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SHORT REPORT

Maternal and perinatal outcomes in pregnant women with confirmed severe and mild COVID-19 at one large maternity hospital in Chile

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ABSTRACT

Objective and methods: We conducted a prospective observational cohort study in 458 pregnant and puerperal women, with confirmed COVID-19 at Hospital San Jose, Santiago, Chile, to determine the impact of COVID-19 on pregnancy and confirm safety and feasibility of a management protocol based on clinical presentation of the disease.

Results: 25.5% (117/458) of women were severe and 74.4% (341/458) mild presentation. Three percent (9/341) of mild presentations required a subsequent hospitalization. Overall, 26/458 women (5.6%) were admitted to ICU, and 13/458 (2.8%) required mechanical ventilation. One maternal death occurred at 49-days postpartum. Severe presentation, infection above 24 weeks, and comorbidities were associated with an adverse maternal outcome. Of total deliveries, 16.5% (36/217) were <37 weeks. Perinatal mortality was 6/226 (2.7%), mostly due to the fetal component.

Conclusions: A quarter of the women had severe COVID-19 that, combined with occurrence of disease in the second half of pregnancy, resulted in substantial maternal compromise. Perinatal morbidity and mortality in women with severe disease were high and warrant consideration. Outpatient management was safe for mild cases.

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SARS-CoV-2; COVID-19; pregnancy; intensive care unit; Latin America

Introduction

Pregnant women with COVID-19 may have a more severe presentation of the disease than non-pregnant women of reproductive age, requiring more admissions to intensive care and mechanical ventilation [1]. Approximately, 1–2% of newborns from mothers with COVID-19 test positive for nasopharyngeal SARS-Cov-2 RT-polymerase chain reaction (PCR) [2]. Several protocols for emergency response to COVID-19 epidemic in maternity facilities have been proposed and they need evaluation [3–5].

The purpose of this study was to determine the impact of COVID-19 on pregnancy outcomes in pregnant or puerperal women presenting with severe and mild COVID-19 in a tertiary level hospital in Chile while evaluating the safety and feasibility of a management protocol based on clinical presentation of COVID-19.

Study design

Ethics

This study was approved by the Institutional Ethics Committee on 23/07/2020 (032/2020).

Methods

Prospective observational cohort study including all consecutive pregnant or puerperal women with confirmed PCR for SARS-CoV-2 infection presenting at Hospital San José, in Santiago, Chile, since 8 April 2020–30 August 2020.

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Table 1. Demographic, obstetric, and clinical characteristics of women with confirmed PCR (+) SARS-CoV-2, Chile Metropolitan area hospital: 8 April 2020 to 30 August 2020.

Characteristic	Total $N = 458$ N (%)	Severe cases at presentation requiring hospitalization Group 1 $N = 117$ n (%)	Mild cases with initial outpatient care Group 2 $N = 341$ n (%)	p Value
Pregnancy status at diagnosis of COVID-19				
Pregnant	445 (97.16)	109 (93.16)	336 (98.53)	**.005**
Puerperium-post-abortion	13 (2.83)	8 (6.83)	5 (1.46)	
Age, years				
Mean (SD)	29.04 (6.38)	29.01 (6.38)	29.48(6.24)	NS
<18	10 (2.18)	5 (4.27)	5 (1.46)	.13
19–34	354 (77.29)	92 (78.63)	262 (76.83)	.79
35–39	63 (13.75)	12 (10.25)	51 (14.95)	.34
>40	30 (6.55)	8 (6.83)	22 (6.45)	1
Gestational age at diagnosis of COVID-19 (weeks)				
Mean (SD)	26.1 (9.5)	31.9 (8.0)	24.2 (9.3)	**<.01**
<12	61 (13.31)	8 (6.83)	53 (15.54)	**.017**
13–23 + 6	111 (24.23)	11 (9.4)	100 (29.32)	**<.01**
24–32 + 6	131 (28.6)	26 (22.22)	105 (30.79)	.096
33–36 + 6	83 (18.12)	27 (23.07)	56 (16.42)	.12
>37	68 (14.84)	43 (36.75)	25 (7.33)	**<.01**
Puerperium	4 (0.87)	2 (1.7)	2 (0.58)	.27
Pregnancy characteristics				
Primigravidae	144 (31.44)	51 (43.58)	93 (27.27)	**<.01**
Multiparous	310 (67.68)	65 (55.55)	245 (71.84)	
Multiple pregnancy	10 (2.18)	3 (2.56)	7 (2.05)	.72
Nationality				
Chilean	269 (58.73)	56 (47.86)	213 (62.46)	**.044**
Other	189 (41.26)	61 (52.13)	128 (37.53)	
Preexisting medical condition				
None	231 (50.43)	60 (51.28)	171 (50.14)	NS
Chronic hypertension	16 (3.49)	4 (3.41)	12 (3.51)	1
Type II diabetes	11 (2.4)	4 (3.41)	7 (2.05)	.48
Asthma	7 (1.52)	1 (0.85)	6 (1.75)	.68
Hypothyroidism	22 (4.8)	1 (0.85)	21 (6.15)	**.021**
HIV	4 (0.87)	1 (0.85)	3 (0.87)	1
Obese (BMI >30)	154 (33.62)	41 (35.04)	113 (33.13)	.38
Severe obesity (BMI >39.9 kg/m^2)	17 (3.71)	5 (4.27)	12 (3.51)	.49

Bold values suggest statistically significant at $p < 0.05$.

All pregnant and puerperal women who presented to the triage area and were classified as suspected COVID-19 cases were included in the study (Appendix 1, Supplementary material). Women were diagnosed with severe or mild disease, according to prespecified criteria [6] (Appendix 2, Supplementary material). Women with severe COVID-19 were hospitalized (group 1) while and those with mild disease were managed as outpatients in the antenatal care clinic (group 2). Low molecular weight heparin (LMWH) was used in all hospitalized women [7].

All alive newborns were tested for SARS-CoV-2 within the first 12 h after birth, except in cases in which the contagion was more than 21 days before childbirth. Positive tests were repeated. Data were collected from medical charts and birth records and entered into an electronic anonymous database. Additional information was obtained by telephone.

Data analysis

Demographic, obstetric, and clinical characteristics and maternal and perinatal outcomes in hospitalized (group 1) and outpatient (group 2) women were compared. Chi-square/Fisher's test was performed to compare proportions and percentages between groups using RStudio analytic software (http://www.rstudio.com). A p value of <.05 was considered statistically significant. Multivariable linear and logistic regressions were performed to evaluate the contribution of maternal variables to specific adverse maternal and neonatal outcomes using the software GraphPad Prism 8.3 (La Jolla, CA).

Results

Out of 843 pregnant women who consulted at our hospital with common symptoms of suspected COVID-19, a total of 458 (54.3%) were confirmed with SARS-Cov-2 infection, 97.2% presented during pregnancy and 2.8% during puerperium or post-abortion (Table 1). Twenty-five percent (117/458) of positive women were in group 1 and 75% in group 2. Only nine women from group 2 (2.9%) required subsequent hospitalization due to the worsening of COVID-19 disease.

Table 2. Maternal and pregnancy outcomes among women with confirmed PCR (+) SARS-CoV-2.

Maternal outcome	Total $N = 458$ N (%)	Severe cases at presentation requiring hospitalization Group 1 $N = 117$ n (%)	Mild cases with initial outpatient care Group 2 $N = 341$ n (%)	p Value
COVID-19 severe complications				
ICU admission	26 (5.67)	20 (17.09)	6 (1.75)	**<.01**
Mechanical ventilation	13 (2.83)	11 (9.4)	2 (0.58)	**<.01**
Pregnancy related complications				.077
Preterm PROM	4 (0.87)	2 (1.7)	2 (0.58)	.27
Gestational diabetes	24 (5.24)	4 (3.41)	20 (5.86)	.61
Preeclampsia	6 (1.31)	5 (4.27)	1 (0.29)	**<.01**
Intrahepatic cholestasis	7 (1.52)	1 (0.85)	6 (1.75)	.49
Pregnancy outcomes				
Miscarriage	9 (1.96)	7 (5.98)	2 (0.58)	**.028**
Live birth[a]	217/222 (97.74)	86/90 (95.55)	131/132 (99.24)	.07
Ongoing pregnancy[b]	223/458 (48.68)	19/117 (16.23)	204/341 (59.82)	<.01
Maternal status at end of follow up				
Death	1 (0.21)	1 (0.85)	0 (0)	.4
Still in hospital[c]	3/458 (0.65)	2/117 (1.7)	1/341 (0.29)	.1
At home without complications	454/458 (99.12)	114/117 (97.43)	340/341 (99.7)	.02

Organ dysfunction	Total data	Group 1	Group 2
Lung failure/VM/RDS	13	11	2
Neurological	1	1	0
Renal	5	5	0
Hepatic	3	3	0
DIC	3	2	1
CV/shock	9	8	1
Cardiac	2	2	0
Thromboembolism	2	0	2
ECMO	0	0	0
Sepsis	2	2	0

[a]Based on total birth each group.
[b]At August 30.
[c]Patients hospitalized in a ICU or due to a diagnosis associated with COVID are considered.
Bold values suggest statistically significant at $p < 0.05$.

Mean (SD) maternal age was 29 (6.38) weeks for both groups. Mean gestational age at diagnosis of COVID-19 in group 1 was higher than in group 2 (31.9 vs. 24.2 weeks of gestation, $p<.01$). Half of the positive women (227/458) had a preexisting medical condition (obesity, chronic hypertension, hypothyroidism, type 2 diabetes) with no difference between groups (Table 1).

Maternal and pregnancy outcomes

Overall, 26 women (5.6%) were admitted to the ICU, and 13 required mechanical ventilation (2.8%). Of the women in critical care, two were in the puerperium and 24 were pregnant. Sixteen (66.6%) were delivered, and eight were discharged from the ICU while still pregnant. A case of late maternal death occurred at 49-days postpartum. The mother was delivered by emergency cesarean section due to acute respiratory failure at 38 weeks of gestation and subsequent developed multi-system and septic shock. The newborn was discharged alive.

Severe COVID-19 related complications were significantly different between groups: ICU admission was required in 17% of women in group 1 vs. 1.75% in group 2 ($p<.01$), and mechanical ventilation was utilized in 11 women (9.4%) in group 1, and two women (0.5%) in group 2 ($p<.01$). Most pregnancy-related complications (preterm rupture of membranes-PROM, gestational diabetes, and intrahepatic cholestasis) did not differ significantly between groups. Preeclampsia was more frequent in group 1 ($p<.01$). Seven women (4.6%) in group 1 had miscarriages, with a gestational age ranging from 7 to 15 weeks, vs. two in group 2 (0.6%) ($p=.028$) (Table 2).

Perinatal outcomes

A total of 221 live births to women included in the study occurred as of 30 August 2020. The overall rates of preterm birth <37 weeks and <34 weeks were 16.5 and 6.4%, respectively.

Rates of prematurity below 37 and 34 weeks were 24.4 and 10.4% respectively in group 1 and 11.4 and 3.8% in group 2 ($p<.01$) (Table 3).

We observed a marginally significant trend for more emergency cesarean sections in group 1 as compared to group 2 (41.6 vs. 29.0%, $p=.06$). The median (IQ range) for neonatal birth weight was statistically

Table 3. Birth and neonatal outcomes among infants[b] born to women with confirmed PCR (+) SARS-CoV-2.

Perinatal outcomes	Total data N = 217 N (%)	Severe cases at presentation requiring hospitalization Group 1 N = 86 n (%)	Mild cases with initial outpatient care Group 2 N = 131 n (%)	p Value
Preterm birth[a]				
Preterm birth <37 sem	36 (16.58)	21 (24.41)	15 (11.45)	**<.01**
Preterm birth <34 sem	14 (6.45)	9 (10.46)	5 (3.81)	**<.01**
Mode of birth[a]				
Vaginal birth	117 (53.91)	44 (51.16)	73 (55.72)	.8
Cesarean section	100 (46.08)	42 (48.83)	58 (44.27)	
Emergency cesarean	74 (34.1)	36 (41.86)	38 (29)	.06
Neonatal outcomes among live births[b]				
Birthweight (g) (median, IQ range)	3172 (2702–3508)	3100 (2562–3455)	3268 (2934–3562)	**<.01**
Birthweight <2500 g	36 (16.28)	21 (23.86)	15 (11.27)	**<.01**
Apgar score <7 at 5 min	4 (1.8)	4 (4.54)	0 (0)	**<.01**
Congenital anomalies	1 (0.45)	0 (0)	1 (0.75)	.4
NICU admission	21 (9.5)	12 (13.63)	9 (6.76)	**.044**
Positive nasopharyngeal PCR SARS-CoV-2 within 24 h after birth (live births only)	10/221 (4.52)	8/88 (9.09)	2/133 (1.5)	**.008**
Positive nasopharyngeal PCR SARS-CoV-2 first and second sample at 24 h after birth	1/221 (0.45)	1/88 (1.13)	0/133 (0)	.2
Neonatal status at end of follow-up				
Stillbirth	5 (2.26)	4 (4.54)	1 (0.75)	.16
Neonatal death <7 days	1 (0.45)	1 (1.13)	0 (0)	.4
Still in hospital[b]	4 (1.8)	1 (1.13)	3 (2.25)	.5
Discharged alive[c]	216 (97.73)	86 (97.72)	130 (97.74)	1.0

[a]Preterm birth is calculated over 217 deliveries from live birth.
[b]Live births only (221); NICU: neonatal intensive care unit.
[c]Based on 221 children born out of 217 deliveries (four twin pregnancies). Stillbirth and those still hospitalized.
Bold values suggest statistically significant at $p < 0.05$..

lower in group 1 with higher incidence of low birth weight (LBW). Four newborns in group 1 had low Apgar score at 5 min, vs. none in group 2 ($p<.01$). NICU admission was higher in group 1 than group 2 (13.6 and 6.7% $p=.04$). A case of fetal aneuploidy was detected in pregnant women from group 2. No other major congenital anomalies were observed.

One hundred and eleven newborns were born with more than 21 days of maternal confirmation of infection and therefore were not tested, and three newborns were not tested due to contingency. One hundred and seven newborns had a nasopharyngeal swap for SARS-CoV-2 taken within 24 h after birth: 95 were negative, two indeterminate, and 10 were positive.

The positivity rate of neonatal PCR was 4.52% (10/221) and 9.3% (10/107) in the tested babies. The positivity rate was higher in group 1 (9 vs. 1.5%) ($p=.03$) (Table 3). In only one newborn, the PCR remained positive after a repeated test 24 h later.

Overall perinatal mortality was 2.65% (6/226), mostly due to fetal mortality. Only one perinatal death (stillbirth) was observed in group 2. The majority of newborns were discharged healthy in both groups at the end of the study period. After neonatal discharge, there were no readmissions for morbidity until 28 days. Two infants were still hospitalized at the end of the study period (30 August 2020).

Main determinants of the maternal and neonatal risk

We performed multivariable analysis to determine the contribution of severe COVID-19 and other factors as maternal age, comorbidities, obstetric pathologies, and foreign nationality to adverse maternal and neonatal outcomes. To establish the risk level, we computed a correlation matrix for maternal and perinatal outcomes (Appendix 3 and 4). In the analysis, we did not exclude twin pregnancies, which could increase morbidity and/or prematurity. However, the number of twins was similar in both groups.

Multiple logistic regression showed that the main factors associated with maternal ICU admission were becoming ill beyond the 24 weeks of gestation (OR 4.58, $p=.02$), severe COVID-19 requiring hospitalization (OR 1.63, $p=.05$), and maternal age (OR 1.07, $p=.02$) (Table 4). Premature birth was associated with maternal age (OR 1.08, $p=.01$ for delivery <37 weeks), obstetrics comorbidity (OR 5.66, $p=.01$, and OR 2.59, $p=.02$ for delivery under 34 and 37 weeks, respectively), and severity of the disease (OR 1.67, $p=.01$, for

Table 4. Multiple logistic regression.

	Maternal outcomes					
	ICU admission			Mechanical ventilation		
Maternal	OR	95% CI	*p* Value	OR	95% CI	*p* Value
Age	1.07	1.01–1.15	.0247	1.07	0.98–1.16	.1439
Nationality: foreign women	1.50	0.64–3.57	.3507	1.18	0.36–3.84	.7752
Obstetric pathology	1.66	0.57–4.28	.3175	1.08	0.16–4.36	.9253
Comorbidities	0.65	0.26–1.57	.3403	0.85	0.25–2.93	.7959
Severe presentation requiring hospitalization	1.63	1.11–3.26	.0506	1.47	0.97–2.43	.0430
Late presentation (>24)	4.58	1.48–20.11	.0180	1.89	0.52–8.94	.3611

	Neonatal outcomes								
	Birth <34 weeks			Birth <37 weeks			Mortality		
Maternal	OR	95% CI	*p* Value	OR	95% CI	*p* Value	OR	95% CI	*p* Value
Age	1.04	0.94–1.15	.4921	1.08	1.02–1.15	.0113	1.17	1.01–1.41	.0460
Nationality: foreign women	3.51	0.89–8.16.86	.0879	1.87	0.84–4.28	.1303	0.10	0.01–0.84	.0637
Obstetric pathology	5.66	1.42–24.40	.0147	2.59	1.08–6.09	.0295	1.34	0.03–13.56	.8159
Comorbidities	1.40	0.37–5.77	.6233	0.86	0.38–1.94	.7121	0.25	0.03–1.83	.1806
Severe presentation requiring hospitalization	1.67	0.89–2.57	.0129	1.42	0.97–2.23	.0554	1.50	0.70–2.39	.1021
GA at disease onset	0.70	0.58–0.80	.0001	0.86	0.79–0.93	.0003	0.82	0.68–0.98	.0292

	Neonatal outcomes		
	Birth weight		
Maternal	Beta	95% CI	*p* Value
Age	−9.88	−23.3 to 3.52	.1477
Nationality: foreign women	9.32	−165.5 to 183.9	.917
Obstetric pathology	−200.6	−412.9 to 11.79	.0640
Comorbidities	123.3	−54.9 to 301.4	.1740
Severe presentation requiring hospitalization	−157.2	−258.7 to −55.7	.0025
GA at disease onset	42.4	23.6–61.1	.0001

delivery under 34 weeks). Maternal age was the main associated factor with perinatal mortality (OR 1.17, $p=.04$). Maternal age was the main associated factor with perinatal mortality ($p=.04$).

Multiple linear regression confirmed a negative association between severe COVID-19 requiring hospitalization with birth weight ($p=.002$) and a positive association of the gestational age at diagnosis of COVID-19 and birth weight ($p=.001$), preterm delivery ($p<.003$), and perinatal mortality ($p=.02$).

Obesity, comorbidities, or nationality were not associated with the risk of negative pregnancy outcomes.

Discussion

This is one of the largest studies of COVID-19 and pregnancy outcomes in Latin America. It includes information from only one institution, which improves data quality and consistency but might reduce generalizability of the results to other populations.

We observed a high rate (25%) of severe COVID-19 among pregnant women that is consistent with the rate reported by the Centers for Disease Control in North America (26%) [8]. Rates of ICU admission (6%) and mechanical ventilation (3%) are also consistent with published data [2,9]. In our cohort, the risk for maternal and perinatal complications increased when the disease occurred at advanced gestational age, as reported in the literature [2,9]. The higher rate of complications during the second and third trimesters has been reported as well in previous epidemics of influenza, SARS, and MERS [10,11]. The prematurity (<37 weeks) and LBW (<2500 g) rates in this study are significantly higher than nationally representative rates, 16% vs. 9%, and 17% vs. 6%, respectively [12]. High preterm birth rates in women with COVID-19 are consistent with data from a recently published systematic review [2] and could be explained by induced preterm births, rather than be a direct cause of the disease. The observed perinatal mortality (26/1000), mostly due to stillbirth, was higher than previously described, and warrant further investigations in larger cohorts [2]. Almost half of the population in this study was from Latin American countries other than Chile and it is possible that social and health related-behaviors, as well as health systems issues and disparities in access to care, may have contributed to the observed high rate of COVID-19 and associated complications [13]. For what concerns the risk of vertical transmission of the disease, the rate of positivity for SARS-CoV-2 in infants was comparable with data and published diagnostic criteria for neonatal infection

from the literature, and only one newborn had a second positive test result [2,14].

Importantly, our data confirm that an outpatient management is safe for mild presentations of COVID-19 in pregnant women. Women with mild disease who received ambulatory had low risk of negative maternal and perinatal outcomes and only few of them were subsequently hospitalized for COVID-19 related indications.

Conclusions

Pregnant women who initially presenting with severe symptoms of COVID-19 and at advanced gestational age are at increased risk for poor maternal and perinatal outcomes than women with mild disease and earlier presentation of symptoms for whom an outpatient management is suitable and safe. We observed a low maternal mortality rate consistent with results of other studies; however, the levels of COVID-19 related maternal complications and perinatal morbidity and mortality in our cohort among women with severe disease are high and merit further consideration. The vulnerability of pregnant and recently pregnant women with COVID-19 and their infants described in this article must be taken into account in public policy making to improve the living conditions and prevent severe complications during pregnancy and in planning post pandemic policies [15].

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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