infección confirmada por SRAS-CoV-2: un análisis de 13.062 embarazos de madres positivas en México, de las cuales 176 murieron

RESUMEN

Objetivo. La mortalidad en el embarazo debida a la enfermedad por coronavirus 2019 (COVID-19) es una prioridad sanitaria actual en los países en desarrollo. La identificación de los factores de riesgo clínicos y sociodemográficos relacionados con la mortalidad en mujeres embarazadas con COVID-19 podría informar las políticas públicas y animar a estas mujeres a aceptar la vacunación. El objetivo fue evaluar la asociación de enfermedades concomitantes y de determinantes socioeconómicos con la mortalidad relacionada con COVID-19 y las enfermedades graves en mujeres embarazadas en México.

Métodos. Se trata de un estudio de cohorte prospectivo a nivel nacional que incluyó a todas las mujeres embarazadas con un resultado positivo de la reacción en cadena de la polimerasa con transcriptasa inversa para el coronavirus 2 del síndrome respiratorio agudo severo (SRAS-CoV-2) del Registro Nacional de Coronavirus de México. El resultado primario fue la muerte materna por COVID-19. Se estudió la asociación de las enfermedades concomitantes y las características socioeconómicas con la muerte materna mediante un modelo de regresión log-binomial ajustado para posibles factores de confusión.

Resultados. Se produjeron 176 (1,35%) muertes maternas por COVID-19 en una cohorte consecutiva de 13.062 mujeres embarazadas con SRAS-CoV-2. La edad materna, como variable continua (riesgo relativo ajustado [RRa], 1,08 [IC 95%, 1,05–1,10]) o categórica, se asoció con la muerte materna debida a COVID-19; las mujeres de 35–39 años (RRa, 3,16 [IC 95%, 2,34–4,26]) o de 40 años o más (RRa, 4,07 [IC 95%, 2,65–6,25]) tuvieron un mayor riesgo de mortalidad, en comparación con las de edad <35 años. Otros factores de riesgo clínicos asociados a la mortalidad materna fueron la diabetes preexistente (RRa, 2,66 (IC 95%, 1,65–4,27)), la hipertensión crónica (RRa, 1,75 (IC 95%, 1,02–3,00)) y la obesidad (RRa, 2,15 (IC 95%, 1,46–3,17)). La vulnerabilidad social muy alta (RRa, 1,88 (IC 95%, 1,26–2,80)) y la vulnerabilidad social alta (RRa, 1,49 (IC 95%, 1,04–2,13)) se asociaron con un mayor riesgo de mortalidad materna, mientras que la vulnerabilidad social muy baja se asoció con un riesgo reducido (RRa, 0,47 (IC 95%, 0,30–0,73)). Ser pobre o extremadamente pobre fueron también factores de riesgo de mortalidad materna (RRa, 1,53 (IC 95%, 1,09–2,15) y RRa, 1,83 (IC 95%, 1,32–2,53), respectivamente).

Conclusión. Este estudio, que abarca la mayor cohorte prospectiva consecutiva de mujeres embarazadas con COVID-19 hasta la fecha, ha confirmado que la edad materna avanzada, la diabetes preexistente, la hipertensión crónica, la obesidad, la alta vulnerabilidad social y el bajo nivel socioeconómico son factores de riesgo de mortalidad materna relacionada con COVID-19.

并存病、贫困和社会脆弱性作为确诊感染 SARS-CoV-2 的孕妇死亡率的风险因素：对墨西哥 13062 名阳性妊娠（含 176 名孕产妇死亡）的分析

摘要

目的由于新型冠状病毒（Covid-19）引起的妊娠期死亡率是发展中国家目前的一个健康优先考虑事项。识别感染 COVID-19 孕妇死亡率相关的临床与社会人口风险因素，将会引导公共政策并鼓励孕妇接受疫苗的接种。我们旨在评估并存病和社会经济影响因素与墨西哥的 COVID-19 相关孕妇死亡率和重症的关联。

方法这是一项仍在进行中的全国性前瞻性群组研究，包含墨西哥国家新冠登记册中严重急性呼吸综合征冠状病毒 2（SARSSARS-CoV-2）逆转录定量聚合酶链反应结果为阳性的所有孕妇。主要结局是因 Covid-19 造成的孕产妇死亡。采用一个根据可能干扰因子调整后的 log-binomial 回归模型来探索并存病和社会经济特征与孕产妇死亡的关联。

结果在 13062 名 SARS-CoV-2 连续阳性的孕妇中，有因 COVID-19 造成 176 名孕产妇死亡（占 1.35%）。作为一个持续变量（调整后的相对风险（aRR），1.08（95%CI，1.05 – 1.10））或分类变量，孕妇年龄与因 COVID-19 造成的孕产妇死亡相关；与年龄小于 35 岁的孕妇相比，年龄在 35-39 岁之间（aRR，3.16（95% CI，2.34 – 4.26））或在 40 或 40 岁以上的孕妇（aRR, 4.07（95% CI，2.65 – 6.25））死亡率更高。与产妇死亡率相关的其他临床风险因素有预先存在的糖尿病（aRR，2.66（95% CI，1.65 – 4.27））、慢性高血压（aRR，1.75（95% CI，1.02 – 3.00））和肥胖症（aRR，2.15（95% CI，1.46 – 3.17））。非常高的社会脆弱性（aRR，1.88（95% CI，1.26 – 2.80））和高社会脆弱性（aRR，1.49（95% CI，1.04 – 2.13））与产妇死亡率增加性风险相关，而非常低的社会脆弱性（aRR，0.47（95% CI，0.30 – 0.73））与风险降低相关。贫困或极其贫困也是产妇死亡率的风险因素（分别为 aRR，1.53（95% CI，1.09 – 2.15）和 aRR，1.83（95% CI，1.32 – 2.53）。

结论本研究包含目前为止感染 COVID-19 孕妇的最大前瞻性、连续性群组，确定了孕妇高龄、预先存在糖尿病、慢性高血压、肥胖症、高社会脆弱性和低社会经济地位，都是与 COVID-19 相关的产妇死亡率的风险因素。

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