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CLINICAL ARTICLE

Obstetrics

Maternal characteristics and pregnancy outcomes of hospitalized pregnant women with SARS-CoV-2 infection in South Africa: An International Network of Obstetric Survey Systems-based cohort study

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Abstract

Objective: To describe risk factors and outcomes of pregnant women infected with SARS-CoV-2 admitted to South African healthcare facilities.

Methods: A population-based cohort study was conducted utilizing an amended International Obstetric Surveillance System protocol. Data on pregnant women with SARS-CoV-2 infection, hospitalized between April 14, 2020, and November 24, 2020, were analyzed.

Results: A total of 36 hospitals submitted data on 673 infected hospitalized pregnant women; 217 (32.2%) were admitted for COVID-19 illness and 456 for other indications. There were 39 deaths with a case fatality rate of 6.3%: 32 (14.7%) deaths occurred in women admitted for COVID-19 illness compared to 7 (1.8%) in women admitted for other indications. Of the women, 106 (15.9%) required critical care. Maternal tuberculosis, but not HIV co-infection or other co-morbidities, was associated with admission for COVID-19 illness. Rates of cesarean delivery did not differ significantly between women admitted for COVID-19 and those admitted for other indications. There were 179 (35.4%) preterm births, 25 (4.7%) stillbirths, 12 (2.3%) neonatal deaths, and 162 (30.8%) neonatal admissions. Neonatal outcomes did not differ significantly from those of infected women admitted for other indications.

Conclusion: The maternal mortality rate was high among women admitted with SARS-CoV-2 infection and higher in women admitted primarily for COVID-19 illness with tuberculosis being the only co-morbidity associated with admission.

KEYWORDS
COVID-19, low- and middle-income country, perinatal, pregnancy, SARS-CoV-2

1 | INTRODUCTION

South Africa reported its first case of SARS-CoV-2 infection in March 2020, the same month that WHO declared SARS-CoV-2 a global pandemic.[1] The first wave of infections peaked in South Africa in July 2020, reaching a nadir by October 2020, with just over 700 000 infections reported.[2] Paralleling the evolution of the pandemic, reports on a multitude of topics related to SARS-CoV-2 infection abounded. In contrast, pregnancy-related research in the field remains sparse, in particular for low- and middle-income countries (LMICs).

An early report from the United Kingdom Obstetric Surveillance System (UKOSS) highlighted that a high proportion of pregnant women admitted to hospital with SARS-CoV-2 infection were from black or other ethnic minority groups, overweight, had pre-existing medical disorders, or were of advanced maternal age.[3] A systematic review and meta-analysis reported that SARS-CoV-2 infection is associated with an increased risk of admission to the intensive care unit (ICU) for the mother, and preterm birth and admission to the neonatal ICU (NICU) for the infant.[4]

Literature available from Africa after the first wave of the pandemic is comparatively sparse, comprising mostly opinion pieces, literature reviews, case studies, and small retrospective analyses with several limitations.[5–8] Treatment of pregnant women with SARS-CoV-2 has therefore relied on guidance for the general population. Pregnancy cohort data are required as a matter of priority given the prevalence in Africa of the risk factors for severe illness identified in studies from Western populations.

The primary aim of the present study was to describe the characteristics and outcomes of hospitalized pregnant women infected with SARS-CoV-2 in South Africa who were admitted for treatment of clinical SARS-CoV-2 illness or other indication, in order to inform evidence-based guidance for pregnant women in South Africa.

2 | MATERIALS AND METHODS

A multicenter observational cohort study was conducted based on the protocol originally developed by the UKOSS, and subsequently adopted by the International Obstetric Surveillance System (INOSS) to enable a coordinated and standardized international approach to the study of SARS-CoV-2 infection in pregnancy.[3] As a national Obstetric Surveillance System had not been formalized in South Africa at the time of the study launch, the present study was communicated through the South African Society of Obstetricians and Gynecologists and clinical networks. Lead clinicians of obstetric units wishing to participate contacted the study team and were registered as center leads.

Lead clinicians were provided with case report forms (CRFs) containing a unique site number, along with guidance on form completion. Data were obtained through review of medical records. Hospitalized women were included in the study if they had a laboratory confirmed SARS-CoV-2 polymerase chain reaction (PCR) test and were pregnant or within 42 days of delivery (or miscarriage/termination of pregnancy [TOP]). CRFs were completed during admission to hospital, or if the woman was still pregnant at discharge, additional information was collected at pregnancy outcome. Data collected included background information (sociodemographic information, nutritional status, behavioral factors, medical and obstetric history) and information on the following: index pregnancy; SARS-CoV-2 infection (symptoms, testing, and treatment administered); and maternal, neonatal, and pregnancy outcome. Completed CRFs were submitted to the central study team, where the information was captured into the electronic database (REDCap) using the double entry method.

During the study period, women were tested for SARS-CoV-2 infection if they were symptomatic or according to local hospital policy (case contact history or as mandatory screening before admission). Clinicians were asked to complete CRFs for all PCR-confirmed cases of SARS-CoV-2 infection in their unit. In addition, clinicians were sent a monthly email to encourage ongoing reporting and inform them of study progress. Submission of CRFs was closed on November 30, 2020 for this analysis.

The present study received ethical approval from the University of Pretoria, Faculty of Health Sciences Research Ethics Committee as overseeing approval, and subsequently received ethical approval from the University of KwaZulu-Natal, University of Cape Town, Stellenbosch University, Walter Sisulu University, University of Witwatersrand, and Sefako Makgatho University. Institutional approvals were obtained for each participating facility.

Statistical analysis is primarily descriptive, reporting the mean and standard deviation for continuous data, and frequencies with percentages for the categorical variables. The Shapiro–Wilk test was used to test for normality of continuous data, followed by the non-parametric Mann–Whitney *U*-test when comparing the independent groups. The χ^2 test was used to investigate if categorical variables of interest showed differences between the different groups being compared. All tests were performed at a 5% level of significance. Comparison was made between two groups based on primary indication for hospital admission: women admitted for clinical SARS-CoV-2 infection were compared to women admitted for other indications. For this comparison, women admitted solely for purposes of isolation were excluded.

3 | RESULTS

A total of 36 hospitals across six provinces in South Africa enrolled in the present study. Completed CRFs were received for 673 women admitted between April 14, 2020, and November 24, 2020, the majority (96%) from state-subsidized hospitals.

3.1 | Maternal characteristics

The age range of the women was 11–47 years, with 64.6% aged 20–34 years. Using body mass index (BMI, calculated as weight

TABLE 1 Characteristics of the study population[a]

	Number of women ($n = 673$)
Age (years) ($n = 536$)	
<20	32 (6.0)
20–34	346 (64.6)
≥35	158 (29.5)
BMI (kg/m^2) ($n = 460$)	
Underweight (<18)	5 (1.1)
Normal (18–25)	94 (20.4)
Overweight (25.1–30)	108 (23.5)
Obese (>30)	253 (55.0)
MUAC (cm) ($n = 333$)	
Underweight (<23)	20 (6.0)
Normal (23–32)	194 (58.3)
Overweight (≥33)	119 (35.7)
Nationality ($n = 655$)	
South African	554 (84.6)
Black	472 (85.2)
Colored	52 (9.4)
Indian	9 (1.6)
White	3 (0.5)
Unknown	18 (3.2)
Non-South African	101 (15.4)
Woman in paid work ($n = 512$)	164 (32.0)
Smoking status ($n = 521$)	
Never	499 (95.8)
Currently smoking	14 (2.7)
Gave up before pregnancy	5 (1.0)
Gave up during pregnancy	3 (0.6)
Alcohol use ($n = 498$)	
Never	431 (86.5)
Current alcohol use	18 (3.6)
Gave up before pregnancy	29 (5.8)
Gave up during pregnancy	20 (4.0)
Pre-existing medical conditions	
Women with no pre-existing medical conditions	314 (46.7)
Women with ≥1 pre-existing medical condition	322 (47.8)
HIV ($n = 658$)	220 (33.4)
Viral loads ($n = 182$)	
LDL/<50 copies/mL	132 (72.5)
>50 copies/mL	50 (27.5)
CD4 count ($n = 164$)	
≤50 cells/mm^3	4 (2.4)
51–200 cells/mm^3	24 (14.6)
>200 cells/mm^3	136 (82.9)
On antiretroviral medication	207 (94.1)
Hypertension ($n = 653$)	70 (10.7)
Endocrine disorders ($n = 652$)	28 (4.3)
TB ($n = 633$)	26 (4.1)
Asthma ($n = 654$)	23 (3.5)
Chronic cardiac disease ($n = 654$)	15 (2.3)
Other ($n = 630$)	12 (1.9)
Chronic kidney disease ($n = 651$)	4 (0.6)
Chronic pulmonary disease ($n = 654$)	4 (0.6)
Hematological disorders ($n = 651$)	4 (0.6)
Psychiatric disorders ($n = 652$)	4 (0.6)
Autoimmune disease ($n = 652$)	3 (0.5)
Cancer ($n = 652$)	2 (0.3)
Chronic neurologic disease ($n = 652$)	2 (0.3)
Chronic liver disease ($n = 652$)	1 (0.2)
Nulliparous ($n = 671$)	172 (25.6)
Multiple pregnancy	24 (3.6)

Abbreviations: BMI, body mass index; MUAC, mid upper arm circumference; TB, tuberculosis.

[a]Values are given as number (percentage).

in kilograms divided by the square of height in meters), 55% of women were classified as obese in comparison to using mid-upper arm circumference (MUAC), which identified the majority (58%) of women to be in the normal range. However, MUAC was only recorded for half of the women. Of the women, 84.6% were South African. The vast majority of South African women were classified ethnically as black ($n = 472$, 85.2%), with 9.4% colored, 1.6% Indian, and less than 1% white. Current use of cigarettes and alcohol was reported among 2.7% and 3.6% of women, respectively.

Nearly half the women ($n = 322$, 47.8%) had at least one pre-existing medical condition. HIV infection was the most prevalent ($n = 220$, 33.4%), followed by hypertension ($n = 70$, 10.7%). The most recent HIV viral load was available for over 80% of women infected with HIV, identifying 72.5% as virally suppressed. The majority (94.1%) of women infected with HIV were on antiretroviral therapy.

Nearly three-quarters of the women were multiparous. Of them, 24 (3.6%) had multiple pregnancies (Table 1).

3.2 | SARS-CoV-2 illness

The majority ($n = 539$, 83.3%) of women were in the third trimester of pregnancy at the time of SARS-CoV-2 testing, with 226 (34.9%) at term and 16 (2.5%) women at less than 14 weeks of pregnancy. Indications for admission included delivery or TOP (38.6%),

admission for COVID-19 illness (32.2%), hospital care for other medical indications (19.5%), and isolation in the absence of illness ($n = 59$, 8.8%). At the time of admission, 483 (72.0%) women were pregnant but not in labor, 133 (19.8%) were in labor, 38 (5.7%) were postpartum, and 17 (2.5%) were post-TOP or miscarriage. The median duration of admission was shortest for women admitted for delivery or TOP (4 days) and longest for women admitted for other medical indications (10 days).

Nearly one-quarter (23.3%) of women were asymptomatic at the time of SARS-CoV-2 diagnosis. For women who were symptomatic, cough, fever, and shortness of breath were the most frequently reported symptoms (70.2%, 44.5%, and 42.3%, respectively). Loss of taste or smell was reported infrequently but relied on spontaneous reporting as this symptom was not included in the CRF. Respiratory symptoms predominated with very few reports of headache, diarrhea, or other system involvement.

Pharmacotherapy for SARS-CoV-2 infection was frequent and included the administration of antibiotics to 287 (44.1%) women, and corticosteroids for respiratory symptoms in 122 (18.7%) or to enhance fetal lung maturity in 76 (11.6%) women. "Other therapies" were administered to 193 (29.9%) women. These included, but were not limited to, low-molecular weight heparin, and zinc and vitamin supplementation. Few women received antiviral, antimalarial, antifungal, and/or experimental drugs. Information on respiratory support (e.g. oxygen and nebulizers) was reported occasionally but not routinely collected. In total, 106 (15.9%) women required critical care, with 4 (0.6%) receiving extracorporeal membrane oxygenation. There were 39 maternal deaths (31 women were postpartum and eight died while pregnant), resulting in a case fatality rate of 6.3% for the total cohort. Severe acute respiratory infection, most likely due to SARS-CoV-2 infection, was the major cause of maternal death ($n = 29$, 74.4%). The remaining 10 deaths were attributed to "other" direct causes ($n = 5$), hypertensive disease ($n = 1$), and in four women the cause of death was unknown. In the remaining 10 cases, a causal association with SARS-CoV-2 infection was uncertain due to the presence of other risk factors and maternal morbidities (Table 2).

3.3 | Pregnancy outcomes

At the time of data analysis, pregnancy outcomes were available for 575 (85.4%) women. Miscarriage, ectopic, or molar pregnancy was reported for 31 (5.4%) women and two women underwent a TOP. Of the 505 women who delivered, 326 (64.6%) gave birth at term. Of the 505 women, 316 (63%) had a cesarean delivery: 35.9% before labor and 27.1% during labor. Fetal distress (31.3%) and previous cesarean delivery (29.1%) were the commonest indications for cesarean delivery.

Neonatal outcomes were available for 551 babies. A total of 162 (30.8%) neonates were admitted to the high care unit or NICU. In total, 37 (7.0%) perinatal deaths were reported: 25 babies were stillborn; five early neonatal deaths were attributed to complications of

TABLE 2 Description of COVID-19 disease[a]

	Number of women ($n = 673$)
Primary reason for admission	
Delivery/termination of pregnancy	260 (38.6)
Duration of admission in days	220; 4 (2–9)
Care needed for COVID-19	217 (32.2)
Duration of admission in days	124; 7 (3–12)
Care needed for other medical indication	131 (19.5)
Duration of admission in days	100; 10 (5, 14)
Isolation needed but otherwise well	59 (8.8)
Duration of admission in days	29; 7 (1–14)
Unknown/other	6 (0.9)
Woman's status upon admission ($n = 671$)	
Pregnant, not in labor	483 (72.0)
Pregnant, in labor	133 (19.8)
Postpartum	38 (5.7)
Post-abortion/miscarriage	17 (2.5)
Gestational age at time of COVID-19 positive test (weeks) ($n = 647$)	
<14	16 (2.5)
14–22	21 (3.2)
22–27	53 (8.2)
28–31	108 (16.7)
32–36	205 (31.7)
≥37	226 (34.9)
Postpartum	18 (2.8)
Maternal symptoms at diagnosis of COVID-19 ($n = 656$)	
Asymptomatic	153 (23.3)
Symptomatic	503 (76.7)
Cough	353 (70.2)
Fever	224 (44.5)
Shortness of breath	213 (42.3)
Sore throat	98 (19.5)
Headache	75 (14.9)
Tiredness/lethargy	61 (12.1)
Limb or joint pain	48 (9.5)
Vomiting	42 (8.3)
Diarrhea	20 (4.0)
Rhinorrhea	17 (3.4)
Chest pain[b]	9 (1.8)
Loss of taste[b]	9 (1.8)
Loss of smell[b]	7 (1.4)
Treatment given for COVID-19	
Intravenous fluids ($n = 655$)	188 (28.7)
Antiviral drugs ($n = 659$)	20 (3.0)
Antibiotics ($n = 651$)	287 (44.1)
Corticosteroids (for respiratory disease) ($n = 652$)	122 (18.7)

(Continues)

TABLE 2 (Continued)

	Number of women (n = 673)
Corticosteroids (for fetal lung maturation) (n = 656)	76 (11.6)
Antifungal agents (n = 663)	10 (1.5)
Antimalarial agents (n = 663)	6 (0.9)
Experimental agents (n = 664)	4 (0.6)
Other therapies (n = 645)	193 (29.9)
Extracorporeal membrane oxygenation (n = 661)	4 (0.6)
Women needing level 3 critical care (n = 667)	106 (15.9)
Maternal deaths (n = 621)	39 (6.3)
Suspected primary cause of death	
Severe acute respiratory infection	29 (74.4)
Other direct cause	5 (12.8)
Unknown	4 (10.3)
Hypertensive disorder	1 (2.6)

[a]Values are given as number (percentage) or number; median (IQR).
[b]Ad hoc reporting.

prematurity, birth asphyxia (n = 2), congenital abnormality (n = 2), and other (n = 2) or unknown cause (n = 1) (Table 3).

3.4 | Stratified analysis by indication for hospital admission

History of maternal tuberculosis (current or previous) was more frequent among women admitted for treatment of COVID-19 than those admitted for other indications; however, maternal age, BMI, MUAC, and pre-existing morbidities (including HIV infection) did not differ significantly. SARS-CoV-2 symptoms, especially respiratory symptoms, were more commonly reported in the group of women who were admitted for COVID-19. There was no difference for rhinorrhea and diarrhea.

Women admitted for the management of COVID-19 were significantly more likely to need critical care and to die than women infected with SARS-CoV-2 admitted primarily for other medical conditions or for delivery (32.3% vs 8.6%, $P < 0.0001$ and 14.7% vs 1.8%, $P < 0.0001$, respectively). Severe acute respiratory failure was the leading primary cause of death in both groups but occurred at a higher frequency among women admitted for clinical SARS-CoV-2 infection (Table 4).

Women infected with SARS-CoV-2 requiring admission for management of the infection were at a significantly higher risk of ventilation ($P < 0.0001$), adult respiratory distress syndrome ($P < 0.0001$), pulmonary edema ($P = 0.02$), septicemia ($P = 0.03$), and renal failure ($P = 0.04$). Gestational age at delivery, mode of delivery, infant birth weight, neonatal mortality, and respiratory distress syndrome rates were, however, comparable across groups.

TABLE 3 Pregnancy outcomes of the study population[a]

Pregnancy outcome	Number of women (n = 575)
Miscarriage/ectopic pregnancy/molar pregnancy	31 (5.4)
Termination of pregnancy	2 (0.3)
Delivery	542 (94.3)
Delivery outcome	Number of women (n = 542)
Gestational age at time of delivery (weeks) (n = 505)	
22–27	12 (2.4)
28–31	25 (5.0)
32–36	142 (28.1)
≥37	326 (64.6)
Mode of delivery (n = 502)	
Normal vertex delivery	177 (35.3)
Breech vaginal delivery	4 (0.8)
Assisted (vacuum/forceps) vaginal delivery	5 (1.0)
Cesarean delivery before labor	180 (35.9)
Cesarean delivery during labor	136 (27.1)
Primary indication for cesarean delivery (n = 316)	
Fetal distress	99 (31.3)
Previous cesarean delivery	92 (29.1)
Maternal medical condition	27 (8.5)
Pre-eclampsia/eclampsia	22 (7.0)
Failure of labor to progress	15 (4.7)
Other	12 (3.8)
Placental abruption	9 (2.8)
Failed induction	9 (2.8)
Abnormal fetal presentation	8 (2.5)
Placenta previa	6 (1.9)
Cephalo-pelvic disproportion	4 (1.3)
Previous uterine surgery	3 (0.9)
Multiple gestation	3 (0.9)
Premature rupture of membranes	3 (0.9)
Suspected fetal growth restriction	2 (0.6)
Reduced fetal movement	1 (0.3)
Unknown	1 (0.3)
Timing of COVID-19 infection and delivery (n = 524)	
COVID-19 >7 days before delivery	195 (37.2)
COVID-19 within 7 days before delivery	230 (43.9)
COVID-19 within 7 days after delivery	76 (14.5)
COVID-19 >7 days after delivery	23 (4.4)
Neonatal outcome	Number of infants (n = 551)
Birth weight (g) (n = 520)	
<1000	11 (2.1)
1000–1499	19 (3.7)

(Continues)

TABLE 3 (Continued)

Pregnancy outcome	Number of women (n = 575)
1500–2499	116 (22.3)
≥2500	374 (71.9)
Congenital abnormality (n = 535)	18 (3.4)
Perinatal death (n = 530)	37 (7.0)
Primary cause of perinatal death (n = 37)	
Stillbirth	25 (67.6)
Complications of prematurity	5 (13.5)
Birth asphyxia	2 (5.4)
Congenital abnormality	2 (5.4)
Other	2 (5.4)
Unknown cause of neonatal death	1 (2.7)
Neonatal admission to high care/intensive care unit (n = 526 infants born alive)	162 (30.8)
Neonatal complications (n = 526 infants born alive)	
Infants without complications	395 (75.1)
Infants with ≥1 complication	112 (21.3)
Respiratory distress syndrome	81 (15.4)
Other	27 (5.1)
Severe jaundice requiring phototherapy	23 (4.4)
Severe infection	14 (2.7)
Neonatal encephalopathy	6 (1.1)
Necrotizing enterocolitis	3 (0.6)
Intraventricular hemorrhage	2 (0.4)
Chronic lung disease	1 (0.2)

[a]Values are given as number (percentage).

Of note, "maternal medical condition" was the primary indication for cesarean delivery in 30.8% of women admitted for COVID-19 compared to 1.4% of women admitted for other reasons, where the commonest indication was "previous cesarean delivery" (32.6%) (Tables 4 and 5).

4 | DISCUSSION

The present multicenter, national observational study assessing the symptoms and associations between SARS-CoV-2 infection in pregnancy and maternal and neonatal outcomes in a South African cohort shows that approximately 7.5% of all admitted women required invasive ventilation, three-quarters of whom were admitted specifically for the management of COVID-19. Women with respiratory symptoms and admitted primarily for clinical SARS-CoV-2 illness were more likely to require invasive ventilation, need critical care, and were at higher risk of mortality. The INTERCOVID Multinational Cohort Study demonstrated similar results, where the presence of any symptom increased the association with adverse outcomes compared with the group of pregnant women uninfected with SARS-CoV-2.[9]

More than half (61%) the women admitted for clinical SARS-CoV-2 illness were obese (using BMI) and just over one-third (33%) were aged 35 years and older. However, late booking is common in South Africa, and MUAC, which may be considered a more reliable marker of nutritional status,[10] identified the majority (61%) to be within the normal range. Unfortunately, MUAC was only recorded in under half of the women admitted for clinical SARS-CoV-2 infection hence no firm conclusions can be drawn. The overall prevalence of HIV infection in the present population is 33.4% compared to a national average of 30.7% among antenatal clinic attendees.[11] No significant difference in prevalence of HIV infection was observed between women admitted for clinical SARS-CoV-2 illness and those with SARS-CoV-2 infection admitted for other reasons. Of note, the majority of HIV-infected women in our cohort were on antiretroviral therapy (94.1%) and virally suppressed (72.5%). This may provide some reassurance to South Africa, a country heavily burdened by HIV infection, that treated HIV infection may not be an independent predictor of adverse outcome in pregnant women infected with SARS-CoV-2, though further studies are needed.

At the time of analysis, 85.4% of women had pregnancy outcomes available. Approximately 35% were preterm deliveries, 63% were cesarean deliveries, with maternal medical condition being the leading primary indication for cesarean delivery among women primarily admitted for the management of COVID-19. Similarly, high rates of cesarean delivery, around 50% and above, have been described in both high-income countries and LMICs in many large studies of women admitted with SAR-CoV-2 infection.[9,12–14]

Of concern is the high mortality rate in the present cohort, in particular among those admitted primarily due to clinical SARS-CoV-2 illness. Mortality rates in the present cohort are higher than those identified in the UKOSS study,[12] which was based on the same protocol and focused on hospitalized women but predominantly in a high-income setting. The majority of women in the present cohort were from state-subsidized hospitals representing a predominantly low-income population. The INTERCOVID Study showed a risk of maternal mortality of 1.6%, that is, 22 times higher among pregnant women with a diagnosis of COVID-19 than uninfected pregnant women. Deaths were concentrated in institutions from less-developed regions, suggesting greater lethality in lower-income settings.[9] In the present study, mortality was also high for pregnant women admitted for clinical SARS-CoV-2 illness, most of whom were from low-income settings, and also appear to be at higher risk of mortality than women in the UKOSS study.

The present study is strengthened through multi-provincial collaboration, with seven of the eight medical universities in South Africa participating. Planning and implementation were timely, allowing for robust data collection during the first wave of the COVID-19 pandemic, both from state-subsidized and a small number of privately funded healthcare facilities. The study is based on an established UKOSS/INOSS protocol and locally adapted CRF to facilitate the comparison of data across countries. Importantly, the indication for admission to hospital was recorded. Furthermore, the

TABLE 4 Comparison between women admitted for COVID-19 illness and women admitted for other medical indications (excluding isolation): Characteristics and description of COVID-19 illness[a]

	Admitted for COVID-19 illness ($n = 217$)	Admitted for other medical indications (excluding isolation) ($n = 397$)	*P* value
Age (years)	$n = 153$	$n = 337$	0.24
<20	6 (3.9)	24 (7.1)	
20–34	97 (63.4)	221 (65.6)	
≥35	50 (32.7)	92 (27.3)	
BMI (kg/m^2)	$n = 129$	$n = 291$	0.16
Underweight (<18)	0 (0.0)	4 (1.4)	
Normal (18–25)	19 (14.7)	64 (22.0)	
Overweight (25.1–30)	31 (24.0)	71 (24.4)	
Obese (≥30)	79 (61.2)	152 (52.2)	
MUAC (cm)	$n = 93$	$n = 213$	0.71
Underweight (<23)	7 (7.5)	13 (6.1)	
Normal (23–32)	57 (61.3)	124 (58.2)	
Overweight (≥33)	29 (31.2)	76 (35.7)	
Pre-existing medical conditions			
Women with no pre-existing medical condition	96 (44.2)	187 (47.1)	
Women with ≥1 pre-existing medical condition	107 (49.3)	191 (48.1)	
HIV	74 (34.1)	130 (32.7)	0.46
Hypertension	24 (11.1)	41 (10.3)	0.78
Endocrine disorders	8 (3.7)	19 (4.8)	0.41
TB	13 (6.0)	11 (2.8)	0.01
Asthma	8 (3.7)	12 (3.0)	0.48
Chronic cardiac disease	7 (3.2)	8 (2.0)	0.34
Other	4 (1.8)	8 (2.0)	**
Chronic kidney disease	3 (1.4)	1 (0.3)	**
Chronic pulmonary disease	3 (1.4)	1 (0.3)	**
Hematological disorders	0 (0.0)	4 (1.0)	**
Psychiatric disorders	2 (0.9)	2 (0.5)	**
Autoimmune disease	0 (0.0)	3 (0.8)	**
Cancer	0 (0.0)	2 (0.5)	**
Chronic neurologic disease	1 (0.5)	1 (0.3)	**
Chronic liver disease	0 (0.0)	1 (0.3)	**
Gestational age at time of COVID-19 (weeks)	$n = 202$	$n = 372$	
<14	3 (1.5)	12 (3.2)	
14–22	10 (5.0)	10 (2.7)	
22–27	27 (13.4)	17 (4.6)	
28–31	50 (24.8)	40 (10.8)	
32–36	73 (36.1)	116 (31.2)	
≥37	39 (19.3)	177 (47.6)	
Maternal symptoms at diagnosis of COVID-19			
Cough	169 (77.9)	146 (36.8)	<0.0001
Shortness of breath	148 (68.2)	49 (12.3)	<0.0001
Fever	94 (43.3)	108 (27.2)	0.0001

(Continues)

TABLE 4 (Continued)

	Admitted for COVID-19 illness ($n = 217$)	Admitted for other medical indications (excluding isolation) ($n = 397$)	*P* value
Sore throat	40 (18.4)	41 (10.3)	0.02
Tiredness/lethargy	36 (16.6)	16 (4.0)	<0.0001
Headache	34 (15.7)	32 (8.1)	0.01
Other	31 (14.3)	31 (7.8)	0.04
Limb or joint pain	24 (11.1)	14 (3.5)	0.0009
Vomiting	24 (11.1)	15 (3.8)	0.0018
Diarrhea	10 (4.6)	8 (2.0)	0.18
Rhinorrhea	4 (1.8)	8 (2.0)	0.94
Women needing level 3 critical care	70 (32.3)	34 (8.6)	<0.0001
Maternal deaths	32 (14.7)	7 (1.8)	<0.0001
Suspected primary cause of death			
Severe acute respiratory infection	26 (81.3)	3 (42.9)	
Other direct cause	3 (9.4)	2 (28.6)	
Unknown	3 (9.4)	1 (14.3)	
Hypertensive disorder	0 (0.0)	1 (14.3)	

Abbreviations: BMI, body mass index; MUAC, mid upper arm circumference; TB, tuberculosis.

[a]Values are given as number (percentage).

TABLE 5 Comparison between women admitted for COVID-19 illness and women admitted for other medical indications (excluding isolation): Pregnancy, delivery, and neonatal outcomes[a]

	Admitted for COVID-19 illness ($n = 148$)	Admitted for other medical indication (excluding isolation) ($n = 382$)	*P* value
Major maternal morbidity			
Required ventilation	30 (20.3)	10 (2.6)	<0.0001
Adult respiratory distress syndrome	28 (18.9)	5 (1.3)	<0.0001
Other	26 (17.6)	24 (6.3)	<0.0001
Septicemia	9 (6.1)	9 (2.4)	0.03
Renal failure	8 (5.4)	8 (2.1)	0.03
Pulmonary oedema	6 (4.1)	6 (1.6)	0.03
Pregnancy outcome			
Miscarriage/ectopic pregnancy/molar pregnancy	6 (4.1)	25 (6.5)	**
Termination of pregnancy	1 (0.7)	1 (0.3)	**
Delivery	141 (95.3)	356 (93.2)	**
Delivery outcome	$N = 141$	$N = 356$	*P* value
Gestational age at time of delivery (weeks)	130; 37.0 ± 3.5	336; 37.0 ± 3.4	0.56
22–27	2 (1.5)	9 (2.7)	
28–31	7 (5.4)	17 (5.1)	
32–36	40 (30.8)	95 (28.3)	
≥37	81 (62.3)	215 (64.0)	
Final mode of delivery	$n = 115$	$n = 349$	0.33
Normal/breech/assisted vaginal delivery	37 (32.2)	134 (38.4)	
Cesarean delivery	78 (67.8)	215 (61.6)	
Primary indication for cesarean delivery: leading indications	$n = 78$	$n = 215$	

(Continues)

TABLE 5 (Continued)

	Admitted for COVID-19 illness ($n = 148$)	Admitted for other medical indication (excluding isolation) ($n = 382$)	*P* value
Maternal medical condition	24 (30.8)	3 (1.4)	
Fetal distress	22 (28.2)	69 (32.1)	
Previous cesarean delivery	12 (15.4)	70 (32.6)	
Failure of labor to progress	6 (7.7)	9 (4.2)	
Pre-eclampsia/eclampsia	5 (6.4)	17 (7.9)	
Timing of COVID infection and delivery	$n = 136$	$n = 346$	
COVID-19 >7 days before delivery	71 (52.2)	95 (27.5)	
COVID-19 within 7 days before delivery	48 (35.3)	173 (50.0)	
COVID-19 within 7 days after delivery	10 (7.4)	65 (18.8)	
COVID-19 >7 days after delivery	7 (5.1)	13 (3.8)	
Neonatal outcome	Admitted for COVID-19 illness ($n = 143$)	Admitted for other medical indication (excluding isolation) ($n = 361$)	*P* value
Birth weight (g)	127; 2809 ± 713	347; 2883 ± 783	0.36
<1000	2 (1.6)	7 (2.0)	
1000–1499	5 (3.9)	12 (3.5)	
1500–2499	32 (25.2)	75 (21.6)	
≥2500	88 (69.3)	253 (72.9)	
Congenital anomaly	5 (3.5)	11 (3.0)	0.62
Perinatal death	10 (7.0)	24 (6.6)	0.68
Primary cause of perinatal death			
Stillbirth	5 (50.0)	20 (83.3)	
Complications of prematurity	2 (20.0)	2 (8.3)	
Birth asphyxia	0 (0.0)	1 (4.2)	
Congenital abnormality	1 (10.0)	0 (0.0)	
Unknown cause of neonatal death	0 (0.0)	1 (4.2)	
Other	2 (20.0)	0 (0.0)	
Admission to neonatal high care/intensive care unit	44 (31.9)	108 (31.7)	
Neonates without complications	96 (69.6)	263 (77.1)	
Neonates with ≥1 complication	27 (19.6)	77 (22.6)	
Respiratory distress syndrome	23 (16.7)	51 (15.0)	
Other	4 (2.9)	22 (6.5)	
Severe jaundice requiring phototherapy	6 (4.3)	16 (4.7)	
Severe infection, e.g. septicemia, meningitis	0 (0.0)	12 (3.5)	
Neonatal encephalopathy	0 (0.0)	5 (1.5)	
Necrotizing enterocolitis	1 (0.7)	1 (0.3)	
Intraventricular hemorrhage	1 (0.7)	1 (0.3)	
Chronic lung disease	0 (0.0)	1 (0.3)	

[a]Values are given as number (percentage) or number; mean ± SD.

prevalence of HIV infection in the present population is comparable to the national average and is therefore likely to be representative of the wider pregnant population in South Africa.

The present study has some limitations. First, the study lacks a control group and institutional maternity statistics to allow for comparison and calculation of pre-pandemic morbidity and mortality outcomes. Second, lead clinicians in the facilities participated on a voluntary basis as there was limited funding for the study. This, together with the overwhelming clinical burden during the pandemic, means that not all cases may have been reported. Lastly, the CRFs were designed at the beginning of the pandemic, when delineation of the disease, especially in pregnant women, was incomplete. Some

variables were not routinely collected and may therefore have been underreported.

The present study identifies that mortality is increased among pregnant women admitted for clinical SARS-CoV-2 illness compared to infected women admitted for other indications. There appears to be a greater risk of mortality in pregnant women admitted with SARS-CoV-2 infection in low-income settings with tuberculosis as the only co-morbidity associated with admission. Symptomatic pregnant women should be advised to seek medical attention early, and pregnant women in South Africa must be considered a vulnerable group to be prioritized in vaccination programs for COVID-19.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

SB and VV were joint National Principal Investigators for the study and are joint first authors. LY and SM were both National co-Principal investigators and are joint final authors. SB, VV, LY, and SM were involved in the conception and design of the study. All co-authors contributed to data collection. Data analysis was performed by TB and interpretation by SB, VV, LY, and SM. The article was drafted by SB, VV, LY, and SM. Critical revision and final approval of the version to be published was undertaken by all listed co-authors in the article. All authors contributed to and approved of the final version of the manuscript.

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