ORIGINAL RESEARCH

Epidemiology of severe maternal morbidity and maternal mortality among pregnant women with COVID-19 in the department of Caldas, Colombia

Comportamiento epidemiológico de la morbilidad materna extrema y la mortalidad materna en gestantes con COVID-19 del departamento de Caldas, Colombia

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Abstract

Introduction: Given the serious implications of severe COVID-19 in pregnant women, more strict epidemiological surveillance of severe maternal morbidity (SMM) and maternal mortality in the context of COVID-19 is required.
Objective: To determine the epidemiology of SMM and maternal mortality among pregnant women with COVID-19 in the department of Caldas (Colombia) between 2019 and 2021.
Materials and methods: Observational, descriptive, and retrospective study. Data analysis was conducted using records from the notification forms for COVID-19, SMM, and maternal mortality events. Cases of pregnant women with COVID-19 and cases of SMM and maternal mortality reported in Caldas between 2020 and 2021 and between 2019 and 2021, respectively, were included. Maternal health indicators were calculated, including SMM ratio, maternal mortality ratio, case fatality rate, and the relationship between SMM and maternal mortality cases.
Results: Data from 102 cases of pregnant women with COVID-19 were analyzed, finding that 90.90% had a low socioeconomic status and 81.81% were under 30 years of age. Between 2020 and 2021, there were 4 cases of SMM due to severe preeclampsia in pregnant women with COVID-19 and 20 cases of maternal mortality, including 4 indirect deaths due to COVID-19. An increase was observed between 2019 and 2021 in SMM ratio (34.45 vs. 93.85 per 1 000 live births), maternal mortality ratio (38.57 vs. 176.82 per 100 000 live births), and case fatality rate (1.10% vs. 1.84%).
Conclusion: The behavior of the SMM ratio and the maternal mortality ratio in Caldas during the study period showed an increasing trend compared to 2019, and these indicator values were higher than those reported for the country. The case fatality rate reflected an increase of almost 2 maternal deaths per 100 cases of SMM in 2021.

Resumen

Introducción. Dadas las implicaciones de la COVID-19 grave en las gestantes, se requiere una vigilancia epidemiológica más estricta de la morbilidad materna extrema (MME) y la mortalidad materna en el contexto de la COVID-19.
Objetivo. Determinar el comportamiento epidemiológico de la MME y la mortalidad materna en gestantes con COVID-19 del departamento de Caldas (Colombia) entre 2019 y 2021.
Materiales y métodos. Estudio observacional, descriptivo, retrospectivo. Se realizó un análisis de datos obtenidos de las fichas de notificación de los eventos COVID-19, MME y mortalidad materna. Se incluyeron los casos de gestantes con COVID-19 y los casos de MME y mortalidad materna notificados en Caldas entre 2020 y 2021 y entre 2019 y 2021, respectivamente. Se calcularon los indicadores de salud materna: razón de MME, razón de mortalidad materna, índice de letalidad y relación entre casos de MME y de mortalidad materna.
Resultados. Se analizaron los datos de 102 casos de gestantes con COVID-19, de las cuales 90.90% eran de nivel socioeconómico bajo y 81.81% tenían menos de 30 años de edad. Entre 2020 y 2021 hubo 4 casos de MME por preeclampsia severa en las gestantes con COVID-19 y 20 casos de mortalidad materna, de los cuales 4 fueron muertes indirectas por COVID-19. Se observó un aumento de la razón de MME entre 2019 y 2021 (34.45 vs. 93.85 x 1 000 nacidos vivos), la razón de mortalidad materna (38.57 vs. 176.82 x 100 000 nacidos vivos) y el índice de letalidad (1.10% vs. 1.84%).
Conclusión. El comportamiento de la razón de MME y la razón de mortalidad materna en Caldas durante el periodo de estudio mostró una tendencia al aumento en comparación con 2019; además, los valores de estos indicadores fueron superiores a los reportados para el país. El índice de letalidad reflejó un aumento de hasta casi 2 muertes maternas por cada 100 casos de MME para 2021.

Introduction

Due to the serious health and economic consequences associated with COVID-19 world-wide, the disease was declared a pandemic by the World Health Organization in March 2020.[1] In Colombia, the first confirmed case of COVID-19 was reported on March 6, 2020, and 6 days later, by means of Resolution 385, the Ministry of Health and Social Protection[2] declared a health emergency nationwide.

The health crisis caused by the pandemic put different population groups, including pregnant women, at greater risk. Hernández *et al.*[3] demonstrated that although the clinical manifestations of SARS-CoV-2 infection in pregnant women, as in the general population, range from asymptomatic disease to severe disease requiring admission to an intensive care unit (ICU), there are differences associated with pregnancy and its physiological characteristics that should be considered when providing medical care to this specific population group.

While it has been reported that pregnant women do not seem to be more susceptible to contracting COVID-19,[4] they do have an increased risk of severe COVID-19 and, therefore, an increased risk of requiring admission to the ICU and invasive mechanical ventilation, as well as increased mortality compared to non-pregnant women.[5] Likewise, SARS-CoV-2 infection is associated with an increased risk of pregnancy-specific complications, such as preeclampsia, preterm delivery, and fetal death.[6]

Despite the fact that pregnancy induces changes in the immune system, COVID-19 in this population is usually mild[5] and asymptomatic in 13.5-60% of cases.[3] On the other hand, it has been reported that about 20% of pregnant women infected with SARS-CoV-2 develop severe COVID-19, and that risk factors include advanced maternal age, acquiring the infection in the third trimester of pregnancy, and having comorbidities such as chronic cardiopulmonary diseases, obesity, and diabetes mellitus.[7] It should be noted that severe COVID-19 may occur in any trimester of pregnancy, but it has been reported to occur more frequently in the third trimester, and that COVID-19 pneumonia is the most frequent indirect cause of maternal mortality in these patients.[3]

As mentioned above, the impact of COVID-19 in pregnant women varies depending on the risk factors of each patient. In this regard, the situation in Brazil at the beginning of the pandemic attracted worldwide attention due to the high number of maternal deaths, since 124 (12.7%) of the 978 pregnant and puerperal women diagnosed with COVID-19 as of June 18, 2020, had died. This led to a significant increase in maternal mortality rates, which were already high before the pandemic.[8]

In Colombia, severe maternal morbidity (SMM)[9] and maternal mortality[10] events are of public health interest and must be reported to the *Sistema de Vigilancia en Salud Pública* (National Public Health Surveillance System or SIVIGILA by its Spanish acronym). In 2020, 24 451 cases of SMM were reported to SIVIGILA, with an SMM ratio of 39.3 cases per 1 000 live births,[11] which was higher than the one reported in 2019 (37.1 cases per 1 000 live births).[12] Moreover, according to figures from the *Instituto Nacional de Salud* (National Institute of Health or INS by its Spanish initials),[11] the preliminary SMM ratio for 2021 was 48.4 cases per 1 000 live births, and the department of Caldas was one of the territorial entities with the highest SMM ratios.

Concerning maternal mortality in Colombia, this event showed a decreasing trend between 2009 and 2019.[13] However, with the onset of the COVID-19 pandemic, this trend reversed: the INS reported 299 cases in 2019, with a maternal mortality ratio of 46.8 cases per 100 000 live births nationwide, while 403 and 456 cases were reported in 2020 and 2021, respectively (maternal mortality ratios of 65.1 and 81.4 cases per 100 000 live births).[14]

In view of this situation, there was a need for a specific analysis of SMM events and maternal mortality in relation to COVID-19 in pregnant women. Accordingly, the objective of the present study is to determine the epidemiology of SMM and maternal mortality among pregnant women with COVID-19 in the department of Caldas between 2019 and 2021.

Materials and methods

Study type

Observational, retrospective, descriptive study.

Data used

Data were obtained from a review of the SIVIGILA notification forms for SMM (code 549), maternal mortality (code 551), and COVID-19 (code 346) events reported between 2020 and 2021, 2019 and 2021, and 2020 and 2021, respectively. Maternal mortality was analyzed using the year 2019 as a point of comparison prior to the pandemic to assess the behavior of this outcome.

Cases were selected according to the following inclusion criteria based on the INS definitions of the events:

- SMM case reported during the study period by any municipality of Caldas to SIVIGILA.
- Maternal mortality case reported during the study period by any municipality of Caldas to SIVIGILA.
- COVID-19 case in pregnant women reported during the study period by any municipality of Caldas to SIVIGILA.
- Maternal mortality case that was also reported in the *Registro Único de Afiliados* (Single Registry of Beneficiaries or RUAF by its Spanish acronym) (death certificate).

Taking into account the aforementioned, 102 cases of pregnant women with COVID-19 were included.

Procedures and variables

Once the research protocol was approved by the *Dirección Territorial de Salud de Caldas* (Caldas Territorial Health Department or DTSC by its Spanish initials), the databases of the notification forms for each event were reviewed and the quality of the data was verified and cleaned in order to eliminate duplicate records. Data were sorted in ascending order by date of event notification.

Based on the notification forms review, information on the following variables was collected for each case of pregnant women with COVID-19: age at infection acquisition, gestational age at infection acquisition, trimester of gestation at infection acquisition, nationality, municipality of notification, date of notification, source of notification (routine notification, institutional active search, intensive surveillance, active community search, research), classification of the COVID-19 case as defined by the INS protocol, area of incidence (municipal seat, population center, rural area), health system coverage, socio-economic status, occupation, hospital treatment requirements (COVID-19), and mortality

due to COVID-19. Furthermore, to characterize the pregnant women for whom maternal mortality was reported, data were also collected on: place of origin, main cause of death (in accordance with the code of the tenth edition of the International Classification of Diseases [ICD-10] registered), type of death (direct, indirect, external, or not established), gestational age at the beginning of prenatal checkups, and number of prenatal checkups.

COVID-19 cases were classified as per the INS protocol definitions[15] as follows:

Suspected case of COVID-19: A) patient with acute respiratory disease (fever and at least one sign/symptom of respiratory disease such as cough or respiratory distress) and history of travel to a location where community transmission of COVID-19 was reported within 4 days prior to symptom onset, or living in an area with such characteristics; B) patient with acute respiratory disease who had contact with a confirmed or probable case of COVID-19 within 14 days prior to symptom onset; C) patient with acute respiratory disease (requiring inpatient care) with no alternative diagnosis that fully explains the clinical manifestations.

Probable case of COVID-19: A) suspected case in whom the COVID-19 test is inconclusive; B) suspected case in whom the test has not been performed for some reason.

Confirmed case of COVID-19: person with a laboratory test confirmation for SARS-CoV-2 infection, regardless of clinical signs and symptoms.

It is worth pointing out that socioeconomic status in Colombia is divided into 6 strata depending on the people's place of residence and access to basic services (strata 1 and 2 refer to people with low income, strata 3 and 4 to people with medium income, and strata 5 and 6 to people with high income).[16] Health insurance coverage varies according to the insurance scheme, which may be contributory, subsidized, special or exceptional, depending, among other factors, on the capacity to pay and the solidarity component of the system; therefore, most of the people with the lowest socioeconomic status are covered by the subsidized scheme.[17,18]

To analyze the direct and indirect causes of SMM and maternal mortality, the ICD-10 codes of the basic cause of death were considered.

Data analysis

Data are described using absolute frequencies and percentages for qualitative variables and means and standard deviations for quantitative variables. The distribution of the data was normal (Kolmogorov-Smirnov test).

Based on the comparison of the case databases, the pregnant women with COVID-19 who presented SMM and maternal mortality were identified. To calculate maternal health indicators, the technical data sheets of the indicators of each INS protocol were used:[9,10]

SMM ratio

Numerator: number of SMM cases over a time period.
Denominator: number of live births in the same time period.
Time period: 2019-2020-2021
Multiplication coefficient: x 1 000

Maternal mortality ratio

Numerator: number of maternal mortality cases over a time period.
Denominator: number of live births in the same time period.
Time period: 2019-2020-2021
Multiplication coefficient: x 100 000

Relationship between SMM cases and maternal mortality

Numerator: number of SMM cases over a time period.
Numerator: number of maternal mortality cases over a time period.
Time period: 2019-2020-2021.

Case fatality rate

Numerator: number of maternal mortality cases over a time period.
Denominator: number of maternal mortality cases + number of SMM cases in the same time period.
Time period: 2019-2020-2021
Multiplication coefficient: x 100

The case fatality rate reflects the percentage of maternal deaths per 100 cases of SMM. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25 for Windows.

Ethical considerations

The study followed the ethical principles for biomedical research involving human subjects established in the Declaration of Helsinki,[19] as well as the scientific, technical and administrative standards for health research contained in Resolution 8430 of 1993 of the Colombian Ministry of Health.[20] Also, it was approved by the Bioethics Committee of the Faculty of Health Sciences (Minutes 005 of 2022 dated April 19, 2022) and by the Research Ethics and Bioethics Committee of the DTSC (official letter CEBI-2022-3-1 dated June 6, 2022).

Results

Out of the 102 COVID-19 cases in pregnant women reported by the department of Caldas in the study period, 88 were reported in 2020 and 14 in 2021; SMM was reported in 4 of such cases. Between 2020 and 2021, there were 20 maternal mortality events, of which 4 were indirect deaths due to COVID-19.

Sociodemographic characteristics

The mean age of the cases reported in 2020 was 23.83 years (SD=6.47; minimum age: 15 years, maximum age: 45 years) and for the cases reported in 2021 it was 27.07 years (SD=6.15; minimum age: 19 years, maximum age: 39 years). In 2020, by age group, most cases occurred in the 20-24 years age group (32.95%), while the majority of cases in 2021 occurred in the 25-29 years age group (35.71%). Table 1 lists the sociodemographic characteristics of the pregnant women with COVID-19 included in the study.

Table 1. Sociodemographic characteristics of cases of pregnant women with COVID-19 treated in Caldas (Colombia) between 2020 and 2021.

Variable	Categories	2020 n=88		2021 n=14	
		Frequency	%	Frequency	%
Nationality	Colombian	87	98.86	13	92.90
	Venezuelan	1	1.14	1	7.10
Place of origin	Municipal seat	72	81.82	12	85.71
	Scattered rural settlement	16	18.18	1	7.14
	Population center	0	0	1	7.14
Age (years)	15-19	27	30.68	1	7.14
	20-24	29	32.95	4	28.57
	25-29	16	18.18	5	35.71
	30-34	8	9.09	2	14.29
	35-39	5	5.68	2	14.29
	40-44	2	2.27	0	0
	45-49	1	1.13	0	0
Health insurance scheme	Subsidized	80	90.91	2	14.29
	Contributive	5	5.68	8	57.14
	Special/exception	1	1.14	0	0
	Not insured	0	0	3	21.43
	No data	2	2.27	1	7.14
Socioeconomic status	Low	80	90.91	7	50.00
	Medium	1	1.14	7	50.00
	High	1	1.14	0	0
	No data	6	6.84	0	0
Occupation	Housewife	80	90.91	6	42.84
	Student	6	6.84	1	7.14
	Factory/company employee	1	1.14	5	35.70
	Health personnel	0	0	1	7.14
	No data	1	1.14	1	7.14

By reporting municipality, it was found that in 2020 most cases of pregnant women with COVID-19 were reported in La Dorada (92.04%), followed by Manizales (3.40%), while in 2021 most were reported in Manizales (64.29%), followed by Supía (21.43%) (Table 2).

Table 2. Distribution by municipality reporting cases of pregnant women with COVID-19 treated in the department of Caldas (Colombia) between 2020 and 2021.

Municipio	2020 n=88		2021 n=14	
	Frequency	%	Frequency	%
Manizales	3	3.40	9	64.28
Anserma	1	1.14	0	0
Chinchiná	1	1.14	0	0
La Dorada	81	92.04	1	7.14
Palestina	1	1.14	0	0
Villamaría	1	1.14	0	0
Filadelfia	0	0	1	7.14
Supía	0	0	3	21.43
Total	88	100	14	100

Epidemiological characteristics

In both 2020 and 2021, most cases were routinely notified (2020: 97.7%; 2021: 78.6%). On the other hand, while the majority of notifications (93.2%) were classified as probable cases in 2020, in 2021 the majority (85.7%) were laboratory-confirmed cases. Finally, only 4 pregnant women required hospital care for COVID-19 and none died as a direct result of the disease (Table 3).

Table 3. Epidemiological characteristics of pregnant women with COVID-19 treated in Caldas (Colombia) between 2020 and 2021.

Variable	Category	2020		2021	
		Frequency	%	Frequency	%
Notification source	Routine notification	86	97.72	11	78.57
	Active institutional search	1	1.14	3	21.43
	Intensified surveillance	0	0	0	0
	Active community search	0	0	0	0
	Research	1	1.14	0	0
COVID-19 case classification	Suspect	0	0	0	0
	Probable	82	93.19	2	14.29
	Laboratory confirmed	6	6.81	12	85.71
Inpatient care	Yes	2	2.28	2	14.29
	No	86	97.72	12	85.71
Final status	Alive	88	100	14	100
	Dead	0	0	0	0

Regarding the monthly behavior of cases of pregnant women with COVID-19, it was observed that the highest number of cases in 2020 occurred in June (n=60), whilst the highest number of cases in 2021 occurred in April (n=3) (Figure 1).
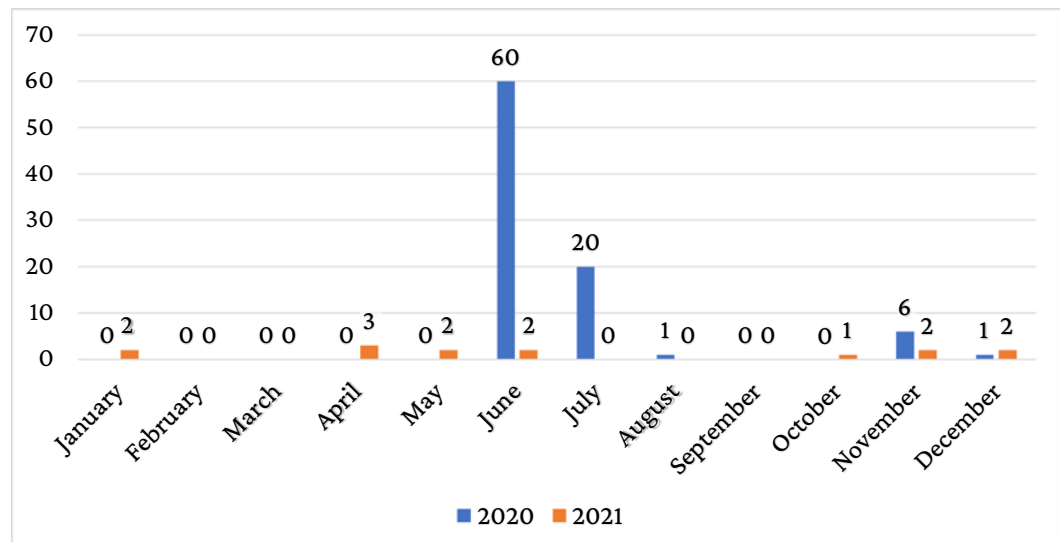

Figure 1. Number of cases of pregnant women with COVID-19 reported per month in Caldas (Colombia) in 2020 and 2021.

Regarding gestational age at the time of COVID-19 diagnosis, the following was found: the mean in 2020 was 20.8 weeks (SD=9.5); the median was 21 weeks; the mode was 20.86 weeks; and the gestational age in quartile 3 was 28 weeks. In 2021, the mean was 23 weeks (SD=10.70); the median was 22.5 weeks; the mode was 24 weeks; and the gestational age in quartile 3 was 33.5 weeks. Moreover, when grouped by pregnancy trimester, it was found that the highest number of COVID-19 cases occurred in pregnant women in the second trimester in both years (Table 4).

Table 4. Distribution of cases of pregnant women with COVID-19 treated in the department of Caldas (Colombia) in 2020 and 2021 by pregnancy trimester.

Pregnancy trimester	2020		2021	
	Frequency	%	Frequency	%
1 (1-12 weeks)	21	23.86	3	21.43
2 (13-26 weeks)	40	45.46	6	42.86
3 (27-42 weeks)	27	30.68	5	35.71
Total	88	100	14	100

SMM in pregnant women with COVID-19

Four cases of SMM were reported in the pregnant women with COVID-19 included in the study, with severe preeclampsia being the main cause (Table 5).

Table 5. Main characteristics of the cases of pregnant women with COVID-19 treated in the department of Caldas (Colombia) in 2020 and 2021 and in whom severe maternal morbidity was reported.

Characteristics	Case 1	Case 2	Case 3	Case 4
Year	2020	2020	2020	2021
Municipality of residence	La Dorada	La Dorada	La Dorada	Manizales
Age (years)	15	23	27	27
Area of incidence	Scattered rural	Municipal seat	Municipal seat	Municipal seat
Occupation	Student	Housewife	Housewife	Secretary
Insurance scheme	Subsidized	Subsidized	Subsidized	Contributive
Number of prenatal checkups	6	6	3	7
Beginning of checkups (weeks of gestation)	12	20	13	10
Primary cause (ICD-10)	Severe preeclampsia	Severe preeclampsia	Severe preeclampsia	Severe preeclampsia
Inclusion criteria for case definition of severe maternal morbidity *	Disease-related (1) severe pre-eclampsia †	Disease-related (2) blood clotting and severe pre-eclampsia †	Related to organ dysfunction and respiratory disease (4), severe preeclampsia, sepsis, and obstetric hemorrhage †	Disease-related (1) eclampsia †

* A case of severe maternal morbidity was defined as the occurrence of a severe complication during pregnancy, delivery, or within 42 days of pregnancy termination that did not result in death but put the pregnant woman's life at risk and meets at least 1 of the following criteria: related to organ dysfunction (cardiovascular, renal, hepatic, cerebral, respiratory, and/or coagulation/hematologic failure); disease-related (eclampsia, severe pre-eclampsia, sepsis, or severe systemic infection, severe obstetric hemorrhage and/or uterine rupture); treatment-related (need for emergency surgical procedure).[9]
† The number in parentheses represents the number of inclusion criteria met by the case.

Maternal mortality in the context of the COVID-19 pandemic

Regarding maternal mortality, taking 2019 (before the pandemic) as a comparison point, there was an increase in the number of cases in Caldas, going from 3 deaths in 2019 to 7 in 2020 and 13 in 2021. Of the total maternal deaths in the study period (2019-2021), 60.86% (n=14) were indirect, of which 28.57% (n=4) were caused by COVID-19. All cases of maternal mortality due to COVID-19 (indirect cause) occurred in women of low socioeconomic status (Table 6).

Table 6. Main characteristics of maternal mortality cases in Caldas between 2019 and 2021 (n=23).

Year	Total cases	Municipality	ICD-10 diagnosis code	Type
2019	3	Manizales	1. Intentional self-harm by hanging, strangulation, and suffocation	External
		Victoria	2. Intracardiac thrombosis, not elsewhere classified	Indirect
		Villamaría	3. Cardiac arrhythmia, unspecified	Indirect
2020	7	Riosucio	1. Other immediate postpartum hemorrhage (atonic)	Direct
		Manizales	2. Neoplasm of uncertain or unknown behavior, unspecified	Indirect
		Chinchiná	3. Choriocarcinoma NOS	Direct
		Manizales	4. Unspecified asthma	Indirect
		San José	5. Obstetric hypovolemic shock	Direct
		Manizales	**6. COVID-19, virus identified**	Indirect
		Manizales	7. Sequelae of transport accidents	External
2021	13	Aranzazu	1. Allergic shock (anaphylactic)	Indirect
		La Dorada	**2. COVID-19, virus identified**	Indirect
		Belalcázar	3. Acute lymphoblastic leukemia	Indirect
		Villamaría	**4. COVID-19, virus identified**	Indirect
		La Dorada	**5. COVID-19, virus identified**	Indirect
		Aranzazu	6. Shock	Not specified
		Aguadas	7. Placental disorder, unspecified	Direct
		Belalcázar	8. Malignant neoplasm of cecum	Indirect
		Pácora	9. Other specified carcinomas of liver	Indirect
		Villamaría	10. Malignant neoplasm: colon, unspecified.	Indirect
		Aranzazu	11. Peritonitis	Not specified
		Belalcázar	12. Other hereditary and idiopathic neuropathies	Indirect
		Villamaría	13. Leiomyoma of uterus	Direct

Finally, all the maternal health indicators considered showed an upward trend during the study period (Table 7).

Table 7. Indicators of severe maternal morbidity and maternal mortality in Caldas (Colombia). 2019-2021.

Year	SMM ratio (x 1 000)	Maternal mortality ratio (x 100 000)	Relationship between SMM cases and maternal mortality	Case fatality rate (%)
2019	34.45	38.57	89.33	1.10
2020	73.07	92.99	78.57	1.25
2021	93.85	176.82	53.07	1.84

SMM: severe maternal morbidity.

Discussion

The first COVID-19 case reported in Caldas was confirmed on March 15, 2020, and the first death from this disease was notified on April 1 of the same year. As of December 31, 2020, there were 32 204 confirmed cases of COVID-19 and 633 deaths in this department.[21]

At the beginning of the pandemic, the Colombian Ministry of Health and Social Protection[22] published guidelines for the care of pregnant women in the context of the COIVD-19 pandemic in the country, since this population is considered one of the important groups to address due to the presence of physiological and adaptive conditions that differentiate them from the general population and that can lead to diagnostic and therapeutic errors.

In this regard, Lira-Lucio *et al.*,[23] in a study conducted in 2020 in Mexico with data from 84 pregnant women with SARS-CoV-2 infection and 2 836 women of reproductive age with this infection, found that pregnant women are more susceptible to infection by respiratory pathogens given the adaptive changes of pregnancy, such as elevation of the diaphragm, increased oxygen consumption, airway mucosal edema, and low tolerance to compensatory mechanisms of hypoxia, and are therefore more vulnerable to developing COVID-19.

Similarly, in a study of 2 130 pregnant women (706 with COVID-19 and 1 424 without COVID-19) from 18 countries to assess the risks associated with COVID-19 during pregnancy and maternal and neonatal outcomes, Villar *et al.*[24] found that a COVID-19 diagnosis was associated with an increase in severe maternal morbidity and maternal mortality, as well as an increase in neonatal complications.

In the present study, 102 cases of pregnant women with COVID-19 reported in Caldas in 2020 (n=88) and 2021 (n=14) were analyzed, which were characterized by being mainly young women (with a mean age of 24 years in 2020 and 27 years in 2021). Additionally, only 1 case was found in the 45-49 age group in 2020 and 2 cases in the 35-39 age group in 2021. Care was mainly provided on an outpatient basis (96.08%, n=98), which shows that most of the patients did not have severe symptoms that required in-hospital or ICU admission. This is consistent with what has been described in the literature, as advanced maternal age is reported to be a factor associated with severe COVID-19.[3,6]

A noteworthy finding in the present study is the relatively high proportion of adolescent pregnant women (27.45%), which differs from other studies conducted in the region. For example, Guevara-Ríos *et al.*[25] conducted a study in Peru in 2 419 pregnant women admitted between April 15 and May 15, 2020, to a tertiary care maternal institute, where only 6.5% (n=170) of the patients with positive results in the anti-SARS-CoV-2 serologic test were adolescents.

The pregnancy trimester in which the infection is contracted is also important, as severe forms of COVID-19 have been reported to occur more frequently in the third trimester.[7] In the present study, most cases in both 2020 and 2021 occurred in the second trimester (2020: 45.45%; 2021: 42.85%); however, when analyzing gestational age at the time of infection, we found that infection occurred at a later gestational age in 2021 than

in 2020 (75% of pregnant women were less than 33.5 weeks in 2021 and 75% were less than 28 weeks in 2020). Despite this, in 2021 there were fewer cases of pregnant women with COVID-19 and only 2 cases required hospital care.

This research showed that the number of COVID-19 cases in pregnant women (n=14) was lower in 2021 compared to 2020 (n=88). This decline may be attributed to the advancements made in the National Vaccination Plan against COVID-19, which initiated in February 2021 and consisted of 3 stages, with pregnant women being prioritized in the first stage alongside the elderly and healthcare workers.[26]

The relatively low number of COVID-19 deaths found in the present study (n=4) can be associated with the behavior of COVID-19 mortality in the general population in the department of Caldas, where, as of October 15, 2021, a higher frequency of COVID-19 deaths was reported in men (66.7%; n=2).[27]

The diagnosis and treatment of SMM during the pandemic was more complex because, among other reasons, clinical manifestations similar to HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome, such as elevated transaminases and thrombocytopenia, were observed in patients with COVID-19.[22] In our study, severe preeclampsia was the main cause of SMM in the four cases who were diagnosed with COVID-19; accordingly, given that HELLP syndrome is also one of the initial manifestations of preeclampsia, clinically differentiating these two conditions is difficult.

As for maternal mortality ratio, in Caldas, according to the results of the present study, there was an increase during the pandemic, going from 38 cases per 100 000 live births in 2019 to 93 cases per 100 000 live births in 2020 and 177 cases per 100 000 live births in 2021. These figures exceed those reported at the national level, as the maternal mortality ratio in Colombia was 65.1 deaths per 100 000 live births in 2020 and 76.1 deaths per 100 000 live births in 2021. It should be noted that Caldas is one of the 19 territorial entities in the country where an increase in maternal mortality cases was registered after the declaration of the COVID-19 pandemic.[28]

Based on these findings, it may be concluded that the increase in SMM cases in Caldas between 2019 and 2021 could be related to the increase in case fatality and not to the strengthening of epidemiological surveillance, since the case fatality rate in our study went from 1.10% in 2019 to 1.25% in 2020 and to 1.84% in 2021, that is, there was an increasing trend of up to almost 2 maternal deaths for every 100 cases of SMM.

The leading cause of indirect maternal death in Colombia in 2021 was COVID-19 pneumonia (35.1%).[29] In Caldas, during the study period (2019-2021), there were 4 indirect maternal deaths due to COVID-19 and the remaining maternal deaths (n=19) were from other causes, most notably oncological diseases (Table 6). It should be noted that while the main cause of morbidity in all SMM cases (n=4) was severe preeclampsia, none of the cases of maternal mortality was due to a hypertensive disorder. This could indicate that care for these conditions has been strengthened in the health services of Caldas.

The study's limitations include the lack of detailed information on pre-existing comorbidities in pregnant women (e.g., hypertension, diabetes, among others), making it impossible to accurately assess the influence of comorbidities on the severity of COVID-19 infection during pregnancy, despite the existing evidence linking these medical conditions to more severe forms of the disease in this population.[3,6] Another limitation lies in the failure to analyze the vaccination status against COVID-19 in pregnant women during the study period (2021), a relevant factor for further studies of greater scope given that vaccination has been shown to considerably reduce the risk of severe COVID-19.[30]

Finally, we highlight the importance of this study to guide decision making in accordance with the behavior of the event in the territories. In this case, evidence from this

study leads us to recommend prioritizing prevention and health education actions in the municipality of La Dorada and evaluating the follow-up of non-obstetric causes of maternal mortality such as cancer.

Conclusions

Most COVID-19 cases in pregnant women reported in the department of Caldas in 2020 and 2021 occurred in young women of low socioeconomic status. The behavior of the SMM ratio and maternal mortality ratio in Caldas during the study period showed an upward trend compared to 2019. Furthermore, the values of these indicators were higher than those reported for the country. The case fatality rate reflected an increase of up to almost 2 maternal deaths per 100 cases of SMM in 2021.

Conflicts of interest

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