# Master of Medicine Obstetrics and Gynaecology Thesis


## Post caesarean section complications in women with COVID-19 disease.

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## Abstract-Open

**Title:** Post caesarean- section complications in women with COVID-19 disease

**Background:** The COVID-19 pandemic had a multifaceted impact on maternal health and pregnancy outcomes. This study aimed to determine the impact of the COVID-19 on caesarean section outcomes in pregnant women with COVID-19 infection in South Africa.

**Objective:** To evaluate post-operative outcomes in women who were diagnosed with COVID-19 infection, who underwent a caesarean section delivery while hospitalized in South Africa, during the pandemic.

**Methods:** A secondary analysis was conducted on data from a multicentre national database by the International Network of Obstetric Survey Systems (INOSS). The dataset included hospitalized pregnant women diagnosed with the COVID-19 disease between 14 April 2020 and 9 December 2021 in South Africa. Statistical analyses were performed to determine the association between mode of delivery, postoperative complications and mortality.

**Results:** Among 456 women who delivered by caesarean section. Complications were seen in 74 of 456 (16.2%) women. There was a statistically significant association between caesarean delivery and post-operative complications ($p = 0.04$). Mortality in COVID-19 positive women undergoing caesarean was 6.1%. Elective caesarean sections (9.02%) were associated with a notably higher rate of mortality compared to emergency procedures (2.5%). Notably 71.4% of maternal deaths amongst those who delivered by caesarean section were due to COVID-19 related respiratory complications.

**Conclusion:** Caesarean section in COVID-19 positive women was associated with increased postoperative complications, especially in the elective cases. Mortality in this cohort was mainly due to respiratory complications. These findings suggest the need for more refined clinical protocols and careful surgical decision-making during pandemics, especially in resource constrained settings.

## Keywords

- Caesarean section
- Complications
- COVID-19
- Post operative
- Pregnancy
- SARS-CoV-2

## List of Abbreviations

- ARDS: Acute Respiratory Distress Syndrome
- BMI: Body Mass Index
- CNS: Central Nervous System
- COVID-19: Coronavirus Disease 19
- CRF: Case Report Forms
- CS: Caesarean Section
- CVS: Cardiovascular System
- DRC: Department Research Committee
- ELCS: Elective Caesarean Section
- EMCS: Emergency Caesarean Section
- H1N1: Swine Flu
- HICs: High-Income-Countries
- HPT: Hypertensive Disorder
- HREC: Human Research Ethics Committee
- ICU: Intensive Care Unit
- INOSS: International Network of Obstetric Survey Systems
- LMICs: Lower Middle-Income Countries
- MERS: Middle East Respiratory Syndrome
- MICs: Middle-Income Countries
- NICU: Neonatal Intensive Care Unit
- NVD: Normal Vaginal Delivery
- PPH: Post Partum Haemorrhage
- SARS: Severe Acute Respiratory Syndrome
- SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2
- SSI: Surgical Site Infection
- UMIC: Upper-Middle Income Country
- UKOSS: United Kingdom Obstetric Surveillance System
- USA: United States of America
- WHO: World Health Organization

# 1. Introduction

The first coronavirus COVID-19 cases were reported in December 2019 by the World Health Organization (WHO) following a cluster of pneumonia cases in Wuhan City, Hubei Province of China. South Africa reported its first case of COVID-19 on the 5 March 2020, by the end of March 2021 there more than 1.5 million cases reported the same month the WHO declared COVID-19 a global pandemic (Jassat et al., 2021).

There have been many research studies about a latitude of topics related to COVID-19. However, research on COVID-19 disease in pregnancy remains limited in low and middle-income countries (LMICs) (Budhram et al., 2021; Kuandyk et al., 2024).

Pregnant women exhibit a heightened vulnerability to respiratory infections, a state attributed to the significant physiological adaptations occurring in their cardiac, respiratory, and immune systems. (Li et al., 2020). Some reports early in the outbreak showed that patients who underwent surgery while COVID-19 disease positive had a higher risk of morbidity than patients who were COVID-19 disease negative (Collaborative, 2020).

An early international cohort across 116 LMICs showed that post-surgical morbidity and mortality risks were higher within six weeks of diagnosis however patients with less adverse outcomes had infections older than six weeks and were often from high-income countries (HICs). This may have alluded to how health systems in the different income categories had an impact on COVID-19 outcomes on patients (COVIDSurg Collaborative & GlobalSurg Collaborative, 2021).

Literature in LMICs highlighted the financial burden faced by women in LMICs, where economic factors may have had a crucial role in shaping maternal health outcomes (Eleje et al., 2022). This study aimed to describe post-operative complications in obstetric participants who were admitted to a hospital with COVID-19 disease, in South Africa, which is an upper-middle income country (UMIC).

## 2. Literature on COVID-19 in Pregnancy

COVID-19 is from the coronavirus family, and other pathogens from this family have recently manifested a range of viral infections in humans, including Middle East Respiratory Syndrome (MERS) and COVID-19 disease. The predominant method of transmission is through respiratory droplets or contact with bodily fluids. People affected may have mild or severe disease, but most fatal cases were in patients who had co-morbidities (Wloch et al., 2012)

The symptoms of COVID-19 disease vary from asymptomatic infection to pneumonia and life-threatening complications, including cardiovascular disease (CVS), diabetes, multi-system organ failure, hypertension, acute respiratory distress syndrome (ARDS), and death (Nachon-Acosta et al., 2021). Pregnant women exhibit heightened vulnerability to viral respiratory infections and severe pneumonia as a result of the physiological alterations in their immune and cardiopulmonary systems (Asalkar et al., 2022).

The COVID-19 virus has remained elusive as data on variants surfaced, with changes in the symptoms and extent of the disease. In addition to respiratory disease, women with severe symptoms manifested electrolyte imbalances, placental disease and higher mortality rates. A national study in the United Kingdom, based on data from the United Kingdom Obstetric Surveillance System (UKOSS), showed that COVID-19 disease during pregnancy was found to be associated with an increased risk of preeclampsia, preterm birth, stillbirth, Intensive Care Unit (ICU) admission, lower birth weight, and Neonatal Intensive Care Unit (NICU) admission compared to no infection (Knight et al., 2020). Symptomatic COVID-19 disease in pregnancy was associated with an increased risk of preterm birth and Caesarean delivery compared to asymptomatic COVID-19 disease.

A systematic review and meta-analysis by (Wei et al., 2021) analyzed data from 42 observational studies involving 438,548 pregnant individuals worldwide, and indicated that severe COVID-19 disease was strongly associated with preeclampsia, preterm birth, gestational diabetes, ICU admission, mechanical ventilation, caesarean delivery, low birth weight, and NICU admission compared to mild COVID-19.

The need to understand the impact of COVID-19 disease on post-operative recovery to inform clinical decision-making is now more compelling after the COVID-19 pandemic (Nachon-Acosta et al., 2021).

Data from other coronaviruses, such as the Swine Flu (H1N1), Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), suggests that pregnant women had severe progression of symptoms and a higher likelihood of severe morbidity and mortality than the non-pregnant population (Sunuwar et al., 2022). Studies have shown that women who delivered with COVID-19 disease had higher rates of complications: ICU admission, preterm delivery, mortality and other complications (Chinn et al., 2021). A high BMI leads to metabolic and hormonal dysregulation, which itself is already a known risk factor for different diseases like diabetes, hypertension, stroke, hyperlipidaemia, coronary heart disease, and some malignancies. During the COVID-19 pandemic, studies demonstrated that obesity plays a profound role in the risk for death from COVID-19 (Wei et al., 2020).

## 2.1. Mode of Delivery in Women with COVID-19

In 2021, (Chinn et al., 2021) showed that women who had COVID-19 disease irrespective of mode of delivery, normal vaginal or caesarean, had markedly higher rates of ICU admission, intubation and mechanical ventilation and higher rates of in-patient mortality and higher peripartum mortality rates. This study also found that women who were Black or Hispanic had more adverse outcomes with the COVID-19 disease than those who did not have COVID-19 disease.

In one meta-analysis conducted at a hospital in Turkey, the mortality rate of non-pregnant COVID-19 hospitalized women were 6.4%, while the mortality rate of all pregnant women was 11.3%. This study showed pregnant COVID-19 women had a high probability of maternal morbidity, ICU admission, mechanical ventilation, and perinatal death. In comparison with non-pregnant women (aged 35 to 44 years with COVID-19), pregnant women in the same age group were found approximately four times more likely to require invasive ventilation and were twice as likely to die (Aydin Güzey & Uyar Türkyilmaz, 2022).

Initial studies suggested that COVID-19 disease did not pose a higher risk of complications in pregnancy, but more recent research has indicated an increased risk of severe outcomes. follow up case series demonstrated an increase in maternal mortality and recommended more research to investigate this (Asalkar et al., 2022).

During the COVID-19 pandemic, research demonstrated that obesity correlates with an increased risk of severe disease progression and poorer clinical presentations and outcomes in infected individuals (Yang et al., 2022). Morbidity and mortality associated with high-grade obesity, diabetes, gestational diabetes, and advanced maternal age (over 35) were evaluated as potential prognostic indicators of COVID-19 severity. Furthermore, a study at Duke University, USA, identified that pregnant individuals with COVID-19 and pre-existing risk factors for severe illness, such as elevated BMI, exhibited a higher probability of requiring a Caesarean Section (Craig et al., 2022).

## 2.2. The Effects of COVID-19 on Surgery

At the beginning of the COVID-19 pandemic, new guidelines were developed for patients undergoing surgery as they were at risk of COVID-19 exposure if admitted to the hospital (Collaborative, 2020; Nachon-Acosta et al., 2021). Some initial studies aimed to determine the general impact of COVID-19 on hospital services and healthcare workers and the attributes and outcomes of COVID-19 disease-positive patients (Knight et al., 2020; Nachon-Acosta et al., 2021). Nachon-Acosta et al., 2021 in Mexico reviewed the characteristics and outcomes of patients undergoing general and oncology surgery during the COVID-19 period in 2020 and found higher postoperative morbidity and mortality in COVID-19 disease-positive patients.

The compounding factors associated with higher complication rates were gender, level of function, pre-operative infection and mechanical ventilation, acute kidney injury or chronic kidney disease. On analysis, the study additionally reported an association between COVID-19 disease and Surgical Site Infections (SSIs), respiratory complications, blood and blood product transfusions, renal failure, sepsis, multiple interventions, repeat admissions, and death (Nachon-Acosta et al., 2021).

A study conducted at Motahari Hospital, Iran, aimed to investigate the outcome of obstetric surgeries in patients with COVID-19 disease at the hospital (Ayatollahi, Ghasemzadeh & Ghasemiyan Dizaj Mehr, 2021). Outcomes in Motahari showed that surgery was not directly associated with an increased risk of mortality and complications in patients with COVID-19 disease per se'; it was more the associated underlying co-morbidities such as diabetes, age and whether the surgery was planned or elective that significantly conferred risk of complications (Ayatollahi, Ghasemzadeh & Ghasemiyan Dizaj Mehr, 2021).

A COVID-19 study by (Bhangu et al., 2020) reported thirty-day mortality rates and other complications in patients with perioperative COVID-19 disease. Patients who had pulmonary complications or other co-morbidities and were above 70 years of age were shown to have worse mortality rates. The study was conducted across surgical disciplines, including obstetrics, and examined outcomes in emergency versus elective surgery settings. This study found that emergency surgery had higher complication rates compared to elective surgery, and that elective surgical interventions had less complication rates. Although (Bhangu et al., 2020) did not specifically mention caesarean outcomes it can be inferred that obstetric surgery was caesarean sections and thus emergency caesarean had higher complication rates than elective cases. The results were used to inform the benefits and risks of delaying surgery in specific individuals, especially those above 70 or those with comorbidities, as they had the poorest outcomes in the study. A prospective non-randomized comparative study enrolled a cohort of asymptomatic COVID-19 disease-positive patients by (Pitak-Arnnop et al., 2022) investigated the association between asymptomatic or mildly symptomatic infection and severe acute respiratory syndrome secondary to COVID-19 disease and SSI after repair of craniomaxillofacial injury (Pitak-Arnnop et al., 2022). This study found a significantly increased risk of SSI in patients with mild and asymptomatic COVID-19 disease particularly in patients above 60 years of age who were treated for fractures and had prolonged antibiotic use.

The abovementioned studies, although not directly linked to caesarean section outcomes, provide some insights into the positive impact of COVID-19 disease on post-surgical morbidity and mortality.

A large international prospective cohort study found that risks of postoperative morbidity and mortality were highest if patients had surgery within six weeks of the diagnosis COVID-19 disease, therefore this study suggested that surgery should be delayed for at least seven weeks from being diagnosed with COVID-19 disease (COVIDSurg Collaborative & GlobalSurg Collaborative, 2021).

Brown, Moore & Watters (2021a) performed a meta-analysis which included data from eight studies in Australia encompassing 193 patients with concurrent COVID-19 infection and 910 COVID-19 negative patients. The analysis revealed that patients with COVID-19 had a significantly higher risk of postoperative mortality compared to those without the infection.

Several studies have focused on different aspects of COVID-19 disease, such as its impact on healthcare workers, the use of face masks, and revisiting handwashing as an essential preventative measure for infection. One such study in India evaluated the reinforcement of fundamental principles and how they affected the postoperative incidence of surgical site infections (Pantvaidya et al., 2022). This study evaluated the use of face masks, social distancing and hand hygiene and their influence on the incidence of surgical site infections (SSI's) in major oncology surgical cases. All these measures were demonstrated to decrease the risk of SSI in major oncologic resections (Pantvaidya et al., 2022). A study on post-caesarean complications in those with COVID-19 disease would be informative in improving morbidity and mortality in this cohort and enlighten approaches for future pandemics.

COVID-19 disease has had a global impact and a devastating effect on healthcare systems worldwide. There is a dearth of research, particularly from UMICs such as South Africa, on the impact of COVID-19 infection on surgical outcomes in the obstetric population as pregnancy physiology is different and might influence the nature, extent and prevalence of complications. International Network of Obstetric Survey Systems (INOSS) sought to describe the maternal characteristics and pregnancy outcomes of hospitalized pregnant women with COVID-19 disease. Our study, nested within INOSS, focuses on the post-caesarean section complications of - patients with COVID-19 disease.

# 3. Study Objective and Hypothesis

## 3.1. The objective of the Study

The study aimed to explore the postoperative outcomes in women who tested COVID-19 disease positive and were hospitalized and had a caesarean section.

## 3.2. Hypotheses of the study

- **Null hypothesis:** Pregnant patients with COVID-19 disease did not have increased complications post-Caesarean section.
- **Alternative hypothesis:** Pregnant patients with COVID-19 disease did have increased complications post-Caesarean section.

# 4. Research Methodology

## 4.1. Study Design

This study was a secondary analysis of a multicentre study, the maternal characteristics and pregnancy outcomes of hospitalized pregnant women with COVID-19 disease in South Africa.

This study was based on the protocol developed by the United Kingdom Obstetric Surveillance System (UKOSS) and then adopted by INOSS to standardize an international approach to COVID-19 disease in pregnancy. The study analyzed data obtained by lead clinicians across 30 hospital centres across South Africa over a defined period within the COVID-19 pandemic, from April 2020 to November 2020. All locations were consultant-led obstetric units; they were provided with modified Case Report Forms (CRFs), and data was obtained through medical record review – see Appendix A for a copy (Budhram et al., 2021).

## 4.2. Study Setting

Our study aimed to describe COVID-19 positive pregnant women who underwent Caesarean section delivery in South Africa. This was a secondary analysis of the maternal characteristics and pregnancy outcomes of hospitalized pregnant women with COVID-19 infection from a national database which included all nine South African provinces. Data were extracted from the records of all COVID-19 positive pregnant women who underwent Caesarean section. The study compared adverse events, such as postpartum haemorrhage (PPH), postoperative tachycardia, venous thromboembolism, wound site sepsis, puerperal sepsis and death.

## 4.3. Statistical Analysis

Descriptive statistics are presented in tables and graphs and are presented as frequencies and percentages. Means (± standard deviation) or medians (interquartile range) were applied to continuous variable as appropriate, based on data distribution.

Categorical variables were analyzed using chi-squared tests and were presented as frequencies and percentages, accompanied by confidence intervals and p-values. A p-value of <0.05 was considered statistically significant. Associations with continuous variables were analyzed using t-tests. The data analysis was conducted using Stata 18.0 (BE-Basic Edition), by Stata Corp LLC. 4905 Lakeway Drive. College Station, Texas 77845 USA. Associations between mode of delivery and complications, as well as mortality, were assessed using Pearson's chi-squared tests. Significance was set at $p < 0.05$ (Bhangu et al., 2020).

The Pearson Chi-Squared test was employed for this analysis as it is appropriate for determining whether a statistically significant association exists between two categorical variables. In this context, it was used to assess the relationship between the categorical variable 'Mode of Delivery' (with five levels) and the dichotomous categorical outcome 'Complication' (yes/no). The test evaluates if the observed distribution of complications across different delivery modes differs significantly from what would be expected if there were no association between these variables.

# 5. Results of the Study

## 5.1. Study Population and Sample Definition

Data collection across all participating hospital medical centres initially yielded Case Report Forms (CRFs) from 925 respondents. However, for the primary analyses focusing on outcomes related to delivery within the hospital setting, 174 respondents were excluded. These exclusions were due to incomplete data, and due to instances where the respondent did not deliver during the admission to hospital. This resulted in analytical sample of 751 women hospitalized with COVID-19 for the primary analysis concerning mode of delivery, 456 of these women delivered via caesarean section.

## 5.2. Delivery Methods in the Sample

Out of a total of 456 Caesarean section deliveries, 248 (54.4%) were elective (ELCS), and 208 (45.6%) were emergency (EMCS).

## 5.3. Patient Demographics Characteristics

The demographic characteristics of those who delivered by caesarean section (N=456) are presented below, including distribution across 30 hospital centres in nine South African provinces, the patient's nationality and ethnicity, and anthropometric measurements. While the INOSS registry was designed to capture data from all nine provinces of South Africa, reporting was uneven across hospital centres during the COVID-19 pandemic. At the time of data cleaning and analysis, only four provinces - KwaZulu-Natal, Eastern Cape, Western Cape and Gauteng - had submitted sufficiently complete data to permit inclusion. The hospitals from these provinces represent a range of tertiary, regional, secondary and private care levels, providing a reasonably broad but not nationally exhaustive picture of post-caesarean section outcomes in COVID-19-positive women.

**Table 1:** The Numerical Distribution of Hospital Centres performing Caesarean Section according to Level and Type of Care.

| Province | Tertiary Hospitals | Regional Hospitals | Secondary Hospitals | Private Hospitals | Total Hospitals |
|---|---|---|---|---|---|
| KwaZulu-Natal | 2 | 6 | 5 | 2 | 15 |
| Eastern Cape | 4 | 0 | 0 | 0 | 4 |
| Western Cape | 3 | 0 | 0 | 1 | 4 |
| Gauteng | 6 | 0 | 0 | 1 | 7 |
| Total Count | 15 | 6 | 5 | 4 | 30 |

The largest representation was obtained from the KwaZulu-Natal province (15), followed by the hospitals in Gauteng province (7) as seen in Table 1. The highest number of patients were located in tertiary hospitals (15), then closely followed by patients located in regional hospitals (6) as seen in Table 1.

**Table 2:** Patient's Nationality

| Region | Percentage |
|---|---|
| Southern Africa | 97.4% |
| Central Africa | 1.3% |
| East Africa | 1.1% |
| West Africa | 0.2% |

The patient's nationality was largely self-declared and was recorded as from Southern Africa (97.4%). Among those whose nationality was specified, patients from Central Africa constituted the second largest group (1.3%), followed by patients from East Africa (1.1%). Lastly, there was a small representation of patients from West Africa that were recorded (0.2%) as seen in Table 2.

**Table 3:** Patient's Ethnicity

| Ethnicity | Frequency n (%) |
|---|---|
| Black | 348 (76.4%) |
| Not classified | 77 (16.8%) |
| Coloured | 22 (4.9%) |
| Indian | 6 (1.4%) |
| White | 2 (0.5%) |
| **Total** | **456 (100.0)** |

The majority of patients were identified as Black African (76.4%). A significant portion had ethnicity recorded as "not classified" (16.8%). Coloured (4.9%), Indian (1.4%), and White (0.5%) ethnicities represented smaller proportions of the study sample as indicated in Table 3.

**Table 4:** Caesarean Section Patient's Anthropometric Summary (N=456)

| Statistic | Age (Years) | Height (cm) | Weight (Kg) | Calculated BMI ($kg/m^2$) |
|---|---|---|---|---|
| Minimum | 11 | 97 | 35 | 37.20 |
| Maximum | 44 | 190 | 189 | 52.35 |
| Median | 31 | 160 | 78 | 30.47 |
| Mean | 30 | 159 | 81 | 31.89 |

The patients' ages in Table 4 ranged widely from 11 to 44 years, with a median age of 31 and a mean age of 30 years. The median height was 160 cm, and median weight was 78 kg. The median calculated Body Mass Index (BMI) was 30.47 kg/m², with the mean BMI being 31.89 kg/m², suggesting that the mean respondent fell into the obese category according to standard WHO BMI classification.

## 5.4. Postoperative Complications

**Table 5:** Association Between Mode of Delivery and Postoperative Complications

| Caesarean Section | No Complication n (%) | Complication n (%) | Total n (%) |
|---|---|---|---|
| No | 263 (89.2) | 32 (10.8) | 295 (100.0) |
| Yes | 382 (83.8) | 74 (16.2) | 456 (100.0) |
| Total | 645 (85.8) | 106 (13.8) | 751 (100.0) |
| Pearson Chi-Squared = 3.85, p = 0.0499 | | | |

## 5.5. Complication Categories within the Caesarean Section Cohort

Among the 74 women in the Caesarean section group who experienced complications included in the category analysis, the most common category was COVID-19/Respiratory related complications 45.9%. Hypertensive complications of pregnancy and other obstetric complications formed the next largest group 24.3%. Cardiovascular (CVS) and Sepsis complications each accounted for 14.9% of the complications, while Central Nervous System (CNS) complications were the least frequent category at 5.4%.

**Table 6:** Complication Categories within the Caesarean Section Cohort (N=74)

| Complication Category | Frequency n (%) |
|---|---|
| COVID-19/Respiratory | 34 (45.9) |
| Obstetric/HPT | 18 (24.3) |
| CVS | 7 (9.5) |
| Sepsis | 11 (14.9) |
| CNS | 4 (5.4) |
| **Total Complications in the caesarean cohort** | **74 (100.0)** |

Complications were grouped into direct obstetric causes (e.g., obstetric haemorrhage and hypertensive disorders) and indirect medical causes (e.g., respiratory- including COVID-19 disease, cardiovascular, and sepsis-related complications). The predominance of COVID-19/respiratory complications (45.9%) compared with obstetric causes (24.3%) highlights the substantial burden of indirect complications in this cohort.

## 5.6. Mortality of the patients who gave birth by caesarean section

Mortality data were available for the 456 caesarean section patients (elective or emergency combined) within the study period relevant to the analysis. Overall, 28 maternal deaths occurred among this group, yielding a mortality rate of 6.1%.

Among the 28 maternal deaths recorded, the majority were attributed to severe acute respiratory infection (COVID-19 related), accounting for 20 deaths (71.4%). Obstetric haemorrhage was the second most common cause, responsible for 5 deaths (17.9%). Hypertensive disorder, pulmonary embolism, and cases with unknown causes each accounted for one death (3.6%).

**Table 7:** Primary Causes of Maternal Death Amongst the CS Delivery Group (N=28)

| Primary Cause of Maternal Death | Frequency n (%) |
|---|---|
| Severe Acute Respiratory Infection (COVID-19 related) | 20 (71.4) |
| Obstetric Haemorrhage | 5 (17.9) |
| Hypertensive Disorder | 1 (3.6) |
| Other Direct Cause (Pulmonary embolism) | 1 (3.6) |
| Unknown | 1 (3.6) |
| **Total** | **28 (100.0)** |

**Table 8:** Comparison of Elective versus Emergency Caesarean Section and Associated Risk of Maternal Mortality (N=456)

| Mode of Delivery | Alive n (%) | Dead n (%) | Total n (%) |
|---|---|---|---|
| Elective C-Section | 232 (90.9) | 23 (9.02) | 255 (100.0) |
| Emergency C-Section | 196 (97.51) | 5 (2.5) | 201 (100.0) |
| **Total** | **428 (93.4%)** | **28 (6.1%)** | **456 (100.0%)** |
| Pearson Chi-Squared = 7.23, p = 0.0072 | | | |

When comparing mortality between elective caesarean section (232) versus emergency (196) caesarean delivery (N=456) in Table 8, the difference is statistically significant (Pearson Chi-Squared = 7.23, p = 0.0072). Mortality was 9.02% in the elective caesarean section group compared to 2.5% in the emergency caesarean section group.

## 5.7. Complication Categories and Mortality

Among women who experienced complications (N=74) and had mortality data available (N=28), the type of complication was strongly associated with mortality (Pearson Chi-Squared = 28.33, p = 0. 00001). As illustrated in Table 9 below, mortality was highest among those whose primary complication category was CVS-related (100%) and COVID-19/Respiratory (58.8%). Mortality was considerably lower for those with Sepsis (22.2%) or Obstetric/Hypertensive (HPT) complications (0.05%), and no deaths occurred among those with primarily CNS complications in this subset.

**Table 9:** Association Between Complication Category and Maternal Mortality (N=74)

| Complication Category | Alive n (%) | Dead n (%) | Total n (%) |
|---|---|---|---|
| COVID-19/Respiratory | 14 (41.2) | 20 (58.8) | 34 (100.0) |
| CNS | 6 (100.0) | 0 (0.0) | 6 (100.0) |
| CVS | 0 (0.0) | 5 (100.0) | 5 (100.0) |
| Sepsis | 7 (77.8) | 2 (22.2) | 9 (100.0) |
| Obstetric/HPT | 19 (95) | 1 (5.0) | 20 (100.0) |
| **Total** | **46 (62.2)** | **28 (37.8)** | **74 (100.0)** |
| Pearson Chi-Squared = 28.33, p = 0.00001 | | | |

Some women experienced more than one complication. The difference in survival outcomes across complication categories was statistically significant ($\chi^2 = 28.33$, $p = 0.00001$)

# 6. Discussion

## 6.1. Key Findings

Our study found that women who underwent caesarean section delivery had a high complication rate (16.2%) and mortality (6,1%), compared to women who had a vaginal birth (5.2%). We observed that two thirds of women who delivered whilst admitted with COVID-19 had a caesarean section delivery, of note maternal medical condition was the primary indication for both emergency and elective caesarean delivery in 30.8% women admitted for COVID-19 disease, the most common indication for elective caesarean section was previous caesarean delivery. The most common complication that women with a caesarean section with a diagnosis of COVID-19 disease was respiratory complications related to COVID-19 disease. Other studies such as this have been published, but few studies described or compared clinical findings by the mode of delivery. Chinn et al. (2021) described increased complication rates in women who delivered and had COVID-19 disease; however, they did not delineate between mode of delivery. While (Ayatollahi, Ghasemzadeh & Ghasemiyan Dizaj Mehr, 2021) associated increased post-surgical complications in COVID-19 women with comorbidities, (Nachon-Acosta et al., 2021) and (Bhangu et al., 2020) demonstrated increased mortality and morbidity related to COVID-19 disease in broader surgical populations (including settings like Mexico, a lower- to middle-income country, alongside high-income countries).

Our study, conducted in South Africa (which is an UMIC), extends these findings to the obstetric population within a similar economic context, revealing a higher mortality rate in women with COVID-19 disease who underwent elective caesarean versus emergency caesarean. Notably high-income countries maintained or increased caesarean section rates during the pandemic, with patients often opting for elective caesarean to manage COVID-19-positive pregnant patients (To et al., 2024). The higher caesarean section rates shown by To et al. (2024) likely reflect institutional and physician-driven decision-making rather than increased disease severity. In the Ontario cohort, only 5.2% of pregnant women tested positive for COVID-19, and most had mild disease with no increase in maternal complications. As noted by the authors, non-clinical factors such as increased risk management, infection control measures, and patient or provider

preference in high-income settings probably contributed to the observed trend rather than maternal illness severity.

Severe acute respiratory infection was the leading cause of maternal deaths, with COVID-19 disease being a significant contributor, a finding consistent with (Brown, Moore & Watters, 2021b) and (Chinn et al., 2021). Importantly, our study further categorized complications in women with COVID-19 disease, revealing a highly significant association ($p < 0.001$) between COVID-19-related complications and mortality. This distinction between direct obstetric complications (e.g., hemorrhage, hypertensive disorders) and indirect COVID-19 diseases-related complications, further emphasizes the critical need for multidisciplinary management of pregnant women during infectious outbreaks. Contrary to some prior literature (McLaren et al., 2021) suggesting surgery poses no additional risk of complications in women with COVID-19 disease, our study reveals that both COVID-19 disease and surgical delivery independently contribute to increased maternal risk and mortality. Our study had comparative outcomes with studies such as the one conducted in Italy (Doglietto et al., 2020) which found that COVID-19 directly had increased complications and mortality in various specialities.

To date there is a paucity of studies indicating exclusively caesarean section outcomes in Lower to Middle income countries. Caesarean section rates and outcomes during and before the first wave of covid were lower than prior to covid but complications such as postdatism, fetal distress and anaemia where higher than baseline (Eleje et al., 2022)

A study done in Brazil indicated an elevated incidence of maternal mortality in maternity during COVID-19 (Ferreira et al., 2023). These results align with our study and two studies conducted in middle-income countries, India and Mexico, which also reported a significant surge in maternal deaths during the COVID-19 pandemic. (Kumari, Mehta & Choudhary, 2020) (Lumbreras-Marquez et al., 2020). Although the abovementioned studies did not delineate between modes of delivery they do align with our findings of high mortality rates in LMICs. Our cohort exhibited a notably high maternal mortality rate of 5.6% overall compared to high-income settings (Chmielewska et al., 2021). Our study finding further confounds existing literature in that we observed a significant complication rate among elective caesarean patients, contrary to the rates seen in emergency caesarean sections. The higher mortality rate observed in the elective caesarean section

group may indicate bias as these were performed often for women with maternal medical conditions in women who were admitted with COVID-19 disease and had markedly higher rates of ventilation and death. Emergency caesarean sections were often done for obstetric reasons such fetal distress or previous caesarean section (Budhram et al., 2021).

When comparing to high-middle income countries studies such as (Aydin Güzey & Uyar Türkyilmaz, 2022) done in Turkey reported a much higher mortality rate (11.3%) however most other high income country studies did not show an elevated mortality in women who had caesarean section deliveries and were COVID-19 positive. This difference indicates the role of health system policies and resources being invaluable in outcomes.

Kuandyk et al. (2024) and Ahmed et al. (2021) conducted studies on MICs and LMICs which showed that the pandemic disrupted access to maternal and delivery services; some regions, particularly LMICs, experienced declines due to overburdened health systems.

Our study which was conducted on an elective caesarean cohort (55.9%) was based in South Africa which is a UMIC country the elective caesarean section rates may indicate the delays in health care in the first wave of COVID-19, the under recognition and treatment of comorbidities unlike the well planned, well optimized patients seen in high-income countries (Pattinson et al., 2020).

It is widely accepted that elective caesarean sections should carry a lower risk however in resource limited systems where there was insufficient access to high care units, certain treatment, optimal pre-op assessment and logistical challenges contribute to poorer outcomes (Kuandyk et al., 2024).

Our findings also diverge from general surgical literature where emergency surgery usually yields a higher mortality (Bhangu et al., 2020). Our study showed that elective caesarean in COVID-19 positive women had almost four times higher mortality than emergency caesarean section which further highlight systemic weakness in resources, weakness in pre-operative triage and concerns about clinical and surgical decision making under a pandemic strain. In our cohort the majority of women were from

government subsidized hospitals which represents predominantly the low-income population (Budhram et al., 2021).

The findings from our study confirm the necessity of evidence-based decision-making during pandemics. They indicate a need for robust protocols for COVID-19-positive deliveries in South Africa and other UMICs that prioritize the physiological and clinical status over time-based delivery criteria. In settings where healthcare is increasingly constrained, the decision to proceed with Caesarean section must carefully balance resource allocation, maternal indication, and disease progression.

This research suggests that LMICs require resource-stratified guidance for surgery. In these contexts, well-supported emergency interventions may be more beneficial than potentially harmful delayed or inappropriate elective procedures. Therefore, national pandemic preparedness must prioritise maternal critical care infrastructure, standardized pandemic perioperative pathways, and delivery risk assessment tools tailored for low-resource settings.

## 6.2. Strengths and limitations

This was a multi-centre study based on the INOSS protocol which provided data across South Africa in different settings, which further increased the reliability of the outcomes. Our research provides a focused perspective on post-caesarean mortality in this unique population, considering their distinct cardiac and respiratory physiology, altered immune function, and increased hypercoagulability, which can influence postoperative outcomes. We had a large sample size collected in multicentre hospitals which make our study applicable in different settings. The study was on a specific group of patients, women who had COVID-19 disease and underwent caesarean section which would be able to influence local protocols and other lower-middle income countries. A key limitation was the lack of a control cohort such as those who underwent caesarean section without COVID-19 disease.

Due to the study being secondary data analysis, some variables that were not recorded which further limited the analysis. The time period in which this study was done was the

first covid pandemic wave in a resource limited country where delineation of disease was not yet complete.

These findings emphasize the importance of categorizing COVID-19 related complications separately from obstetric complications in order to improve planning and intervention. The strong association between COVID-19 related complications and mortality provides a rationale for preoperative COVID-19 screening, disease optimization, and strict perioperative protocols.

# 7. Recommendations

## 7.1. Careful Preoperative Risk Assessment

Given the higher complication risks particularly in patients with severe acute respiratory disease the benefits of caesarean section should be considered carefully against the risk. A multi-disciplinary team should be consulted if possible.

## 7.2. Careful Post Operative Follow Up

The patient who undergoes caesarean section while COVID-19 disease positive should be followed up closely for post operative complications.

## 7.3. Future Research

- As the COVID-19 continues to evolve with the emergence of new SARS-CoV-2 variants, it is essential to monitor the spatial and temporal patterns of COVID-19-related maternal deaths to identify countries especially LMICs requiring additional support and to inform clinical practice.
- Systematic review of health policies in lower middle-income countries to develop better strategies in future pandemics.
- Further studies in LMICs particularly comparing caesarean outcomes.
- The impact of careful patient selection for surgery in pregnant populations in pandemics.

## 8. Conclusion

Through secondary analysis of a large multicentre dataset derived from the International Network of Obstetric Survey Systems (INOSS) in South Africa, our study demonstrated that caesarean section in COVID-19 disease positive patients was associated with increased risk of complications and mortality. It underscores the need for careful patient selection and evidence based clinical decision making when deciding on mode of delivery for a COVID-19 positive woman.

This highlights the need for UMICs to implement pathways and better protocols in order to be better prepared for pandemics and their effect in already resource limited countries.

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# 10. Appendix A – Data Capture Instrument

**Post caesarean section complications in women with COVID-19 disease**
**SOUTH AFRICA**

**CRF**

**SECTION - 1: Woman's Details**

1. Centre number

2. Participant number

3. Date of birth
D D M M Y Y Y Y

4. Woman's height at booking (cm)

5. Date of admission
D D M M Y Y Y Y

6. Woman's weight at booking (kg)

$^{2}$

7. Date of discharge or death
D D M M Y Y Y Y

8. What is the woman's nationality?
NATIONALITY

9. Date of form
D D M M Y Y Y Y

10. What is the woman's ethnicity?
ETHNICITY

11. Name and province of hospital the woman is admitted in?
PROVINCE | HOSPITAL NAME

**SECTION 2: Pregnancy Outcome and Delivery**

1. What is the primary reason for admission?
- [ ] a. Woman needs to deliver/terminate the pregnancy
- [ ] b. Woman needs hospital care due to COVID-19 illness
- [ ] c. Woman needs isolation but is otherwise well
- [ ] d. Woman needs care related to non-COVID-19 illness
- [ ] e. Unknown
- [ ] f. Other: please specify _____

2. Gravidity (number of pregnancies including the current one if the woman is pregnant)

3. Number of previous completed pregnancies beyond 24 weeks

4. Number of previous pregnancies ending before or at 24 weeks

5. Does the woman have any of the following pre-existing medical conditions? Yes No

## SECTION 3: Previous Medical History

1 *Tick appropriate answer for each condition mentioned*

| | | | | | | |
|---|---|---|---|---|---|---|
| a. Thrombotic event | ☐ | Yes | ☐ | No | ☐ | Unknown |
| b. Amniotic fluid embolism | ☐ | Yes | ☐ | No | ☐ | Unknown |
| c. Pre-eclampsia/eclampsia | ☐ | Yes | ☐ | No | ☐ | Unknown |
| d. 3 or more miscarriages | ☐ | Yes | ☐ | No | ☐ | Unknown |
| e. Mid trimester loss | ☐ | Yes | ☐ | No | ☐ | Unknown |
| f. Preterm Birth (<37 weeks) | ☐ | Yes | ☐ | No | ☐ | Unknown |
| g. Early neonatal death (0-6 days of life) | ☐ | Yes | ☐ | No | ☐ | Unknown |
| h. Stillbirth | ☐ | Yes | ☐ | No | ☐ | Unknown |
| I. Congenital abnormality / birth defect (if yes specify) | ☐ | Yes | ☐ | No | ☐ | Unknown |
| j. Birth weight > 4500gr | ☐ | Yes | ☐ | No | ☐ | Unknown |
| k. Birth weight < 2500gr | ☐ | Yes | ☐ | No | ☐ | Unknown |
| l. Infant requiring intensive care | ☐ | Yes | ☐ | No | ☐ | Unknown |
| m. Puerperal psychosis | ☐ | Yes | ☐ | No | ☐ | Unknown |
| n. Placenta praevia | ☐ | Yes | ☐ | No | ☐ | Unknown |
| o. Gestational diabetes | ☐ | Yes | ☐ | No | ☐ | Unknown |
| p. Placental abruption | ☐ | Yes | ☐ | No | ☐ | Unknown |
| q. Postpartum haemorrhage requiring transfusion | ☐ | Yes | ☐ | No | ☐ | Unknown |
| r. Surgical procedure in pregnancy | ☐ | Yes | ☐ | No | ☐ | Unknown |
| s. Hyperemesis requiring admission | ☐ | Yes | ☐ | No | ☐ | Unknown |
| t. Dehydration requiring admission | ☐ | Yes | ☐ | No | ☐ | Unknown |
| u. Ovarian hyperstimulation syndrome | ☐ | Yes | ☐ | No | ☐ | Unknown |
| v. Severe other infection e.g. pyelonephritis | ☐ | Yes | ☐ | No | ☐ | Unknown |
| w. Other (if yes specify) | ☐ | Yes | ☐ | No | ☐ | Unknown |

2. Does the woman have any of the following pre-existing medical conditions?

*Tick appropriate answer for each condition mentioned*

| | | | | | | |
|---|---|---|---|---|---|---|
| a. Chronic cardiac disease (congenital or acquired - EXCLUDING hypertension) | ☐ | Yes | ☐ | No | ☐ | Unknown |
| b. Hypertension | ☐ | Yes | ☐ | No | ☐ | Unknown |
| c. Chronic pulmonary disease | ☐ | Yes | ☐ | No | ☐ | Unknown |
| d. Asthma | ☐ | Yes | ☐ | No | ☐ | Unknown |
| e. Chronic kidney disease | ☐ | Yes | ☐ | No | ☐ | Unknown |
| f. Chronic liver disease | ☐ | Yes | ☐ | No | ☐ | Unknown |
| g. Chronic neurologic disease | ☐ | Yes | ☐ | No | ☐ | Unknown |
| h. Psychiatric disorders | ☐ | Yes | ☐ | No | ☐ | Unknown |
| I. Endocrine disorders (e.g. hypo- or hyperthyroidism, diabetes mellitus) | ☐ | Yes | ☐ | No | ☐ | Unknown |
| j. Haematological disorders (e.g. sickle cell disease, diagnosed thrombophilia) | ☐ | Yes | ☐ | No | ☐ | Unknown |
| k. Inflammatory disorders (e.g. inflammatory bowel disease) | ☐ | Yes | ☐ | No | ☐ | Unknown |
| l. Autoimmune disease | ☐ | Yes | ☐ | No | ☐ | Unknown |
| m. Cancer | ☐ | Yes | ☐ | No | ☐ | Unknown |
| n. TB | ☐ | Yes | ☐ | No | ☐ | Unknown |

- ☐ Yes, treatment completed?
- ☐ Yes, on treatment?
- ☐ Yes, untreated?
- ☐ Yes, treatment unknown
- ☐ No
- ☐ Unknown

## SECTION 4: Immunization

1. Has the woman been immunised against seasonal influenza? ☐ Yes ☐ No ☐ Unknown

If yes, please give date when immunised ☐

If no, please give reason for non-immunisation *(Tick only 1 option)*

- ☐ Not offered
- ☐ Not available
- ☐ Contra-indicated
- ☐ Safety concerns
- ☐ Woman's preference

2. Has the woman been immunised against any other type of influenza or respiratory pathogen?

Pneumococcal vaccine ☐ Yes ☐ No ☐ Unknown

*(If yes, give date immunized)* ☐

Tuberculosis vaccine ☐ Yes ☐ No ☐ Unknown

COVID-19 (future) ☐ Yes ☐ No ☐ Unknown

*(If yes, give date immunized)* ☐

3. Final mode of delivery? *Tick only 1 option*

- ☐ Natural Vaginal Delivery
- ☐ Breech
- ☐ Assisted delivery
- ☐ Elective caesarean
- ☐ Emergency caesarean

## SECTION 5: Method Of Delivery

1. If the final mode of delivery is caesarean section, please indicate the primary reason for caesarean section

*Tick only 1 option*

- ☐ Maternal reason
- ☐ Previous caesarean
- ☐ Fetal reason

☐ Yes ☐ No ☐ Unknown

2. Method of anaesthesia used during caesarean section?

*Tick only 1 option*

- ☐ Regional
- ☐ General
- ☐ Unknown

3. Did any of the following major maternal morbidity occur? *Tick appropriate answer for each condition mentioned*

| | | | |
|---|---|---|---|
| a. Persistent vegetative state | ☐ Yes | ☐ No | ☐ Unknown |
| b. Cardiac arrest | ☐ Yes | ☐ No | ☐ Unknown |
| c. Cerebrovascular accident | ☐ Yes | ☐ No | ☐ Unknown |
| d. Adult respiratory distress syndrome | ☐ Yes | ☐ No | ☐ Unknown |
| e. Disseminated intravascular coagulopathy | ☐ Yes | ☐ No | ☐ Unknown |
| f. HELLP syndrome | ☐ Yes | ☐ No | ☐ Unknown |
| g. Pulmonary oedema | ☐ Yes | ☐ No | ☐ Unknown |
| h. Mendleson's syndrome | ☐ Yes | ☐ No | ☐ Unknown |
| I. Renal failure | ☐ Yes | ☐ No | ☐ Unknown |
| j. Thrombotic event | ☐ Yes | ☐ No | ☐ Unknown |
| k. Septicaemia | ☐ Yes | ☐ No | ☐ Unknown |
| l. Required ventilation | ☐ Yes | ☐ No | ☐ Unknown |
| m. Other, if Yes specify: _____ | | | |

# 11. Appendix B – Human Research Ethics Committee Approval

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

## FHS017: Annual Progress Report / Renewal

### Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

| | | | |
|---|---|---|---|
| **HREC office use only (FWA00001637; IRB00001938)** | | | |
| **This serves as notification of annual approval, including any documentation described below.** | | | |
| ☑ Approved | Annual progress report | Approved until/next renewal date | 30.04.2026 |
| ☐ Not approved | See attached comments | | |
| Signature Chairperson of the HREC/ Designee | Signed by candidate | Date Signed | 8/4/2025 |

HUMAN RESEARCH ETHICS COMMITTEE
2 4 APR 2025
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

**Note: Please note that incomplete submissions will not be reviewed.**
**Our website address: https://health.uct.ac.za/home/human-research-ethics**

Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za

**Principal Investigator to complete the following:**

**1. Protocol information**

| | | | |
|---|---|---|---|
| Date (when submitting this form) | 22/04/2025 | | |
| HREC REF Number | 062/2024 | Current Ethics Approval was granted until | 31/01/2025 |
| Protocol title | Post Caesarean Section complications in women with Covid-19 disease | | |
| Principal Investigator | Prof Matjila | | |
| Department and email address | obstetrics and gynaecology<br>mushi.matjila@uct.ac.za | | |
| 1.1 Does this protocol receive US Federal funding? | | ☐ Yes | ☑ No |

**2. Protocol status (tick ✓)**

| | |
|---|---|
| ☐ | Research-related activities are ongoing |
| ☑ | Data collection is complete, data analysis only |
| ☐ | Publication or thesis submitted and final completion? |

Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.

**3. Protocol summary**

| | | |
|---|---|---|
| Total number of records or specimens collected, reviewed or stored since the original approval | | N/A |
| Total number of records or specimens collected, reviewed or stored since last progress report | | N/A |
| Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report. | ☑ Yes | ☐ No |

**Please complete the Closure form (FHS019) if the study is completed within the approval period**

**4. Signature**

| | | | |
|---|---|---|---|
| Signature of PI | Signed by candidate | Date | 24/04/25 |

M. Matjila

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

# Form FHS011: Study deviation

| HREC office use only (FWA00001637; IRB00001938) | | | |
|---|---|---|---|
| This serves as acknowledgement of a protocol deviation as described below. | | | |
| Chairperson of the HREC signature/ Designee | Signed by candidate | Date | 27/4/2025 |

**Note:** Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za. Our website address: https://health.uct.ac.za/home/human-research-ethics

HUMAN RESEARCH ETHICS COMMITTEE
24 APR 2025
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

## Principal Investigator to complete the following:

### 1. Protocol information

| | |
|---|---|
| Date (when submitting this form) | 22/04/2025 |
| HREC REF Number | 062/2024 |
| Project Title | Post Caesarean Section Complications in Women with covid-19 disease |
| Protocol number (if applicable) | |
| Principal Investigator | Prof Matjila |
| Department and Email address | Type text here<br>Obstetrics and Gynaecology |

### 2. Protocol deviation description

| Please describe the deviation below, including the reason why the deviation has occurred. |
|---|
| Delayed submission due to difficulty accesing data |

### 3. Follow-up actions

| 3.1 Please describe any follow-up action(s) taken or planned as a result of this deviation e.g. DSMB reporting, report to sponsor, informing participants. |
|---|
| Completing write up |

| 3.2 Please describe what action(s) have or will be taken to prevent similar deviations in future. |
|---|
| Completing write up |

## 4. Principal Investigator's acknowledgement of responsibility

| The required signature indicates the PI has reviewed the deviation, taken appropriate follow-up action and implemented or plans to implement preventative steps where possible. | | | |
|---|---|---|---|
| Signature of PI | Signed by candidate<br>M. Matjila | Date | 24/4/25 |