CLINICAL CHARACTERISTICS, OUTCOMES AND EPIDEMIOLOGY OF PREGNANT WOMEN HOSPITALISED WITH COVID-19 IN SOUTH AFRICA

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FOREWORD

The COVID-19 pandemic continues unabated. South Africa has weathered two COVID-19 waves to date, the second having been more severe than the first. The DATCOV hospital surveillance system has enabled several epidemiological analyses of the progression of this disease in South Africa, including the identification of risk factors and comorbidities associated with COVID-19. This report compares the progression and severity of COVID-19 infection in hospitalized pregnant women against that of non-pregnant women of childbearing age. The data suggest that COVID-19 positive pregnant women do not have a higher case fatality ratio than non-pregnant women of childbearing age, but pregnant women of older age, and those with hypertension and diabetes, are at higher risk of mortality.

This is the eighth special issue of our COVID-19 series, and we trust that you will find this information useful as we continue to grapple with SARS-CoV-2 and its new variant (501Y.V2).

Prof Basil Brooke - Editor

VOLUME 18. SUPPLEMENTARY ISSUE 8

CLINICAL CHARACTERISTICS, OUTCOMES AND EPIDEMIOLOGY OF PREGNANT WOMEN HOSPITALISED WITH COVID-19 IN SOUTH AFRICA, 5 MARCH 2020 – 20 FEBRUARY 2021

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SUMMARY

As of 20 February 2021, 214,547 laboratory-confirmed COVID-19 hospital admissions were reported to DATCOV in the public and private healthcare sectors of all nine provinces in South Africa. Of these, 48,825 (22.8%) were women of childbearing age (15-49 years). Pregnant women made up 5,105 (10.5%) of all COVID-19 admissions of women of childbearing age. The cumulative incidence of COVID-19 admissions in pregnant women was 543.3 per 100,000 population (Table 1), while the cumulative incidence for non-pregnant women of childbearing age was 287.5 per 100,000 population. The risk ratio for hospital admission among pregnant women of childbearing age was 1.9, indicating that pregnant women were at increased risk of hospitalization compared to non-pregnant women of childbearing age. Western Cape Province had the highest cumulative incidence of COVID-19 admissions in pregnant women (1567.4 per 100,000) and Limpopo Province the lowest (208.6 per 100,000). Most COVID-19 admissions in pregnant women were in four provinces, Western Cape with 1,515 (29.7%), Gauteng with 1,236 (24.2%), KwaZulu-Natal with 769 (15.1%) and Eastern Cape with 476 (9.3%), amounting to 78.3% of all admissions of pregnant women. Of these hospitalizations, pregnant women were generally younger than non-pregnant women of childbearing age and had a lower prevalence of comorbid disease. The in-hospital case-fatality ratio (CFR) for pregnant women was 169/4,887 (3.5%), lower than that of non-pregnant women of childbearing age with 4,102/41,125 (10.0%, p<0.001). From multivariable analysis, risk factors associated with in-hospital mortality among COVID-19 pregnant women were: age 25-34 years [aOR=2.5, 95% CI (1.2-5.5)] and ≥35 years [aOR=3.7, 95% CI (1.7-8.1) compared to <25 years; hospital admission in the public health sector [aOR=2.0, 95% CI (1.3-3.1)]; hypertension [aOR=2.5, 95% CI (1.6-4.1)], diabetes [aOR=1.9, 95% CI (1.1-3.4)], and admission to a facility in Free State Province [aOR=2.3, 95% CI (1.1-4.6)] as compared to Western Cape Province.

VOLUME 18. SUPPLEMENTARY ISSUE 8

BACKGROUND

The coronavirus disease 2019 (COVID-19) pandemic has accelerated at a rapid rate, infecting more than 100 million individuals globally and resulting in over 2.3 million deaths as of 10 February 2021.[1] Infections in South Africa had passed 1.4 million with over 47,000 recorded deaths and an incidence rate of 2,499 per 100,000 population by this date.[1] South Africa experienced a second wave of SARS-CoV-2 with larger case numbers and a higher rate of increase than experienced in the first wave. In addition, a new variant (501Y.V2) of SARS-COV-2 that emerged in September 2020 has become the predominant lineage, as identified through genome sequencing during the second wave.[2]

Pregnant women are considered a vulnerable group for severe COVID-19 according to the World Health Organization (WHO).[3] The extent to which the virus affects pregnant women and pregnancy outcomes is still not clear.[4] Most pregnant women with COVID-19 were reported to have mild disease and a favourable clinical course. Pneumonia and severe COVID-19 disease are evidently more prevalent in overweight or obese pregnant women with underlying medical conditions.[4]

Here we describe the characteristics of hospitalized pregnant women in South Africa infected with SARS-CoV-2 from 5 March 2020 to 20 February 2021, and we report on the risk factors for COVID-19 mortality in this group.

METHODS

Study population

The study population included all SARS-CoV-2 infected women of childbearing age (15–49 years) admitted to hospital who were either pregnant or not pregnant.

Data collection procedure

Data were retrieved from the DATCOV surveillance system for the period of 5 March 2020 to 20 February 2021. DATCOV is a hospital surveillance system for COVID-19 admissions that was initiated on 1 April 2020. Data are submitted by public and private hospitals that have agreed to report COVID-19 admissions in all nine provinces of South Africa. A COVID-19 case was defined as a person with a positive reverse transcriptase polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 or a person who had a positive SARS-CoV-2 antigen test, who was admitted to hospital. An individual with severe disease was defined according to the WHO's criteria, including the requirement of oxygen, ventilation, extracorporeal membrane oxygenation (ECMO) or diagnosis with acute respiratory distress syndrome (ARDS).

The surveillance system was adapted from the WHO COVID-19 case reporting tool,[5] recording the following variables: demographic data, exposures such as occupation, and potential risk factors such as obesity, comorbid disease(s), smoking and pregnancy status. A patient was marked as pregnant or within six weeks post-partum if this was noted by the clinician in the patient's hospital records. Data on the reason for conducting COVID-19 testing was not always available. Some asymptomatic pregnant women were incidentally identified as COVID-19 positive during admission for confinement. Additional variables included level of care, treatment and outcomes of the hospital admission (discharged, transferred out to another hospital, or died).

DATA ANALYSIS

Descriptive statistics such as frequencies and percentages were used for categorical variables, while for continuous variables a median and interquartile range (IQR) was used. For the purpose of this study, we refer to pregnant women as pregnant or within six weeks post-partum, and of childbearing age.

Hospital admissions per 100,000 were calculated for pregnant and non-pregnant women of childbearing age (15-49 years), and determined as the number of admissions divided by the population size. As there are no data on the number of pregnant women in the country, we used live births for the period 2020 as a proxy for the total population of pregnant women. This is an underestimate as not all pregnancies result in a live birth. For non-pregnant women, the number of women aged 15-49 years in the country minus the estimated number of pregnant women of childbearing age according to the Statistics South Africa 2020 mid-year population estimates was used as the denominator. Hospital admissions per week were calculated as number of admissions of pregnant women of childbearing age per week divided by the total population size.

The risk ratio for hospital admission for pregnant women of childbearing age was calculated by dividing the cumulative incidence of admission for pregnant women by the cumulative incidence of admission for non-pregnant women of childbearing age.

The incidence for in-hospital death was calculated separately for pregnant and non-pregnant women of childbearing age. The numerator for pregnant deaths was all pregnant women who died in-hospital divided by the total population of pregnant women of childbearing age. The numerator for non-pregnant women of childbearing age was all non-pregnant women who died in-hospital divided by the total population of non-pregnant women. These incidences were expressed per 1000 population.

We performed multivariable logistic regression analyses to identify factors associated with in-hospital mortality and to compare characteristics of SARS-COV-2 admissions among pregnant women and non-pregnant women of childbearing age. Variables included in the models were age, sex, race, comorbidities (hypertension, diabetes, HIV, tuberculosis, malignancies, chronic kidney disease, chronic cardiac disease, asthma and obesity), health sector, province, level of care and length of stay. For each multivariable model we assessed all variables that were significant at $p<0.2$ on univariate analysis and dropped non-significant factors ($p\geq0.05$) with manual backward elimination. Pairwise interactions were assessed by inclusion of product terms for all variables remaining in the final multivariable additive model. We also reported the univariate association of all covariates evaluated in the analyses described above to the main outcomes (in-hospital mortality). The statistical analysis was implemented using Stata 15 (Stata Corp®, College Station, Texas, USA).

RESULTS

Incidence of COVID-19 admissions in pregnant and non-pregnant women

As of 20 February 2021, 214,547 cumulative laboratory-confirmed COVID-19 admissions were reported on DATCOV from 640 hospitals in nine provinces. Of these, 48,825 (22.8%) were women of childbearing age (15-49 years). Pregnant women made up 5,105 (10.5%) of all COVID-19 admissions among women of childbearing age. The cumulative incidence of COVID-19 admissions in pregnant women was 543.3 per 100,000 (Table 1), and that of non-pregnant women of child-bearing age was 287.5 per 100,000.

The risk ratio for hospital admission among pregnant women of childbearing age was 1.9, indicating that pregnant women were at increased risk of hospitalization compared to non-pregnant women of childbearing age. Western Cape Province had the highest cumulative incidence of COVID-19 admissions in pregnant women (1567.4 per 100,000) and Limpopo Province had the lowest (208.6 per 100,000).

Most COVID-19 admissions in pregnant women were in four provinces (Table 1): Western Cape 1,515 (29.7%), Gauteng 1,236 (24.2%), KwaZulu-Natal 769 (15.1%) and Eastern Cape 476 (9.3%) - amounting to 78.3% of all admissions in pregnant women. These provinces are also the most populous in South Africa.

Table 1. Cumulative incidence of laboratory-confirmed COVID-19 associated admissions in women of childbearing age (15-49 years), South Africa, 5 March 2020 – 20 February 2021, n = 48,825.

Province	Number of women of childbearing age (15-49 years)*	Total live-births (2020) (proxy for numbers of pregnant women)*	Number of cumulative COVID-19 admissions of non-pregnant women of childbearing age (15-49 years) n(%)	Incidence risk of cumulative COVID-19 admissions of non-pregnant women of childbearing age (15-49 years) per 100,000 population	Number of cumulative COVID-19 admissions of pregnant women 5 March 2020 – 20 February 2021 n (%)	Incidence risk of cumulative COVID-19 admissions of pregnant women per 100,000 live-births
Eastern Cape	1,643,734	98,578	5,573 (12.7)	338.3	476 (9.3)	482.8
Free State	786,612	44,279	2,344 (5.4)	315.8	273 (5.3)	616.5
Gauteng	4,546,078	216,592	12,295 (28.1)	284.0	1,236 (24.2)	570.7
KwaZulu Natal	3,106,471	195,527	8,976 (20.5)	308.4	769 (15.1)	393.3
Limpopo	1,497,496	128,476	1,346 (3.1)	98.3	268 (5.3)	208.6
Mpumalanga	1,270,574	83,325	1,523 (3.5)	128.3	313 (6.1)	375.6
North West	1,041,676	56,109	2,915 (6.7)	295.8	195 (3.8)	347.5
Northern Cape	330,693	20,034	856 (1.9)	278.4	60 (1.2)	299.5
Western Cape	1,924,254	96,657	7,892 (18.1)	431.8	1,515 (29.7)	1567.4
Total	16,147,588	939,577	43,720 (100)	287.5	5,105 (100)	543.3

*StatsSA mid-year live-births estimates 2020[6]
Admission rates were calculated as follows. Pregnant women: cumulative COVID-19 admissions of pregnant and post-partum women of childbearing age (15-49 years)/population live births * 100,000. Non-pregnant women: cumulative COVID-19 admissions of non-pregnant women of childbearing age (15-49)/women of reproductive age-livebirths * 100,000

COVID-19 ADMISSIONS AMONGST PREGNANT WOMEN OF CHILDBEARING AGE

The peak in admissions to hospital for the first wave for pregnant and non-pregnant women of childbearing age was in week 29 of 2020, and that for the second wave was in week 1 of 2021. The peak in weekly numbers of admissions of pregnant and non-pregnant women was higher in the second wave than in the first (Figure 1).

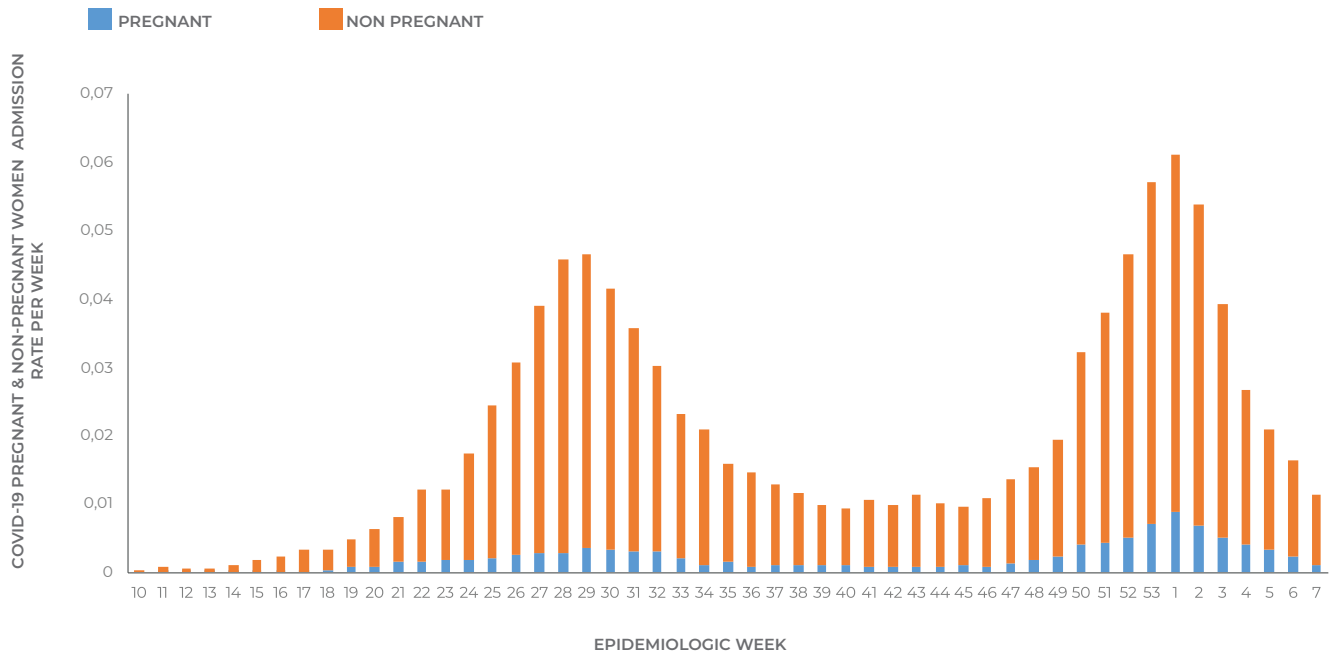

Figure 1. COVID-19 hospital admission rates for pregnant and non-pregnant women of childbearing age by epidemiologic week, South Africa, DATCOV, 5 March 2020 – 20 February 2021, n=48,810.

More COVID-19 admissions in pregnant women were reported in the private sector 2,831/5,105 (55.5%) than in the public sector 2,274/5,105 (44.5%) (p<0001). The peak of admissions in the private sector exceeded that of the public sector in the first wave whereas admissions in the public sector exceeded the private sector in the second wave (Figure 2).

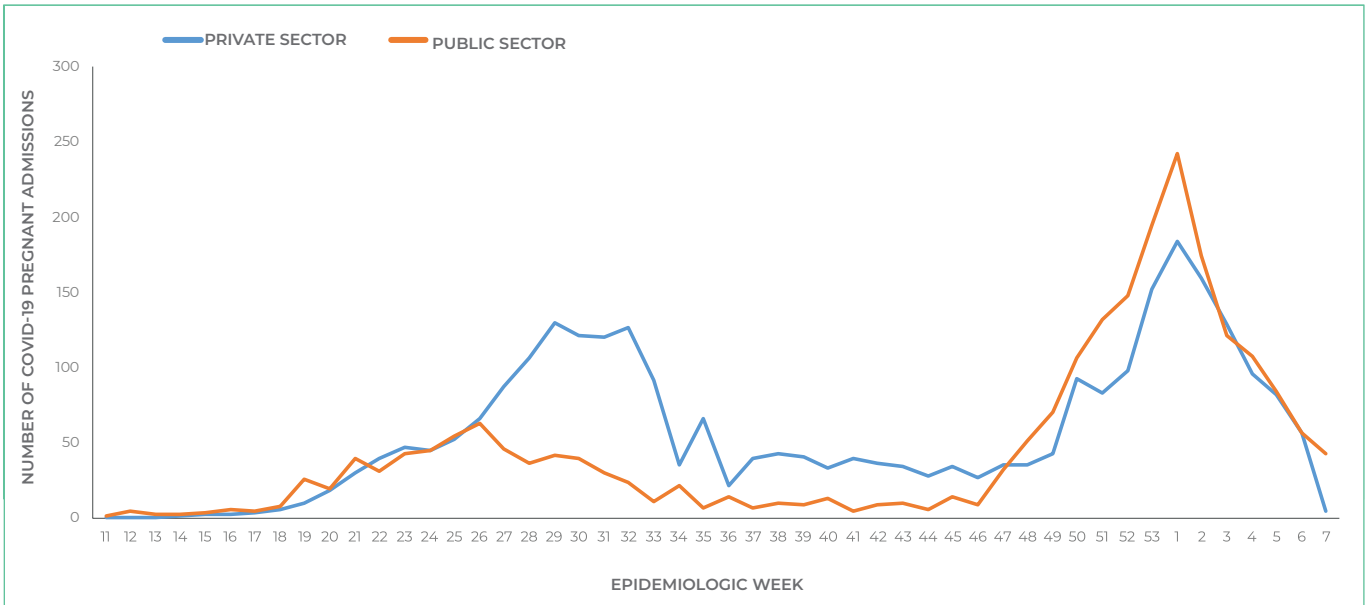

Figure 2. Number of reported COVID-19 admissions in pregnant women of childbearing age, by health sector and epidemiologic week, South Africa, 5 March 2020 - 20 February 2021, n=5,105.

During the first wave, most admissions in pregnant women of childbearing age were in Western Cape and Gauteng provinces. The peak of the second wave exceeded the first wave with most admissions in Western Cape, KwaZulu-Natal, Eastern Cape and Gauteng provinces (Figure 3).

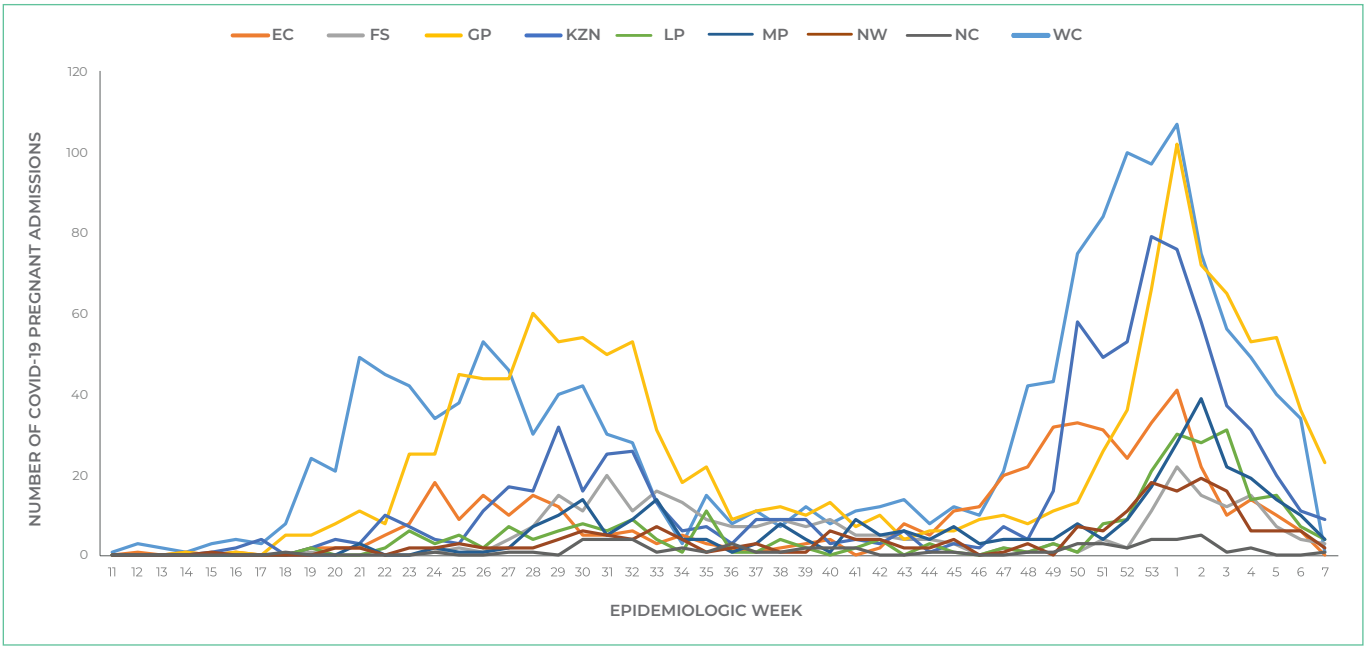

Figure 3. Number of reported COVID-19 admissions of pregnant women of childbearing age, by province and epidemiologic week, South Africa, 5 March 2020 - 20 February 2021, n=5,104.

EC= Eastern Cape Province, FS= Free State Province, GP= Gauteng Province, KZN= KwaZulu Natal Province, LP= Limpopo Province, MP = Mpumalanga Province, NW= North West Province, NC= Northern Cape Province, WC= Western Cape Province.

VOLUME 18. SUPPLEMENTARY ISSUE 8

CHARACTERISTICS OF COVID-19 ASSOCIATED ADMISSIONS IN PREGNANT AND NON-PREGNANT WOMEN OF CHILDBEARING AGE

From multivariable analysis of SARS-CoV-2-positive hospitalized women of childbearing age, pregnant women as compared to non-pregnant women were more likely to be aged 15-24 years [aOR=3.6, 95% CI (3.1-4.2)] and 25-34 years [aOR=4.6, 95% CI (4.1-5.1)] compared to ≥35 years; and were more likely to be Black African race [aOR=1.4, 95% CI (1.1-1.7)] as compared to White race. Pregnant women were, however, less likely to have hypertension [aOR=0.7, 95% CI (0.6-0.8)], diabetes [aOR=0.5, 95% CI (0.4-0.6)], asthma [aOR=0.4, 95% CI (0.3-0.6)], chronic renal disease [aOR=0.2, 95% CI (0.5-0.6)], previous tuberculosis [aOR=0.5, 95% CI (0.3-0.8)], current tuberculosis [aOR=0.2, 95% CI (0.06-0.4)], current and past tuberculosis [aOR=0.2, 95% CI (0.2-0.4)], to be admitted in the public sector [aOR=0.7, 95% CI (0.6-0.8)], and to die in hospital [aOR=0.4, 95% CI (0.3-0.6)] (Table 2).

Among 4,887 pregnant women, 169 deaths were reported (35 per 1,000), and among 41,125 non-pregnant women of childbearing age, 4,102 deaths were reported (100 per 1,000).

The HIV prevalence among pregnant women was 614/4,397 (14.0%), and among non-pregnant women 5,014/28,270 (17.7%). Of those pregnant and non-pregnant HIV-infected women respectively, 298/308 (96.7%) and 2,793/2,992 (93.3%) were receiving antiretroviral treatment (ART); 426/614 (69.4%) and 3,693/5 014 (73.6%) had high viral load (HIV-RNA≥1000 copies/ml); and 27/614 (4.4%) and 271/5,014 (5.4%) were severely immunosuppressed (CD4 count<200 cells/µl).

The in-hospital case-fatality ratio (CFR) for pregnant women was 169/4,887 (3.5%), lower than that of non-pregnant women of childbearing age, at 4,102/41,125 (10.0%, p<0.001). There were statistically significant differences in the proportion of COVID-19 admissions among pregnant women in different provinces (Table 2).

Table 2. Characteristics of pregnant and non-pregnant women aged 15-49 years with laboratory-confirmed SARS-COV-2 infection admitted to DATCOV hospitals, 5 March 2020 – 20 February 2021, South Africa (N=48,825).

Characteristics*	Pregnant n/N (%)	Non-pregnant n/N (%)	OR (95% CI)*	p-value	aOR (95%CI)*	p-value
Age group						
15-24 years	882/5 105 (17.3)	4 472/43 720 (10.2)	3.8 (3.5-4.2)	≤0.001	3.6 (3.1-4.2)	≤0.001
25-34 years	2 797/5 105 (54.8)	11 682/43 720 (26.7)	4.6 (4.3-5.0)	≤0.001	4.6 (4.1-5.1)	≤0.001
≥35 years	1 426/5 105 (27.9)	27 566/43 720 (63.1)	Reference		Reference	
Sector						
Private	2 831/5 105 (55.5)	20 302/43 720 (46.4)	Reference		Reference	
Public	2 274/5 105 (44.5)	23 418/43 720 (53.6)	0.7 (0.6-0.7)	≤0.001	0.7 (0.6-0.8)	≤0.001
Race						
White	114/2 896 (3.9)	1 365/30 947 (4.4)	Reference		Reference	
Black African	2 582/2 896 (89.1)	26 389/30 947 (85.3)	1.2 (0.9-1.4)	0.112	1.4 (1.1-1.7)	0.003
Coloured	123/2 896 (4.3)	1 913/30 947 (6.2)	0.8 (0.6-1.0)	0.052	0.9 (0.6-1.2)	0.386

Indian	77/2 896 (2.7)	1280/30 947 (4.1)	0.7 (0.5-0.9)	0.031	1.0 (0.7-1.4)	0.976
Presence of comorbidity†						
None	3 360/4 500 (74.7)	17 070/30 333 (56.3)	Reference			
1 comorbidity	860/4 500 (19.1)	8 275/30 333 (27.3)	0.5 (0.5-0.6)	≤0.001		
≥2 comorbidities	280/4 500 (6.2)	4 988/30 333 (16.4)	0.3 (0.2-0.3)	≤0.001		
Hypertension						
No	4 050/4 414 (91.7)	23 361/29 099 (80.3)	Reference		Reference	
Yes	364/4 414 (8.3)	5 738/29 099 (19.7)	0.4 (0.3-0.4)	≤0.001	0.7 (0.6-0.8)	≤0.001
Diabetes						
No	4 152/4 382 (94.8)	24 368/28 810 (84.6)	Reference		Reference	
Yes	230/4 382 (5.2)	4 442/28 810 (15.4)	0.3 (0.2-0.3)	≤0.001	0.5 (0.4-0.6)	≤0.001
Cardiac Disease						
No	4 319/4 335 (99.6)	26 789/27 088 (98.9)	Reference		Reference	
Yes	16/4 335 (0.4)	299/27 088 (1.1)	0.3 (0.2-0.5)	≤0.001	0.5 (0.2-1.2)	0.099
HIV						
No	3 783/4 397 (86.0)	23 256/28 270 (82.3)	Reference			
Yes	614/4 397 (14.0)	5 014/28 270 (17.7)	0.8 (0.7-0.8)	≤0.001		
Asthma/CPD						
No	4 240/4 328 (98.0)	26 212/27 813 (94.2)	Reference		Reference	
Yes	88/4 328 (2.0)	1 601/27 813 (5.8)	0.3 (0.3-0.4)	≤0.001	0.4 (0.3-0.6)	≤0.001
Chronic renal disease						
No	4 309/4 313 (99.9)	26 612/27 012 (98.5)	Reference		Reference	
Yes	4/4 313 (0.1)	400/27 012 (1.5)	0.06 (0.02-0.2)	≤0.001	0.2 (0.05-0.6)	0.005
Malignancy						
No	4 315/4 317 (99.95)	26 703/26 888 (99.3)	Reference			
Yes	2/4 317 (0.05)	185/26 888 (0.7)	0.06 (0.01-0.3)	≤0.001		
TB						
None	4 153/4 273 (97.2)	25 447/26 678 (95.4)	Reference		Reference	
Previous	86/4 273 (2.0)	638/26 678 (2.4)	0.8 (0.7-1.0)	0.099	0.5 (0.3-0.8)	0.005
Current	12/4 273 (0.3)	242/26 678 (0.9)	0.3 (0.1-0.5)	≤0.001	0.2 (0.06-0.4)	≤0.001
Current & Past	22/4 273 (0.5)	351/26 678 (1.3)	0.4 (0.2-0.6)	≤0.001	0.2 (0.07-0.4)	≤0.001
Obesity						
No	1 147/1 220 (94.0)	10 966/12 190 (90.0)	Reference			
Yes	73/1 220 (6.0)	1 224/12 190 (10.0)	0.6 (0.4-0.7)	≤0.001		
Ever ventilated						
No	4 982/5 105 (97.6)	42 165/43 720 (96.4)	Reference			
Yes	123/5 105 (2.4)	1 555/43 720 (3.6)	0.7 (0.5-0.8)	≤0.001		
Ever ICU						
No	4 864/5 105 (95.3)	39 733/43 720 (90.9)	Reference			
Yes	241/5 105 (4.7)	3 987/43 720 (9.1)	0.5 (0.4-06)	≤0.001		
Outcomes						
Alive	4 718/4 887 (95.5)	37 023/41 125 (90.0)	Reference		Reference	
Died	169/4 887 (3.5)	4 102/41 125 (10.0)	0.3 (0.3-0.4)	≤0.001	0.4 (0.3-0.6)	≤0.001

Provinces						
Western Cape	1 515/5 105 (29.7)	7 892/43 720 (18.0)	Reference		Reference	
Eastern Cape	476/5 105 (9.3)	5 573/43 720 (12.7)	0.4 (0.4-0.5)	≤0.001	0.4 (0.3-0.5)	≤0.001
Free State	273/5 105 (5.4)	2 344/43 720 (5.4)	0.6 (0.5-0.7)	≤0.001	0.3 (0.2-0.3)	≤0.001
Gauteng	1 236/5 105 (24.2)	12 295/43 720 (28.1)	0.5 (0.5-0.6)	≤0.001	0.4 (0.3-0.5)	≤0.001
KwaZulu-Natal	769/5 105 (15.1)	8 976/43 720 (20.5)	0.4 (0.4-0.5)	≤0.001	0.3 (0.3-0.4)	≤0.001
Limpopo	268/5 105 (5.2)	1 346/43 720 (3.1)	1.0 (0.9-1.2)	0.615	0.7 (0.5-0.9)	0.008
Mpumalanga	313/5 105 (6.1)	1 523/43 720 (3.5)	1.1 (0.9-1.2)	0.317	0.8 (0.6-1.1)	0.118
North West	195/5 105 (3.8)	2 915/43 720 (6.7)	0.3 (0.2-0.3)	≤0.001	0.4 (0.3-0.5)	≤0.001
Northern Cape	60/5 105 (1.2)	856/43 720 (2.0)	0.4 (0.3-0.5)	≤0.001	0.2 (0.1-0.3)	≤0.001
Length of stay						
0-5 days	263/1 430 (18.4)	3 459/23 038 (15.0)	Reference			
>6 days	1 167/1 430 (81.6)	19 579/23 038 (85.0)	0.8 (0.7-0.9)	0.001		
CD4 count						
≤200	27/614 (4.4)	271/5 014 (5.4)	Reference			
>200	587/614 (95.6)	4 743/5 014 (94.6)	1.2 (0.8-1.8)	0.294		
Viral load						
≤1000	188/614 (30.6)	1 321/5 014 (26.4)	Reference			
>1000	426/614 (69.4)	3 693/5 014 (73.6)	0.8 (0.7-0.9)	0.024		

*Abbreviations: OR - odds ratio, aOR - adjusted odds ratio, 95% CI - 95% confidence interval, HIV - human immunodeficiency virus, TB - tuberculosis, ICU - intensive care unit
†Comorbidities: hypertension, diabetes, chronic renal disease, chronic pulmonary disease, HIV, chronic cardiac disease, asthma/CPD (asthma/chronic pulmonary disease).

FACTORS ASSOCIATED WITH IN-HOSPITAL COVID-19 MORTALITY IN PREGNANT WOMEN OF CHILD-BEARING AGE

From multivariable analysis, risk factors associated with in-hospital mortality among COVID-19 pregnant women of childbearing age were: age 25-34 years [aOR=2.5, 95% CI (1.2-5.5)] and ≥35 years [aOR=3.7, 95% CI (1.7-8.1) compared to <25 years; admission in the public health sector [aOR=2.0, 95% CI (1.3-3.1)]; hypertension [aOR=2.5, 95% CI (1.6-4.1)]; diabetes [aOR=1.9, 95% CI (1.1-3.4)]; current and past tuberculosis was borderline significant [aOR=3.1, 95% CI (0.8-11.6)]; and admission to a facility in the Free State Province [aOR=2.3, 95% CI (1.1-4.6)] compared to Western Cape Province (Table 3).

Table 3. Characteristics associated with in-hospital mortality among pregnant women, 15-49 years, with laboratory-confirmed SARS-COV-2 infection with recorded outcomes admitted to hospital, 5 March 2020 - 20 February 2021, South Africa (n=5,105).

Characteristics*	Discharged alive n/N (%)	Died n/N (%)	OR (95% CI)*	p-value	aOR (95%CI)*	p-value
Age						
15–24 years	814/4 178 (17.3)	13/169 (7.7)	Reference		Reference	
25–34 years	2 606/4 178 (55.2)	88/169 (52.1)	2.1 (1.2-3.8)	0.013	2.5 (1.2-5.5)	0.013
≥ 35 years	1 298/4 178 (27.5)	68/169 (40.2)	3.2 (1.8-5.9)	≤0.001	3.7 (1.7-8.1)	0.001
Sector						
Private	2731/4 718 (57.9)	63/169 (37.3)	Reference		Reference	
Public	1 987/4 718 (42.1)	106/169 (62.7)	2.3 (1.7-3.2)	≤0.001	2.0 (1.3-3.1)	0.001
Race						
White	108/2 608 (4.1)	3/98 (3.1)	Reference			
Black African	2 317/2 608 (88.8)	86/98 (87.8)	1.3 (0.4-4.3)	0.626		
Coloured	109/2 608 (4.2)	7/98 (7.2)	2.3 (0.5-9.2)	0.233		
Indian	74/2 608 (2.9)	2/98 (2.0)	0.9 (0.1-5.9)	0.976		
Presence of comorbidity†						
None	3 191/4 192 (76.1)	71/152 (46.7)	Reference			
1 comorbid disease	763/4 192 (18.2)	52/152 (34.2)	3.1 (2.1-4.4)	≤0.001		
≥2 comorbid diseases	238/4 192 (5.7)	29/152 (19.1)	5.4 (3.4-8.6)	≤0.001		
Asthma/CPD						
No	3 980/4 061 (98.0)	135/140 (96.4)	Reference			
Yes	81/4 061 (2.0)	5/140 (3.6)	1.8 (0.7-4.6)	0.202		
Hypertension						
No	3 810/4 118 (92.5)	109/143 (76.2)	Reference		Reference	
Yes	308/4 118 (7.5)	34/143 (23.8)	3.8 (2.5-5.7)	≤0.001	2.5 (1.6-4.1)	≤0.001
Diabetes						
No	3 893/4 096 (95.0)	117/140 (83.5)	Reference		Reference	
Yes	203/4 096 (5.0)	23/140 (16.4)	3.8 (2.3-6.0)	≤0.001	1.9 (1.1-3.4)	0.016
Cardiac Disease						
No	4 054/4 064 (99.8)	139/139 (100)	Reference			
Yes	10/4 064 (0.2)	0	1	-		
HIV						
No	3 571/4 112 (86.8)	111/149 (74.5)	Reference			
Yes	541/4 112 (13.2)	38/149 (25.5)	2.2 (1.5-3.3)	≤0.001		
Chronic renal disease						
No	4 042/4 046 (99.9)	141/141(100)	Reference			
Yes	4/4 046 (0.1)	0 (0)	1	-		

Malignancy						
No	4 049/4 051 (99.95)	140/140 (100)	Reference			
Yes	2/4 051 (0.05)	0 (0)	1	-		
Obesity						
No	1 055/1 106 (95.4)	32/44 (72.7)	Reference			
Yes	51/1 106 (4.6)	12/44 (27.3)	7.7 (3.7-15.9)	≤0.001		
Tuberculosis						
None	3 907/4 018 (97.2)	123/131 (93.9)	Reference		Reference	
Previous	80/4 018 (2.0)	5/131 (3.8)	1.9 (0.8-4.9)	0.145	1.3 (0.4-3.3)	0.650
Current	12/4 018 (0.3)	0	1	-	1	-
Current and past	19/4 018 (0.5)	3/131 (2.3)	5.0 (1.4-17.2)	0.010	3.1 (0.8-11.6)	0.081
Ever ventilated						
No	4 674/4 718 (99.1)	105/169 (62.1)	Reference			
Yes	44/4 718 (0.9)	64/169 (39.9)	64.7 (42.1-99.5)	≤0.001		
Ever ICU						
No	4 599/4 718 (97.5)	73/169 (43.2)	Reference			
Yes	119/4 718 (2.5)	96/169 (56.8)	50.8 (35.6-72.5)	≤0.001		
Province						
Western Cape	1 442/4 718 (30.5)	54/169 (31.9)	Reference		Reference	
Eastern Cape	454/4 718 (9.6)	17/169 (10.1)	0.9 (0.6-1.7)	1.000	0.9 (0.4-1.8)	0.776
Free State	241/4 718 (5.1)	16/169 (9.5)	1.7 (1.0-3.1)	0.051	2.3 (1.1-4.6)	0.015
Gauteng	1 123/4 718 (23.8)	29/169 (17.2)	0.7 (0.4-1.0)	0.112	1.1 (0.6-1.9)	0.861
KwaZulu-Natal	680/4 718 (14.4)	29/169 (17.2)	1.1 (0.7-1.8)	0.580	1.5 (0.9-2.8)	0.129
Limpopo	253/4 718 (5.4)	7/169 (4.1)	0.7 (0.3-1.6)	0.458	1.4 (0.6-3.2)	0.430
Mpumalanga	301/4 718 (6.4)	8/169 (4.7)	0.7 (0.3-1.5)	0.372	0.9 (0.3-2.6)	0.827
North West	168/4 718 (3.6)	6/169 (3.5)	0.9 (0.4-2.2)	0.914	1.6 (0.6-4.3)	0.326
Northern Cape	56/4 718 (1.2)	3/169 (1.8)	1.4 (0.4-4.7)	0.556	1.1 (0.2-5.0)	0.884

*Abbreviations: OR - odds ratio, aOR - adjusted odds ratio, 95% CI - 95% confidence interval, HIV - human immunodeficiency virus, TB - tuberculosis, ICU - intensive care unit
†Comorbidities: hypertension, diabetes, chronic renal disease, chronic pulmonary disease, HIV, chronic cardiac disease, asthma/CPD (asthma/chronic pulmonary disease).

DISCUSSION

Among a large cohort of hospitalized individuals with SARS-COV-2, we found 10.5% of admissions in women of childbearing age were pregnant. Pregnant women were younger than non-pregnant women, there was a lower prevalence of comorbid disease, and lower in-hospital COVID-19 mortality in pregnant women compared to non-pregnant women of child-bearing age. Older age, hypertension and diabetes were associated with in-hospital COVID-19 mortality of pregnant women of childbearing age.

The COVID-19 in-hospital case fatality rate for pregnant women was significantly lower than women of childbearing age who were not pregnant. A population-based cohort study in the UK reported a case fatality of 1.2% (95% CI 0.4-2.7) among pregnant SARS-CoV-2 positive women.[7] In a systematic review by Chi et al,[17] the case-fatality in SeARS-CoV-2 positive pregnant women (0.4%) was lower than the mortality in SARS-CoV-2 patients reported by the WHO (6.8%) and the Chinese Centre for Disease Control and Prevention (2.3%). [8,9,17] This is in keeping with the low case fatality among pregnant women in our study. There are, however, reports showing higher case fatalities in pregnant women. The COVID-19 in-hospital incidence for death in our study was lower among pregnant women of childbearing age (35 per 1,000) compared to non-pregnant women of childbearing age (100 per 1,000). Another study by the US Centers for Disease Control reported 34 SARS-CoV-2-related deaths (1.5 per 1,000 cases) among 23,434 symptomatic pregnant women, and 447 deaths (1.2 per 1,000 cases) among 386,028 non-pregnant women, representing a 70% increased risk for death associated with pregnancy (aRR = 1.7; 95% CI = 1.2–2.4) [8,9,10,11] Generally, South Africa has a high maternal mortality from other obstetric and non-obstetric causes, and it is highly likely that our relatively high case fatality rate and incidence of death compared to other studies reflects this.

Our data also show that pregnant women had lower prevalences of comorbidities compared to non-pregnant women of child-bearing age. This may be due to pregnant women being of younger age. They may also have been admitted for other obstetric-related indications, with a positive result for COVID-19 being an incidental finding. Non-pregnant women who have been admitted are more likely to have comorbidities that are strongly associated with COVID-19 mortality.

Pregnant women infected with SARS-CoV-2 admitted to hospital were more likely to be Black African. This finding is consistent with a study conducted in the United Kingdom showing that more than half of pregnant women admitted to hospital with SARS-CoV-2 infection in pregnancy were from Black or other ethnic minority groups.[7]

HIV infection was not associated with COVID-19 mortality in pregnant women of childbearing age in our study. Pregnant women in this study had a lower prevalence of HIV infection than non-pregnant women, a higher proportion were receiving ART, and fewer had high viral loads and low CD4 counts. In South Africa, HIV infection is the leading non-obstetric cause of maternal death.[12] There is a lack of knowledge on the interaction of SARS-CoV-2 and HIV.[13] Based on the immune system status, patients on antiretroviral therapy and with CD4 cell counts higher than 200 cells/μL may have a mild or moderate course of SARS-CoV-2, should ARVs have an effect on SARS-CoV-2.[13] However, the interactions between HIV and SARS-CoV-2 need clarification by conducting further studies.[13]

Testing of SARS-CoV-2 is not universal and is primarily for symptomatic patients. Many diagnosed pregnant women are reported to be asymptomatic.[14] Hospital admissions for non-pregnant women

were mainly because of SARS-Cov-2 symptoms whereas admissions for pregnant women were mainly due to delivery and not because of SARS-CoV-2 symptoms.[7,15] Pregnant women are routinely tested for COVID-19 as a requirement for admission in the private sector but not in the public sector.
Our study did not report on trimester phases of pregnancy. It would, however, be of interest to know the trimester phase of the women who died and who required ventilation. Some studies have reported on the development of severe outcomes among SARS-CoV-2 positive pregnant women in the third trimester requiring admission to ICU and mechanical ventilation.[15,16]

CONCLUSION

Although hospitalized COVID-19 positive pregnant women did not appear to have a higher case fatality ratio than non-pregnant women of childbearing age, pregnant women who are at risk for mortality include those who are older, and those with hypertension and diabetes. They should be identified early for active case management. Current and past tuberculosis should also be considered in the early identification for active case management although it was found to be a borderline risk factor for mortality of pregnant women of childbearing age infected with SARS-CoV-2.

LIMITATIONS

- The DATCOV digital platform started as a sentinel surveillance platform for laboratory-confirmed COVID-19 admissions. The platform has expanded to include COVID-19 admissions in both public and private hospitals in all nine provinces. However, some hospitals are still catching-up with the capturing of retrospective data and there may be backlogs in reporting by some provinces.
- Asymptomatic pregnant women admitted for confinement to private hospitals are routinely screened for COVID-19 while those in public sector are not, leading to a difference in reported admissions between private and public hospitals.
- Our study did not have data on whether the admission for pregnant women was due to COVID-19 or whether they tested positive for COVID-19 following routine screening.
- DATCOV has incomplete data on underlying medical conditions and obesity.
- Data on gestational age at delivery, mode of delivery, foetal or neonatal outcomes is incomplete on DATCOV, limiting reporting on other adverse maternal outcomes associated with COVID-19 such as prematurity, stillbirth, neonatal death and miscarriage.
- We used live births as a proxy denominator for pregnant women, which could underestimate the true size of the denominator, therefore overestimating the admission rates.

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