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Association between COVID-19 and adverse pregnancy outcomes in Cape Town: A retrospective study

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Background: Adverse pregnancy outcomes significantly contribute to maternal morbidity and mortality. Despite substantial global evidence, data on the effects of coronavirus disease 2019 (COVID-19) on maternal and neonatal outcomes in South Africa remain limited.

Aim: To investigate the association between COVID-19 and adverse pregnancy outcomes.

Setting: Tygerberg Hospital, Cape Town, South Africa.

Methods: We performed a retrospective analysis of pregnant women tested for COVID-19 (categorised as positive or negative), admitted to Tygerberg Hospital between 01 March 2020 and 31 March 2021. The primary outcome was a composite of stillbirth, preterm birth, neonatal death, low birth weight, and maternal death. Binary logistic regression models were used to evaluate predictors of adverse pregnancy outcomes. Variables with $p < 0.1$ in the univariate model, along with clinically relevant covariates (maternal age, parity, COVID-19, human immunodeficiency virus [HIV], and preeclampsia), were included in the final multivariable model. Statistical analyses were performed via Stata/SE® (version 17.0) at $\alpha = 0.05$.

Results: Of 350 pregnant women (mean age: 29.8 years, [standard deviation {s.d.}: 6.99]), majority were in the third trimester (77.4%) and nulliparous (51.4%). Adverse outcomes occurred in 167 (47.7%) participants, with a higher prevalence among those without COVID-19 (51.4% vs. 43.6%) and those with preeclampsia (68.3% vs. 33.3%) compared to their counterparts. Preeclampsia was significantly associated with a higher risk of adverse pregnancy outcomes (adjusted odds ratio [AOR]: 2.87; 95% confidence interval [CI]: 1.62–5.09), whereas COVID-19 was not (AOR: 0.79; 95% CI: 0.42–1.46).

Conclusion: COVID-19 was not associated with increased risk of adverse pregnancy outcomes. Conversely, preeclampsia significantly predicted adverse outcomes.

Contribution: These findings underscore the importance of targeted antenatal interventions to mitigate maternal and neonatal morbidity during future pandemics.

Keywords: COVID-19; pregnancy; maternal; neonatal; South Africa.

Introduction

Background

The global coronavirus disease 2019 (COVID-19) pandemic has shown an increased burden of morbidity and mortality that has affected many populations worldwide.[1] Evidence suggests that the pandemic has also resulted in additional maternal and newborn mortality, particularly in low- and middle-income countries (LMICs).[2] The effects of COVID-19 on maternal, newborn and child health (MNCH) services in countries such as Bangladesh, Nigeria and South Africa highlight the need for a tailored pandemic response in LMICs.[3]

Maternal deaths during the COVID-19 pandemic raised significant concern, with an estimated 287 000 deaths globally in 2020. Low- and middle-income countries (LMICs) accounted for 95% of these deaths, with sub-Saharan Africa (SSA) contributing 70% (202 000),[4] highlighting the region's critical burden. Similarly, studies in South Africa found high COVID-19-related maternal mortality among pregnant women admitted for COVID-19, with the largest study reporting a 14.7% increase in maternal mortality.[5]

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During the 2020–2021 COVID-19 pandemic, more than 4 million COVID-19-related neonatal deaths occurred globally, with the highest numbers documented from SSA.[6] Similar increases in neonatal mortality were observed in LMICs, with a 27% rise, resulting in 6.7 deaths per 1000 live births.[7] In addition, a global increase in stillbirths was reported, with 1.9 million stillbirths recorded in 2021, over 75% of which occurred in SSA.[8] In South Africa, the first wave of the COVID-19 pandemic in 2020 was associated with a perinatal mortality rate of 57 per 1000 live births, which included 22 stillbirths and 16 neonatal deaths.[9] This rate represented an increase compared to the pre-pandemic period, where the neonatal mortality rate had been relatively stable at 12 per 1000 live births from 2014 to 2019, with a slight decrease to 11 per 1000 in 2018.[10]

The COVID-19 pandemic has further been associated with increases in preterm birth rates and low birth weight (LBW) babies. In 2020, approximately 19.8 million newborns (14.7% of all babies) worldwide were born with LBW.[11] A larger study conducted in 2021 estimated that the pooled prevalence of LBW among infants born in SSA was approximately 9.8%,[12] reflecting a 4.1% increase in LBW from 2018 to 2020.[13] In contrast, South Africa experienced a 3% decrease in the prevalence of LBW infants during the pandemic period, estimated at 11%,[14] compared with a 15% increase in 2019, before the pandemic.[15]

Pregnancy outcomes that diverge from a normal live birth, such as LBW, preterm birth, stillbirth or perinatal death, are classified as adverse.[16] Several determinants have been linked to an increased risk of these adverse pregnancy outcomes, including COVID-19,[17,18] chronic medical conditions,[19] and obstetric factors such as nulliparity, multiparity, grand multiparity,[19,20] preeclampsia,[21] younger maternal age,[20] advanced maternal age of ≥ 35 years,[21] and a history of adverse pregnancy outcomes.[16] Among pregnant women with COVID-19, preexisting comorbidities such as diabetes mellitus, hypertension and anaemia,[22] have also been reported to be associated with an elevated risk of adverse outcomes.

While these factors are well known to negatively impact pregnancy, with the presence of COVID-19, there appears to be a high propensity for maternal and neonatal morbidity and mortality.[23] Studies have shown that pregnant women with COVID-19 have significantly higher odds of preterm birth and stillbirth than women without COVID-19.[18,24,25] Moreover, data from global studies, including in South Africa, have shown an increased risk of maternal death among pregnant women with COVID-19.[17,18,26,27,28] These findings collectively suggest that COVID-19 is a strong predictor of adverse pregnancy outcomes. However, literature regarding predictors of adverse pregnancy outcomes in South Africa and the broader SSA region is lacking, particularly in relation to the specific effects of COVID-19 on maternal and neonatal health during the pandemic. This study aimed to investigate the associations between COVID-19 and adverse pregnancy outcomes among pregnant women admitted to Tygerberg Hospital, Cape Town, South Africa.

Research methods and design

Study design

We conducted a secondary analysis of data from the Department of Obstetrics and Gynecology at Tygerberg Hospital, Cape Town, South Africa, drawn from a larger multi-country retrospective cohort study conducted in SSA. These data were collected during the COVID-19 pandemic period, from pregnant women who were hospitalised at Tygerberg Hospital between 01 March 2020 and 31 March 2021.

Study setting

Located in Parow, Cape Town, Tygerberg Hospital is a prominent tertiary care facility. Officially opened in 1976, it is the largest hospital in Western Cape province and the second largest in South Africa, with a capacity of 1899 beds. The hospital provides services to more than 3.6 million people, either directly or via secondary hospitals, such as Paarl and Worcester Hospitals.[29] During the first through third waves of the COVID-19 pandemic, COVID-19 patients were referred and admitted to this hospital.

Data collection and sources

The dataset on COVID-19 and pregnancy outcomes was sourced from the African Forum for Research and Education in Health (AFREHealth) consortium as part of a multi-country study assessing the effect of COVID-19 on pregnancy. Data collection at the study site was conducted under the COVID-19 Research Response collaboration. Primary data were retrospectively extracted from the medical records of all pregnant women admitted to the Department of Obstetrics and Gynecology at the tertiary hospital, who underwent real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, with results categorised as positive or negative.

Collected data were entered into the Research Electronic Data Capture (REDCap) system, a secure, web-based electronic platform specifically designed for research data management. Variables captured included maternal demographics (age, parity, gestational age at admission), clinical characteristics (human immunodeficiency virus [HIV] serostatus, tuberculosis [TB] status [active and past], malaria, syphilis, asthma, hypertension, diabetes mellitus, and obstetric conditions such as gestational anaemia, preeclampsia, and haemorrhage [antepartum or postpartum], previous stillbirth, previous preterm birth), as well as pregnancy and neonatal outcomes (miscarriage < 28 weeks, stillbirth > 28 weeks, preterm birth < 37 weeks, LBW < 2500 g, neonatal and maternal mortality). In instances of missing data on preexisting comorbidities, the absence of documentation was assumed to indicate the absence of that comorbidity, minimising potential bias.

Study population, eligibility criteria and sample size

All pregnant women admitted to Tygerberg Hospital during the study period were screened for eligibility. Women were eligible for inclusion if they underwent routine SARS-CoV-2 testing by RT-PCR upon admission and had a definitive result (either positive or negative). Only those with complete clinical records for both maternal and neonatal outcomes were included in the analysis. Women with inconclusive SARS-CoV-2 test results or missing outcome data were excluded. A minimum sample size of 385 was estimated to provide sufficient power to detect a significant difference between the comparison groups, assuming an event rate of 50% and a 95% confidence level (CI) (z-value of 1.96). However, after applying the inclusion criteria, 350 eligible records with complete data were available for analysis.

Outcome measures

The main outcome for this study was defined as a composite of adverse pregnancy outcomes, consisting of maternal or neonatal events. For maternal outcomes, we considered death as the adverse outcome. For neonatal outcomes, we considered stillbirth (delivery of a dead foetus at > 28 weeks gestation), preterm birth (birth occurring at < 37 weeks gestation), neonatal death (death of a live birth infant occurring at ≤ 28 days post birth), and LBW (birth weight of < 2500 g) as adverse outcomes. Women who experienced any of these outcomes were considered to have had an adverse outcome.

Exposure variables

The study's exposure variables included COVID-19, which was defined as a positive SARS-CoV-2 test confirmed by RT-PCR assay. Other variables included maternal age, which was defined as an age of ≤ 19 years, 20–34 years and ≥ 35 years, maternal weight, parity (parity of 0, 1–3 and ≥ 4 viable pregnancies), hypertension (blood pressure leading to ≥ 140/90 mmHg), known or newly diagnosed diabetes mellitus (fasting plasma glucose [FPG] leading to ≥ 7 mmol/L at any time during pregnancy and/or 2 h-PG ≥ 11.1 mmol/L in the oral glucose tolerance test [OGTT]), gestational anaemia (< 11 g/dL in the third trimester), HIV (confirmed by the HIV enzyme-linked immunosorbent assay [ELISA] test at or during admission if HIV status was not known), TB (active TB and previous TB history), asthma, syphilis (determined by positive Venereal Diseases Research Laboratory [VDRL] test), and preeclampsia or eclampsia (blood pressure leading to ≥ 140/90 mmHg) from 20 weeks gestation associated with elevated protein levels in the urine. In the context of this study, the term preeclampsia was used to refer to both preeclampsia and eclampsia), haemorrhage (antepartum haemorrhage [vaginal bleeding from 24+ weeks gestation], and postpartum haemorrhage [loss of > 500 mL of blood in 24 h post-vaginal delivery or > 1000 mL of blood post-caesarean section delivery]), and previous history of stillbirth, preterm birth, including a family history of any other of the abovementioned comorbidities.

Data management

Data were systematically entered into the REDCap system by trained personnel following standardised data collection procedures. A data entry supervisor subsequently performed rigorous quality assurance checks to ensure the dataset's accuracy, completeness and integrity. After quality control and data cleaning, the finalised dataset was imported into Stata® version 17.0 (Stata Corp., College Station, Texas, United States [US]) for recoding and statistical analysis. Variables such as maternal age were categorised as '< 19 years, 20–34 years, and 35–45 years'; parity as 'nulliparity: 0, low parity: 1–3, and multiparity: 4–8'; gestational age as '0–12 weeks: first trimester, 13–27 weeks: second trimester, and 28–42+ weeks: third trimester'; and length of hospital stay was grouped into '0–4 days and ≥ 5 days'.

Statistical analysis

Data were analysed using Stata/SE® (version 17.0, Stata Corp LLC, College Station, Texas, US) statistical software. Continuous independent variables were summarised as means with standard deviations (s.d.) for normally distributed data or as medians with interquartile ranges (IQR) for skewed data. Categorical variables were presented as frequencies and percentages.

Comparisons of adverse pregnancy outcome proportions across categorical variables were conducted using Pearson's chi-square test or Fisher's exact test, as appropriate. For continuous variables, independent sample t-tests or Mann–Whitney U tests were applied based on data distribution. Statistical significance for bivariate comparisons was assessed at a two-sided alpha level of 0.05.

Univariate logistic regression analyses were first performed to evaluate the association between each predictor and adverse pregnancy outcomes (see Appendix 1). Variables with $p < 0.20$ in univariable analysis were included in a multivariable logistic regression model to adjust for potential confounding. Adjusted odds ratios (AOR) with corresponding 95% CIs were reported as measures of association. Model fit and multicollinearity were assessed to ensure robustness of the final model. All statistical tests were two-sided, with $p < 0.05$ considered indicative of statistical significance.

The final multivariable logistic regression model was assessed for goodness-of-fit using the Hosmer-Lemeshow test, with a $p > 0.05$ indicating adequate model fit. Multicollinearity was evaluated using variance inflation factors (VIFs), and no evidence of multicollinearity was observed among the included covariates (all VIFs < 2). Residuals and influential observations were reviewed to ensure model stability. These diagnostic checks confirmed that the model assumptions were met and that the final model provided a valid estimate of the association between predictors and adverse pregnancy outcomes.

Ethical considerations

Ethical clearance was obtained from the Health Research Ethics Committee (HREC) for Stellenbosch University (Reference No: S22/11/239_Sub Study N20/04/002_ COVID-19). This study utilised secondary data collected as part of a multinational cohort study conducted in SSA.[28] Informed consent to participate was obtained from all participants in the original cohort study, in accordance with the ethical guidelines and national regulations applicable at the time of data collection.

Results

Sociodemographic characteristics of pregnant women

A total of 350 pregnant women were included in the analysis. The mean maternal age was 29.8 years (s.d. = 6.99), with the majority aged 20–34 years (74.3%). Nulliparity was observed in 51.4% of participants, and 77.4% were admitted during the third trimester. The mean maternal weight was 92.6 kg (s.d. = 25.81). The most prevalent preexisting comorbidities were HIV infection (24.9%) and hypertension (19.7%). Among obstetric conditions, gestational anaemia (44.0%) and preeclampsia (36.8%) were most reported. Coronavirus disease 2019, confirmed by RT-PCR testing, was diagnosed in 47.1% (*n* = 165/350) of participants, while 52.9% (*n* = 185/350) tested negative. The median length of hospital stay was 5 days (IQR: 3–9) (Table 1).

TABLE 1: Sociodemographic and clinical characteristics of pregnant women (N = 350).

Characteristic	*n*	%	Mean	s.d.	Median	IQR
Demographics						
Maternal age group (years):	-	-	-	-	-	-
< 19	17	4.90	-	-	-	-
20–34	260	74.30	-	-	-	-
35–45	73	20.90	-	-	-	-
Parity:	-	-	-	-	-	-
Nulliparity (0)	180	51.40	-	-	-	-
Low parity (1–3)	155	44.30	-	-	-	-
Multiparity (4–8)	15	4.30	-	-	-	-
Maternal weight (kg)	-	-	92.6	25.81	-	-
Gestational age at admission (weeks):	-	-	-	-	-	-
0–12 (first trimester)	11	3.20	-	-	-	-
13–27 (second trimester)	66	19.40	-	-	-	-
28–42+ (third trimester)	263	77.40	-	-	-	-
Preexisting comorbidities						
HIV	87	24.90	-	-	-	-
TB:	-	-	-	-	-	-
Active	7	2.00	-	-	-	-
Past	27	7.70	-	-	-	-
Hypertension	69	19.70	-	-	-	-
Diabetes mellitus	31	8.90	-	-	-	-
Syphilis	7	2.80	-	-	-	-
Asthma	29	8.30	-	-	-	-
COVID-19:	-	-	-	-	-	-
Positive	165	47.10	-	-	-	-
Negative	185	52.90	-	-	-	-
Obstetric conditions						
Gestational anaemia (Hb < 11 g/dL)†	40	44.00	-	-	-	-
Preeclampsia	123	36.80	-	-	-	-
Haemorrhage (antepartum/postpartum)	23	6.90	-	-	-	-
Previous stillbirth	5	5.50	-	-	-	-
Previous preterm birth	12	13.20	-	-	-	-
Hospitalisation						
Length of hospital stay (days):	-	-	-	-	5	3–9
0–4	138	41.10	-	-	-	-
≥ 5	198	58.90	-	-	-	-

Note: The table presents descriptive characteristics of the full study population (N = 350). Some variables appeared more prevalent in specific subgroups; however, statistical significance was not assessed in this table.

COVID-19, coronavirus disease 2019; TB, tuberculosis; HIV, human immunodeficiency virus; IQR, interquartile range; s.d., standard deviation.

†, Denominator based on a subgroup of participants with available haemoglobin data (*n* = 91).

Proportion of adverse pregnancy outcomes by women's characteristics

Table 2 summarises the distribution of adverse pregnancy outcomes by selected maternal sociodemographic and clinical characteristics. The overall prevalence of adverse outcomes in the study cohort was 47.7% (*n* = 167/350). Younger women (< 19 years) exhibited the highest proportion of adverse events compared to those aged 20–34 years and 35–45 years (52.9% vs. 48.1% and 45.2%, respectively), although these differences were not statistically significant (p = 0.825). The mean maternal weight was lower among women with adverse outcomes (87.2 kg, s.d. = 26.42) than among those without these outcomes (87.2 kg, s.d. = 26.42 vs. 96.4 kg, s.d. = 24.96; p = 0.127).

Multiparous women had a higher prevalence of adverse outcomes compared to those with low parity and nulliparity (53.3% vs. 49.7% and 45.6%, respectively; p = 0.682). Interestingly, women with COVID-19 had a lower proportion of adverse outcomes than those without COVID-19 (43.6% vs. 51.4%; p = 0.149). Similarly, adverse outcomes were slightly lower among women with HIV than among HIV-negative women (44.8% vs. 48.7%, p = 0.534).

Among those with preexisting comorbidities, higher proportions of adverse outcomes were observed in women with active TB (71.4% vs. 51.4%), past TB (55.6% vs. 47.1%), syphilis (57.1% vs. 51.2%), hypertension (53.6% vs. 46.3%), asthma (51.7% vs. 47.4%), and diabetes mellitus (58.1% vs. 46.7%); however, none of these associations were statistically significant.

A statistically significant association was identified between preeclampsia and adverse outcomes (68.3% vs. 31.7%; $p < 0.001$). Higher proportions of adverse outcomes were also noted in women with obstetric haemorrhage (56.5% vs. 48.7%), gestational anaemia (47.5% vs. 33.3%), and those with a previous stillbirth (60.0% vs. 37.2%), although these differences were not statistically significant.

Predictors of adverse pregnancy outcomes

Table 3 presents results of the crude and adjusted estimates for adverse pregnancy outcomes. In the univariate analysis, preeclampsia was the only variable

TABLE 2: Proportion of adverse pregnancy outcomes by sociodemographic and clinical characteristics.

Predictor	Adverse outcome (*n*)	%	Mean	s.d.	No adverse outcome (*n*)	%	Mean	s.d.	*p*-value
Overall prevalence	167	47.7	-	-	183	52.3	-	-	-
A) Demographic factors									
Maternal age group (years):	-	-	-	-	-	-	-	-	0.825
< 19	9	52.9	-	-	8	47.1	-	-	-
20–34	125	48.1	-	-	135	51.9	-	-	-
35–45	33	45.2	-	-	40	54.8	-	-	-
Maternal weight (g)	-	-	87.16	26.42	-	-	96.41	24.96	0.127
Parity:	-	-	-	-	-	-	-	-	0.682
Nulliparity	82	45.6	-	-	98	54.4	-	-	-
Low parity	77	49.7	-	-	78	50.3	-	-	-
Multiparity	8	53.3	-	-	7	46.7	-	-	-
B) Preexisting comorbidities									
COVID-19:	-	-	-	-	-	-	-	-	0.149
Positive	72	43.6	-	-	93	56.4	-	-	-
Negative	95	51.4	-	-	90	48.7	-	-	-
HIV:	-	-	-	-	-	-	-	-	0.534
Positive	39	44.8	-	-	48	55.2	-	-	-
Negative	128	48.7	-	-	135	51.3	-	-	-
TB: active:	-	-	-	-	-	-	-	-	0.204
Yes	5	71.4	-	-	2	28.6	-	-	-
No:	162	47.2	-	-	181	52.8	-	-	-
Past	-	-	-	-	-	-	-	-	0.396
Yes	15	55.6	-	-	12	44.4	-	-	-
No	152	47.1	-	-	171	52.9	-	-	-
Syphilis:	-	-	-	-	-	-	-	-	0.758
Yes	4	57.1	-	-	3	42.9	-	-	-
No	125	51.2	-	-	119	48.8	-	-	-
Hypertension:	-	-	-	-	-	-	-	-	0.273
Yes	37	53.6	-	-	32	46.4	-	-	-
No	130	46.3	-	-	151	53.7	-	-	-
Asthma:	-	-	-	-	-	-	-	-	0.652
Yes	15	51.7	-	-	14	48.3	-	-	-
No	152	47.4	-	-	169	52.7	-	-	-
Diabetes mellitus:	-	-	-	-	-	-	-	-	0.227
Yes	18	58.1	-	-	13	41.9	-	-	-
No	149	46.7	-	-	170	53.3	-	-	-
C) Obstetric conditions									
Gestational anaemia (Hb < 11 g/dL):	-	-	-	-	-	-	-	-	0.170
Yes	19	47.5	-	-	21	52.5	-	-	-
No	17	33.3	-	-	34	66.7	-	-	-
Preeclampsia	-	-	-	-	-	-	-	-	**< 0.001**
Yes	84	68.3	-	-	39	31.7	-	-	-
No	79	37.4	-	-	132	62.6	-	-	-
Haemorrhage (antepartum/postpartum):	-	-	-	-	-	-	-	-	0.470
Yes	13	56.5	-	-	10	43.5	-	-	-
No	152	48.7	-	-	160	51.3	-	-	-
Previous stillbirth:	-	-	-	-	-	-	-	-	0.309
Yes	3	60.0	-	-	2	40.0	-	-	-
No	32	37.2	-	-	54	62.8	-	-	-
Previous preterm birth:	-	-	-	-	-	-	-	-	0.695
Yes	4	33.3	-	-	8	66.7	-	-	-
No	31	39.2	-	-	48	60.8	-	-	-

Note: Bolded values indicate statistical significance at $p < 0.05$.
COVID-19, coronavirus disease 2019; TB, tuberculosis; HIV, human immunodeficiency virus; s.d., standard deviation.

significantly associated with an increased risk of adverse pregnancy outcomes (OR = 3.60; 95% CI: 2.25–5.76). After adjusting for maternal age, parity, COVID-19, HIV, TB, syphilis, hypertension, asthma, diabetes mellitus, preeclampsia, and haemorrhage, preeclampsia (AOR = 2.87; 95% CI: 1.62–5.09) remained the only independent predictor of adverse pregnancy outcomes. The COVID-19 in pregnancy was not significantly associated with adverse pregnancy outcomes in the adjusted model (AOR = 0.79; 95% CI: 0.42–1.46).

TABLE 3: Crude and adjusted logistic regression estimates for adverse pregnancy outcomes.

Predictor variable	Crude			Adjusted		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Maternal age (20–34 vs. < 19)	0.82	0.31–2.20	0.698	1.17	0.37–3.74	0.787
Maternal age (35–45 vs. < 19)	0.73	0.25–2.11	0.566	0.76	0.20–2.86	0.684
Maternal weight (continuous)	0.99	0.97–1.00	0.129	-	-	-
Parity (low parity vs. nulliparity)	1.18	0.77–1.81	0.451	1.14	0.59–2.21	0.703
Parity (multiparity vs. nulliparity)	0.84	0.49–1.43	0.522	1.43	0.38–5.33	0.594
COVID-19 (positive vs. negative)	1.36	0.89–2.08	0.150	0.79	0.42–1.46	0.447
HIV (positive vs. negative)	0.86	0.53–1.39	0.534	0.75	0.38–1.46	0.400
Active TB	2.79	0.53–14.59	0.223	2.10	0.35–12.68	0.419
Past TB	1.41	0.64–3.10	0.398	3.47	0.97–12.34	0.055
Syphilis	1.27	0.28–5.79	0.758	1.35	0.25–7.28	0.726
Hypertension	1.34	0.79–2.28	0.274	0.87	0.40–1.88	0.721
Asthma	1.19	0.56–2.55	0.652	1.19	0.41–3.51	0.748
Diabetes mellitus	1.58	0.75–3.33	0.230	1.61	0.60–4.30	0.341
Gestational anaemia (Hb < 11g/dL)	1.81	0.77–4.24	0.172	-	-	-
Preeclampsia	**3.60**	**2.25–5.76**	**< 0.001**	**2.87**	**1.62–5.09**	**< 0.001**
Haemorrhage (antepartum/postpartum)	1.37	0.58–3.21	0.471	2.92	0.27–31.94	0.380
Previous stillbirth	2.53	0.40–15.97	0.323	-	-	-
Previous preterm birth	0.77	0.21–2.79	0.696	-	-	-

Note: Bolded values indicate statistical significance at $p < 0.05$.
COVID-19, coronavirus disease 2019; TB, tuberculosis; HIV, human immunodeficiency virus; CI, confidence interval; OR, odds ratio.
–, indicates the variable was not included in the final adjusted model due to limited data or lack of significance in univariate analysis ($p \geq 0.2$).

Discussion

This study aimed to investigate the association between COVID-19 and adverse pregnancy outcomes among women hospitalised at Tygerberg Hospital in South Africa. Nearly half of the participants (47.7%) experienced at least one adverse outcome, a prevalence higher than that reported in similar studies from SSA,[30,31] where estimates range from 21% to 30%. This discrepancy likely reflects methodological differences. While previous studies focused primarily on neonatal outcomes such as stillbirth, LBW, and preterm birth,[31] this study incorporated both maternal and neonatal endpoints offering a more comprehensive assessment of pregnancy-related risk.

Although differences across age categories were not statistically significant, women aged < 19 years had the highest prevalence (52.9%). This finding is consistent with evidence from Turkey,[32] where younger maternal age has been associated with increased risk of preterm birth and LBW. In contrast, a retrospective study from China reported a nonlinear association, with both younger and older maternal age associated with increased risk of adverse outcomes.[33] These variations may stem from contextual differences in maternal age distribution, healthcare access, and socioeconomic factors across settings. In South Africa, most first births occur between the ages of 20 and 29 years,[34] consistent with this study's age distribution, where most women were aged 20–34 years (74.3%). By comparison, the average age at first birth in China is typically above 30 years.[35] The COVID-19 pandemic likely compounded these risks among younger pregnant women by further disrupting ANC access and amplifying socioeconomic instability.[36,37] In South Africa, where adolescent pregnancy rates remain prevalent,[38] these findings underscore the need for targeted maternal health strategies for younger women, especially during public health emergencies.

Multiparity was also associated with a higher prevalence of adverse outcomes, although the difference was not statistically significant. Evidence on the relationship between parity and pregnancy risk is mixed. While a study from Ethiopia reported increased risk among multiparous women,[39] data from China suggest a potential protective effect in well-resourced settings. These contrasting findings likely reflect differences in health system capacity, population health status, and access to quality ANC. In this study, which included a high proportion of women with preexisting comorbidities and limited healthcare access, the compounded risks of multiparity may have contributed to the observed trend. These findings reinforce the importance of context-specific ANC interventions for multiparous women in LMICs, especially during global health crises.

The prevalence of adverse outcomes was also higher among women with preexisting comorbidities and obstetric conditions. A meta-analysis of 12 international studies involving 13 136 pregnant women similarly identified hypertension, diabetes, and cardiovascular diseases as significant predictors of adverse pregnancy outcomes.[40] Findings from Canada also showed that women with preexisting conditions faced higher risks of maternal morbidity and mortality, which were further exacerbated during the COVID-19 pandemic.[41] In LMICs, these risks were likely intensified by resource limitations, reduced access to routine ANC, and increased socioeconomic barriers. The combined effects of preexisting comorbidities and healthcare system constraints likely contributed to the higher prevalence of adverse outcomes observed in this cohort. These findings emphasise the urgency of prioritising targeted interventions and continuity of care for high-risk pregnant women, particularly during global health emergencies.

Preeclampsia emerged as the only statistically significant independent predictor of adverse pregnancy outcomes in this study. This finding aligns with prior literature,[42] including the INTERCOVID study, which demonstrated a 2.53-fold increase in the risk of preterm birth and perinatal morbidity among women with preeclampsia.[43] The high prevalence of hypertension and preeclampsia in this cohort reinforces the critical role of hypertensive disorders in adverse maternal and neonatal outcomes. Although some studies have reported an association between COVID-19 and increased risk of preeclampsia, our finding did not confirm this relationship. However, the identification of preeclampsia as a key predictor supports the need for early identification, close monitoring, and proactive management of hypertensive disorders during pregnancy, mainly during public health crises like the COVID-19 pandemic.

While preeclampsia was significantly associated with adverse pregnancy outcomes, COVID-19 was not. This contrasts with several large-scale studies reporting increased risks of adverse outcomes among pregnant women with COVID-19.[17,18,24,25,26] Notably, a higher proportion of adverse outcomes was observed among pregnant women without COVID-19 compared to those with COVID-19 (51.4% vs. 43.6%). This unexpected finding may be explained by selection bias, wherein women with severe obstetric complications unrelated to COVID-19 were more likely to be admitted and tested. Unmeasured confounding factors such as reduced access to ANC, socioeconomic disparities, or delays in healthcare-seeking may also have disproportionately affected the COVID-negative group. Furthermore, the lack of association between COVID-19 and adverse outcomes in this study may be attributed to limited statistical power, differences in study design, and contextual variation compared to global data. Studies demonstrating associations typically involved larger cohorts, systematic reviews, or meta-analyses conducted outside SSA, where baseline risk profiles differ. Nonetheless, this study contributes valuable, region-specific evidence that enhances understanding of adverse pregnancy outcomes and their predictors during the COVID-19 pandemic, addressing a critical gap in the South African and broader SSA literature.

One key limitation of this study is its relatively small sample size, which may have reduced the statistical power to detect significant associations within specific subgroups. The retrospective design also introduces the potential for residual confounding, selection bias, and incomplete data capture. Despite these limitations, the use of multivariable modelling allowed for adjustment of key confounders, enhancing the internal validity of our findings. Importantly, this study provides context-specific evidence from a resource-limited setting where empirical data remain scarce. These findings advance our broader understanding of adverse pregnancy outcomes during the COVID-19 pandemic and offer actionable insights to inform clinical decision-making. Future research involving larger, prospective cohorts across diverse settings is warranted to confirm these associations and support the development of targeted maternal health interventions.

Conclusion

In conclusion, while COVID-19 was not independently associated with adverse pregnancy outcomes in this cohort, preeclampsia emerged as a strong and statistically significant predictor. Although not statistically significant, the higher prevalence of adverse outcomes among women aged < 19 years, those with multiparity, and those with preexisting comorbidities highlights important clinical and public health vulnerabilities. These findings underline the imperative to strengthen ANC services, prioritise early detection and management of hypertensive disorders in pregnancy, and implement context-specific maternal health interventions in LMICs, especially amid global health crises. Future prospective studies with larger, more diverse cohorts are essential to validate these findings and inform evidence-based, context-specific maternal health strategies in SSA.

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Competing interests

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Authors' contributions

M.N. and P.S.N. conceived and developed the concept of the presented idea. M.N. performed the data analysis, with verification by I.L.S., M.N. wrote the article, while R.C.M., V.N., I.L.S., L.N.S., P.S.N., and E.L. reviewed and provided critical feedback. All authors contributed to the discussion of the results and gave their approval for the final article.

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Data availability

The data supporting this study's findings are not publicly accessible because of sensitivity considerations, such as human subject data. However, they can be obtained from the corresponding author, P.S.N., upon reasonable request.

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Appendix 1

Logistic regression model

In logistic regression, the model predicts the log odds of the dependent binary variable (often coded as 0 or 1) being 1. The model equation is:

$$\operatorname{Iog}\left(\frac{p}{1-p}\right)=\beta_0+\beta_1 X_1+\beta_2 X_2+\cdots+\beta_k X_k \quad \text{[Eqn 1]}$$

Where:

- p is the probability of the outcome occurring (e.g., probability of adverse pregnancy outcome).
- The variables X_1, X_2..., X_k represent predictor variables.
- p/1−p is the odds of the outcome occurring.
- Log (p/1−p) is the log-odds of the outcome (also known as the logit function).
- β_0 is the intercept term.
- β_1, β_2 ..., β_k are the coefficients for the predictor variables X_1, X_2..., X_k. Each coefficient β_i represents the effect of the corresponding predictor variable X_i on the log-odds of the outcome.

This equation can be rewritten to express the probability p directly:

$$p=\frac{1}{1+e^{-(\beta_0+\beta_1 X_1+\beta_2 X_2+\cdots+\beta_k X_k)}} \quad \text{[Eqn 2]}$$

Assumptions of logistic regression

1. **Linearity of the Log Odds:** Logistic regression assumes a linear relationship between predictor variables and the log odds of the outcome.
2. **Independence of Observations:** Each observation should be independent of the others, ensuring that no data point influences another.
3. **No Perfect Multicollinearity:** Predictor variables should not be perfectly correlated with one another, as perfect multicollinearity makes it impossible to determine the unique effect of each predictor on the outcome.
4. **Sufficient Sample Size:** Logistic regression performs best with an adequate sample size, as small samples can lead to unreliable and unstable estimates.