# *Factors associated with disease severity amongst children admitted with SARS-COV-2 infection in Gauteng and KwaZulu-Natal, 2020 to 2022.*

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**RESEARCH REPORT**
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# DECLARATION

I, Dr Dominique Adrienne Tapamo, declare that this research report is my own work. It is being submitted in partial fulfilment of the requirements for the degree of Master of Science in Epidemiology in the field of Epidemiology & Biostatistics at the University of the Witwatersrand, Johannesburg. This research has not been submitted previously for any degree or examination to any other institution. All sources and references used in this report have been acknowledged.

Signature: 

09 October 2025

# DEDICATION

I dedicate this work to my family, whose unwavering support, encouragement, and love have been the foundation of my academic journey. To my parents—my mother, Mrs. Augustine Chantale Tapamo and my father, Prof. Jules-Raymond Tapamo—thank you for your sacrifices, your constant support and for always believing in my potential. Without you both, this degree would not have been possible. I am deeply grateful for everything.

# ABSTRACT

## Background

Understanding the risk factors associated with severe disease, including mortality, in children infected with SARS-CoV-2 is crucial for guiding public health interventions and clinical management.

## Methods

We conducted a retrospective analysis of paediatric patients (<18 years) admitted with SARS-CoV-2 infection between April 2020 and March 2022 in Gauteng and KwaZulu-Natal. We examined demographic and clinical characteristics associated with mortality and severe disease, using multivariable logistic regression models to estimate adjusted odds ratios (aORs) with 95% confidence intervals (CIs).

## Results

Among 13,577 children admitted, 1,569 (11.6%) developed severe COVID-19. Newborns had the highest odds of severe disease (aOR: 4.7, 95% CI: 3.4–6.5, p<0.001), followed by infants aged 1–11 months (aOR: 2.0, 95% CI: 1.6–2.5, p<0.001). Males had a slightly increased risk (aOR: 1.2, 95% CI: 1.1–1.4, p=0.013). Comorbid conditions significantly contributed to severity, with diabetes (aOR: 3.6, 95% CI: 2.3–5.5, p<0.001) and HIV-positive status (aOR: 1.6, 95% CI: 1.0–2.6, p=0.043) being key predictors. Hospital stays exceeding 15 days were strongly associated with severe disease (aOR: 6.0, 95% CI: 4.8–7.6, p<0.001).

Among 320 paediatric deaths, infants (<1 year) accounted for the highest proportion (43.1%), with newborns at the greatest risk (aOR: 3.2, 95% CI: 2.1–4.8, p<0.001). Adolescents (13–17 years) also had an increased mortality risk (aOR: 1.6, 95% CI: 1.1–2.3, p=0.016). Patients admitted to high-care and intensive care units had markedly higher odds of death (aOR: 2.4 and 8.2, respectively, p<0.001).

**Conclusion**

Younger age (especially newborns), male sex, prolonged hospitalization, and underlying comorbidities significantly increased the risk of severe disease (including mortality) in paediatric COVID-19 patients. These findings emphasize the need for targeted interventions to protect high-risk children and optimize clinical management strategies.

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# ABBREVIATIONS

All the abbreviations used in the research report in alphabetical order.

| Abbreviations | Meaning |
|---|---|
| **ACE2** | angiotensin converting enzyme 2 |
| **ARDS** | acute respiratory distress syndrome |
| **CLD** | chronic lung disease |
| **CLWHIV** | Children living with HIV |
| **COVID-19** | Coronavirus Disease 19 |
| **CRP** | C-reactive protein |
| **DIC** | disseminated intravascular coagulopathy |
| **ESR** | Erythrocyte Sedimentation Rate |
| **GP** | Gauteng Province |
| **HFNPO2** | high flow nasal prong oxygen |
| **HIV** | human immunodeficiency virus |
| **HPRN** | hospital patient registration number |
| **ICU** | intensive care unit |
| **KZN** | KwaZulu-Natal |
| **LOS** | Length of stay |
| **MIS-C** | multi-systematic inflammatory syndrome |
| **NICD** | National Institute for Communicable Diseases |
| **NPO2** | nasal prong oxygen |
| **NS** | Not significant |
| **OR** | odds ratio |
| **PT** | Prothrombin time |
| **PTT** | Partial thromboplastin time |
| **PUI** | patient under investigation |
| **RT PCR** | reverse transcriptase polymerase chain reaction |
| **SARS-COV-2** | severe acute respiratory syndrome coronavirus 2 |
| **SD** | Standard deviation |
| **TB** | Tuberculosis |
| **US** | United States |
| **USA** | United States of America |
| **WHO** | World Health Organization |

# CHAPTER 1

# Introduction

## 1.1. Backgroud

The beginning of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) at the end of 2019 marked a global pandemic which had significant health implications. Initially perceived as primarily affecting adults, the virus causes a range of symptoms from mild to severe illness, predominantly impacting the respiratory system but also affecting the gastro-intestinal and neurological systems (1-4).

Early pandemic data suggested children were less susceptible to COVID-19, with minimal testing and confirmed cases (5, 6). In South Africa, for instance, individuals under 19 years comprised only 12.5% of confirmed cases and 0.7% of COVID-19-associated deaths (6). However, this likely underestimated the true prevalence due to lower testing rates and asymptomatic presentations in this age group (6-8). Although Gauteng province and KwaZulu-Natal (KZN) are the most populous provinces in South Africa (9), Gauteng and the Western Cape recorded the highest numbers of COVID-19–related admissions, with approximately 161,730 and 121,822 admissions, respectively, while KwaZulu-Natal had 90,336 admissions (9). A study by Chiwandire et al., covering the period from March 2020 to February 2022, found that although children accounted for nearly 35% of the population, they represented only 13.6% of total SARS-CoV-2 tests, 11.8% of laboratory-confirmed cases, 5.8% of COVID-19–associated hospital admissions, and 0.7% of COVID-19–associated deaths (7).

Research globally has identified several risk factors for severe COVID-19 in children, including underlying comorbidities such as asthma, chronic lung diseases, diabetes, HIV, and tuberculosis. Additional risk factors include young age (particularly newborns and infants), prematurity, and in some studies, male sex. The severity of disease varies, with approximately 30% of hospitalized children experiencing critical conditions (10-16).

The introduction of COVID-19 vaccination was crucial in mitigating severe disease. In South Africa, the vaccination program began in February 2021, with eligibility for children aged 12 and above initially introduced in December 2021, and extended to the 5-11 age group in December 2022 with children below the ages of 5 not being eligible for the vaccine (17, 18). From existing literature, newborns and infants demonstrated a higher risk of severe disease. While those falling in these age groups are not eligible for COVID-19 vaccination, evidence indicates that vaccinating pregnant women significantly reduces the risk of severe disease in their infants, particularly those under six months of age (19).

## 1.2. Problem statement

Since the beginning of the pandemic, similar studies have examined the paediatric population, though most were conducted in high-income countries (12-14, 16). These studies found that comorbidities significantly increased the risk of severe COVID-19 in children (12, 15, 16, 20, 21). This study would assist in identifying the factors associated with hospital admission and disease severity in our setting. Looking at the paediatric population, from 0 – 17 years would identify which age groups are highest at risk of severe disease and factors associated with severe disease. Gauteng Province and KwaZulu-Natal Province are 2 of the most populated provinces in the country (9), therefore

identifying local risk factors in these provinces is essential to guide targeted interventions, resource allocation, and health policy.

Although most children infected with SARS-CoV-2 experience mild or asymptomatic disease, a subset develop severe or critical illness. Severe manifestations commonly include respiratory complications such as acute respiratory distress syndrome (ARDS), hypoxemia requiring supplemental oxygen, and pneumonia. Cardiovascular involvement may occur, including myocarditis, pericarditis, shock, and hypotension, and in some cases, children develop multisystem inflammatory syndrome (MIS-C), characterized by fever, mucocutaneous involvement, cardiac dysfunction, and systemic inflammation. Neurological complications, such as seizures, altered mental status, or rarely stroke, have also been reported. Gastro-intestinal symptoms may include severe abdominal pain, vomiting, diarrhea, and hepatic dysfunction, particularly in MIS-C. Hematologic and immunologic abnormalities, including coagulopathy, thrombocytopenia, and hyperinflammatory states, are also features of severe disease. Multi-organ failure may occur in the most critical cases, and children with underlying comorbidities—such as chronic lung disease, congenital heart disease, obesity, or immunocompromised states—are at higher risk of developing severe outcomes (1, 22).

In general, children < 5 years are a vulnerable population group who are susceptible to infections and illnesses due to their physiology and immunity. Therefore, preventing these diseases is crucial for children's survival to adulthood. School-going children are often exposed to pathogens from their peers, which can lead to increased school absences

and hospital visits. These illnesses can also affect their caregivers, who may need to miss work to care for sick children, potentially impacting the family's income (23, 24).

In children ≥ 5 years, where the COVID-19 vaccine has been approved, identifying and prioritizing vaccination efforts for high-risk groups in our resource-limited setting would help justify which populations should be prioritized.

## 1.3. Justification

Identifying clinical and demographic factors associated with severe COVID-19 in children in our setting can help guide targeted preventive measures, such as advocating for the prioritization of vaccinations for those at highest risk. It can also support informed clinical decision-making and improve risk communication with parents and caregivers. Additionally, these findings will aid policymakers and clinicians in developing future COVID-19 guidelines and optimizing resource allocation in our already resource-limited setting.

While several studies have described risk factors for severe pediatric COVID-19 in high-income countries, there remains a paucity of data from low- and middle-income countries, including South Africa, where health system constraints and population characteristics differ (11, 13, 14, 16, 20, 21, 25). Understanding these factors is particularly relevant in the post-COVID era, as health systems prepare for potential resurgences of SARS-CoV-2 and integrate lessons learned into broader pandemic preparedness and child health strategies.

Although the vaccine has not yet been approved in children < 5 years, this study could serve as a future guide in this age group should there be a need. Gauteng and Kwa-Zulu Natal were chosen as the two most populous provinces in the country and contributed the highest and 3rd provinces with the most COVID-19 related admissions respectively (6).

The time period, 2020-2022, was selected to capture the height of the pandemic, covering four of the five waves. The waves covering the periods of analysis were as follows: the first wave, driven by the D614G B.1 variant (June 7–Aug 22, 2020); the second wave, dominated by the Beta B.1.351 variant (Nov 15, 2020–Feb 6, 2021); the third wave, associated with the Delta B.1.617.2 variant (May 9–Sept 18, 2021); and the fourth wave, linked to the Omicron BA.1 and BA.2 variants (Nov 28, 2021–Feb 5, 2022) (26).

## 1.4. Literature review

Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), a virus causing the disease called Coronavirus diseases 19 (COVID-19), was first discovered in Wuhan, China, towards the end of 2019, spread rapidly globally causing severe morbidity and mortality. SARS-COV-2 infection ranged from asymptomatic to severe illness in humans with adults being predominantly affected (1, 3, 27). Children were initially described as being asymptomatic or developing mild symptoms (2). In the early stages of the pandemic, the confirmed SARS-COV-2 positive tests in children accounted for between 1% and 2% of the total positive test from surveillance studies done in several countries (28-30). Complications of SARS-COV-2 infection in children described included (i) acute respiratory failure and ARDS (acute respiratory distress syndrome), (ii) sepsis and septic shock, (iii) acute kidney failure, (iv) neurological complications such as meningitis and encephalitis, (v) hypercoagulable state, (vi) myocarditis(10), (vii) post-infectious multi-systematic inflammatory syndrome (MIS-C) and (viii) long covid syndrome (27).

### 1.4.1. Prevalence, clinical manifestations and complications of COVID-19

In South Africa, from March 2020 until February 2022, children aged ≤ 18 years accounted for approximately 11.8% of laboratory-confirmed cases, 5.8% of COVID-19 associated hospital admissions, and 0.7% of COVID-19 associated deaths (7). They also reported that Gauteng Province had the highest percentage of tests done, confirmed cases, and hospital admissions (6). Due to children being mostly asymptomatic and having a lower rate of being tested, it is thought that the prevalence of COVID-19 is underestimated in

this group. In the United States of America, they estimated asymptomatic infection in children to range from 10% to 42% (8). Clinical presentation includes fever, cough, rhinorrhoea, sore throat, headache, vomiting, diarrhoea, difficulty breathing, dyspnoea, myalgia, fatigue, and tachycardia (3, 8). A significant number of children had mild upper respiratory tract infections (URTI), but some developed lower respiratory tract infections (LRTI). These include pneumonia and the acute respiratory distress syndrome (ARDS). As previously mentioned, it is described that COVID-19 affected the respiratory system, but extra pulmonary manifestations can also occur which include cardiac involvement such as myocarditis, heart failure, and arrhythmias; neurological involvement such as anosmia and ageusia which is reported as a symptom in older children, others included headache, encephalopathy, seizures, weakness, Guillain-Barre Syndrome, movement disorders and psychiatric disorders (8, 31). Some children with pre-existing neurological pathologies experienced worsening or exacerbations in their symptoms. Other systems involvement include renal, dermatological, and gastro-intestinal manifestations such as diarrhoea, vomiting, loss of appetite, and abdominal pain (8).

MISC is a complication of COVID-19 in children and notifiable medical condition in South Africa. The Centers for Disease Control and Prevention (CDC) and the WHO defined criteria to diagnose MISC which include clinical presentation, laboratory findings, and organ involvement (8). This syndrome has been described in children and adolescents between the ages 0 to 19 years, with ≥ 3day history of fever, with a confirmed current or recent positive SARS-COV-2 test or likely contact with COVID patients, elevated inflammatory markers such as Erythrocyte Sedimentation Rate (ESR), C-reactive protein

(CRP), pro-calcitonin, fibrinogen, ferritin and D-dimer (8, 32), and 2 of the following: rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet); hypotension or shock; features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiogram findings or elevated troponin/NT-pro Brain natriuretic peptide); evidence of coagulopathy (by PT, PTT, elevated D-dimers), acute gastro-intestinal problems (diarrhoea, vomiting, or abdominal pain). There should also be no other plausible diagnosis (10). The abdominal symptoms occur in approximately 60% of children with MISC and can be severe (10).

Long COVID is described as persistent symptoms of COVID-19 after a confirmed or probable SARS-COV-2 infection, usually 3 months after the onset of COVID symptoms, and last for at least 2 months and cannot be explained by another diagnosis (8). Symptoms include cough, fatigue, headache, insomnia, decreased concentration, and muscle and joint pain (8).

### 1.4.2. Risk factors associated with severe COVID-19

Numerous studies conducted in Europe and America aimed to identify risk factors for severe disease in children. Severe disease was defined as requiring critical care admission, developing COVID-19-related complications, or resulting in COVID-19-related death. These factors will be described below.

Age has consistently been described as an important predictor of disease severity. A systematic review reported that infants (<1 year of age) and children aged 10–14 years were more likely to require critical care and had higher mortality compared with other age groups (12). In the United States, Woodruff et al. found that children under 12 months had a higher risk of severe disease and intensive care admission (13). A Brazilian study similarly reported that newborns (<30 days) had the greatest risk, with an adjusted odds ratio (aOR) of 9.5 (95% CI 3.0–30.1), while children aged 6–10 years also had elevated risk with an aOR 2.3 (95% CI 0.8–6.4) (15). In sub-Saharan Africa, infants <1 year demonstrated an aOR of 4.89 (95% CI 1.44–16.61) for severe outcomes including ICU admission and mortality (33). A South African national analysis confirmed that children < 1 year had significantly higher mortality with an OR 4.11 (95% CI 1.08–15.54) (11). In addition, Graff et al. found that infants ≤3 months were at particularly high risk (16). Among older children, Schober et al. reported that adolescents aged ≥12 years had increased odds of severe disease, particularly in the presence of obesity (OR 2.2, 95% CI 1.3–3.7) (14).

The presence of underlying medical conditions is strongly associated with poor outcomes. A systematic review showed a stepwise increase in risk, with odds of moratlity nearly five-fold higher in children with ≥3 comorbidities (OR 4.98, 95% CI 3.78–6.56) compared with those with one (12). In Brazil, children with one comorbidity had an aOR of 5.3 (95% CI 2.7–10.3), increasing to an aOR 9.9 (95% CI 4.5–22.2) with ≥2 comorbidities (15). Similarly, Schober et al. reported ORs of 1.6 (95% CI 1.05–2.5) for one comorbidity and 2.6 (95% CI 1.6–4.2) for two (14). Sub-Saharan African data showed comparable patterns, with one comorbidity associated with an aOR of 1.95 (95% CI 1.08–3.50) and

≥2 with an aOR of 3.75 (95% CI 1.71–8.22) (33). In South Africa, non-communicable comorbidities were impactful, showing that having ≥ 1 non-communicable comorbidity present had an OR of 12.09 (95% CI 4.19 – 34.89) (11).

Obesity was also among the most frequently identified risk factors. Schober et al. found it conferred nearly five-fold increased odds of severe disease (OR 4.7, 95% CI 2.3–9.7) (14). Antoon et al. reported an aOR of 2.2 (95% CI 1.6–2.8) (21), while Graff et al. also demonstrated obesity as a significant risk factor for severe outcomes (16). Non-asthma pulmonary disease was consistently associated with severe outcomes: aRR 2.2 (95% CI 1.1–4.3) in U.S. children <2 years (13), OR 3.1 (95% CI 1.5–6.6) in Schober et al. (14), and aOR 2.7 (95% CI 1.8–3.9) in Antoon et al. (21). Sub-Saharan African data similarly showed increased risk (aOR 2.97, 95% CI 1.65–5.37) (33).

Evidence for asthma as a risk factor had mixed findings. Some studies reported increased odds of severe disease (16, 20) and increased odds of hospitalization (21), while others found no significant association with severe disease (13, 21). This inconsistency may reflect differences in disease control, with uncontrolled or severe asthma showing a higher risk of severe disease (25).

Cardiac disease was identified as a strong predictor. Woodruff et al. found an aRR of 1.7 (95% CI 1.3–2.3) in children <2 years (13). Antoon et al. reported the highest effect size among comorbidities, with an aOR of 3.1 (95% CI 2.6–3.7) (21). Schober et al. similarly observed increased odds in younger children (14).

Neurological disorders in children <2 years were associated with an aRR of 2.0 (95% CI 1.5–2.6) (13). Antoon et al. reported neuromuscular disease as a significant risk factor with an aOR of 1.6 (95% CI 1.2–2.0) (21).

Diabetes mellitus was consistently reported as a significant risk factor. In U.S. children ≥2 years, the aRR was 1.9 (95% CI 1.6–2.3) (13). Antoon et al. reported an aOR of 2.2 (95% CI 1.6–2.8) (21), and Graff et al. identified it as an important contributor to severe outcomes (16).

Hypertension was associated with increased risk in multiple studies. Schober et al. reported an OR of 2.8 (95% CI 0.8–9.5) (14), while sub-Saharan African data showed a strong association (aOR 5.91, 95% CI 1.89–18.50) (33).

Premature infants were also at higher risk, with an aRR of 1.6 (95% CI 1.3–2.1) in children <2 years (13). Among children ≥2 years, feeding tube dependence was associated with aRR 2.0 (95% CI 1.5–2.5) for severe disease (13). Sub-Saharan African data reported haematological disorders as an independent risk factor (aOR 3.10, 95% CI 1.04–9.24) (33). Schober et al. identified chromosomal abnormalities as a significant predictor, with an OR of 3.6 (95% CI 1.0–12.6) (14).

In sub-Saharan Africa, HIV infection showed a non-significant trend towards increased risk (aOR 2.02, 95% CI 0.97–4.20; p=0.06) (33). In South Africa, HIV, tuberculosis, and malignancy were common among hospitalized children, though no deaths were reported in those with HIV or chronic pulmonary disease in this particular study (11).

Findings regarding sex were inconsistent. Some studies reported higher risk among males (16, 21, 34), while others suggested higher risk in females (14, 20). However, these differences did not reach statistical significance.

Beyond biological risk factors, health system disparities contributed to outcomes. In South Africa, admission to public hospitals was independently associated with higher mortality (OR 5.07, 95% CI 2.01–12.76) (11).

Existing literature shows that children at risk of severe COVID-19 disease include those living with one or more comorbidity, such as chronic lung disease, cardiac disease, diabetes mellitus, and hypertension. It also shows that having more than one comorbidity increased the risk of severe disease further. This study describes the factors associated with disease severity amongst children admitted with SARS-COV-2 infection in Kwa-Zulu Natal Province and Gauteng Province from April 2020 to March 2022.

## 1.5. Research Question

What are the factors associated with disease severity amongst children admitted with SARS-COV-2 infection in Kwa-Zulu Natal Province and Gauteng Province from April 2020 to March 2022?

## 1.6. Aim:

To describe the demographic and clinical characteristics of children < 18 years hospitalized with COVID-19 and to determine factors associated with disease severity

among those admitted with SARS-CoV-2 infection in KwaZulu-Natal and Gauteng Provinces from April 2020 to March 2022.

## 1.7. Specific objectives:

1. To describe the clinical characteristics and demographics of children aged < 18 years admitted with SARS-COV-2 in hospitals in KwaZulu-Natal Province and Gauteng Province from April 2020 to March 2022
2. To determine the factors associated with disease severity in children < 18 years of age admitted with SARS-COV-2 infection in KwaZulu-Natal Province and Gauteng Province from April 2020 to March 2022.

# CHAPTER 2

# Methods

This chapter provides an overview on the data collection, the study setting, the study population, the analysis was conducted, including the variables analysed and the ethics consideration.

## 2.1. Data collection and Primary data source

The primary data was from the data for COVID-19 (DATCOV), which was a national active surveillance for COVID-19 admissions. This surveillance system was started in April 2020 during the pandemic, about 666 hospitals, both public and private hospitals, were involved until December 2022 when the DATCOV surveillance system ended (35-37). The surveillance system, which was a prospective, electronic-based, active, hospital-based sentinel surveillance, captured SARS-COV-2 positive related admissions in South Africa from March 2020 to December 2022, and was funded by the National Department of Health and National Institute for Communicable Diseases (NICD). Patients were identified on admission and followed up to their in-hospital outcome were possible.

The primary aim of this hospital surveillance system was to “describe the epidemiology of the COVID-19 outbreak” and “the distribution of hospital admissions” (36). The patients were captured using their identification number, hospital patient registration number (HPRN) or a NICD case ID. Any patient who tested positive for SARS-COV-2 test on reverse transcriptase polymerase chain reaction (RT PCR) assay, or antigen test from a

nasopharyngeal swab, nasal swab, oropharyngeal swab, or occasionally a lower respiratory tract specimen (sputum, tracheal aspirate, and broncho-alveolar lavage) was enrolled (11).

The patients were classified as a case on the DATCOV database if the test was positive irrespective of the reason for admission (ie. COVID-19 related or not). The variables that were collected for each patient were the patient's demographics such as age, sex, race, and the province they were admitted from, their comorbidities, clinical characteristics, complications, length of hospital stay, type of ward admitted in, medical treatment given, and type of oxygen administered and the admission outcomes (36).

The DATCOV data management included removing duplicates and extracting source data from other surveillance systems to minimize missing data. Additional sources used included the notifiable medical condition (NMC) platform and patient under investigation (PUI) database to extract and correlate data. (36)

## 2.2. Study setting

This study was a secondary data analysis, were the focus was in 2 provinces: Gauteng and KwaZulu-Natal. The data was from private and public hospitals in Gauteng and KwaZulu-Natal, in children < 18 years of age admitted with SARS-COV-2 infection, will be analysed. Gauteng is the most populous but smallest province of South Africa, with 1.4% of the total surface area of the country with an area of 18 178km² (38). In 2024, the

mid-year population was estimated the population of Gauteng to be approximately 15.8 million people which made up 25.1% of South Africa's population (39). KZN is the third smallest province of South Africa, and the second most populous province, with a total surface area of 94 361km² (40) and a total population of approximately of 12.3 million people which is 19.6% of South Africa's total population with 27.5% of the population being <15 years of age in South Africa (39). Over half were from the private sector, including hospital groups such as Melomed, Life Hospitals, Medicross, and Lenmed, while the public hospitals represented urban, semi-urban, and rural areas (9).

## 2.3. Study design

The study design was a cross-sectional study through secondary analysis of data from DATCOV hospital surveillance in South Africa.

## 2.4. Study population

The study population included participants < 18 years of age, who were admitted to the paediatric or medical department, AND had a documented, laboratory-confirmed positive SARS-COV-2 result. The patients who were admitted in KwaZulu-Natal and Gauteng from April 2020 to March 2022 were included.

## 2.5. Study sample

The study included all participants aged < 18 years with laboratory-confirmed SARS-CoV-2 infection who were admitted to hospitals in Kwazulu-Natal and Gauteng and enrolled in

the DATCOV hospital surveillance system from April 2020 to March 2022. These two provinces are the most populous in South Africa and had the highest number of COVID-19-related admissions during the pandemic, with Gauteng reporting the most cases and KwaZulu-Natal ranking third.

### 2.5.1. Inclusion Criteria:

- Children aged < 18 years with laboratory confirmed SARS-CoV-2 admitted to public or private hospitals in the KwaZulu-Natal and Gauteng provinces.
- Laboratory-confirmed SARS-CoV-2 positive cases, from any testing laboratories associated with the hospitals.
- Participants with laboratory confirmed SARS-CoV-2 admitted to general wards, high care units, or intensive care units (ICUs).

### 2.5.2. Exclusion Criteria:

- Participants from KwaZulu-Natal and Gauteng provinces with unknown outcomes.
- Participants who had COVID-19, but where the classification of disease severity was not possible.

## 2.6. Sample size

All children under 18 years of age with laboratory-confirmed COVID-19, admitted to hospitals in KwaZulu-Natal and Gauteng provinces and enrolled in the DATCOV surveillance from April 2020 to March 2022, who met the inclusion criteria, were included

in the analysis and report. After cleaning and removing duplicates in the dataset, the sample size was 13577.

## 2.7. Data collection

The data analyzed were a secondary data analysis from DATCOV dataset.

COVID-19 has been described with 5 categories of disease severity, ranging from asymptomatic to critical

### 2.7.1. Data collection

#### 2.7.1.1. Dependent Variable:

**Severity of Disease**: Categorized as Severe Disease or Non-severe Disease, as detailed in Table 1.

***Table 1*****:** A table to show the categories of COVID-19 disease severity[1] [2]

| Severity | Symptoms experienced |
|---|---|
| **Asymptomatic** | No symptoms experienced |
| **Mild** | Mild symptoms such as cough and fever but no evidence of pneumonia |
| **Moderate** | Clinical features of pneumonia, oxygen saturation >92% |
| **Severe** | Requiring supplementary oxygen, admission to high care |
| **Critical** | Developing ARDS, septic shock, organ failure, requires admission to ICU and mechanical ventilation |

Literature defined mild disease as a patient with various symptoms of COVID-19 such as cough and fever but no signs of pneumonia, moderate disease was defined by clinical signs of pneumonia with oxygen saturation > 92% to 94%. Severe disease was defined

[1] https://www.ncbi.nlm.nih.gov/books/NBK570371/pdf/Bookshelf_NBK570371.pdf
[2] https://www.nicd.ac.za/wp-content/uploads/2021/12/COVID-19-in-Children-week-48.pdf

as a patient who required supplementary oxygen or had infiltrates affecting more than 50% of the lungs. Critical disease are patients who were admitted to high care facility or ICU, developed complications from SARS-COV-2 infection including respiratory failure, acute respiratory distress syndrome (ARDS), organ failure, MIS-C, septic shock, and COVID-19 related deaths (1, 6). Severe and critical disease may overlap in some cases.

In this data analysis, the classification above was categorized to define severe disease as patients presenting with severe or critical illness, while non-severe disease was defined as those with mild or moderate illness. The following classifications were used: non severe disease included children admitted to the general ward or isolation who did not require oxygen therapy. Severe disease included children admitted to high care or the intensive care unit, those who required supplementary oxygen or were intubated, and patients who experienced in-hospital mortality.

Independent variables included the presence of pre-existing comorbidities, such as chronic lung disease, asthma, chronic kidney failure, cardiac disease, hypertension diabetes mellitus, HIV infection, tuberculosis, malignancies, and obesity (11). Additional predictor variables in the dataset included the type of healthcare facility (private vs. public sector), nutritional status, and treatments received.

### 2.7.1.2. Independent Variables:

- **Comorbidities**: Presence of any comorbidity (Yes/No).

- **Risk Factors**: other risk factors, such as CLWHIV, diabetes mellitus, cardiac disease, previous or current tuberculosis, obesity, sex and race/ ethnic background. These variables will be listed below.

## 2.7.2. Other independent variables

***Table 2:*** Summary of variables included in the analysis

| Types of variables | Variable | Categories |
|---|---|---|
| **2.7.2.1. Continuous Variables** | Duration of Hospital Stay | Median and interquartile range (IQR) |
| | Age (in years) | Median and interquartile range (IQR) |
| **2.7.2.2. Categorical Variables** | Age Groups | Newborns (≤28 days of life), 1–11 months, 1–4 years, 5–12 years, 13–17 years |
| | Race | Black, Other race (Indians, Coloureds, other races), Unknown |
| | Comorbidities | Presence/absence of: Chronic lung disease, asthma, chronic renal failure, cardiac conditions, diabetes mellitus, hypertension, HIV infection, tuberculosis (previous/current), malignancies |
| | Nutritional Status | Obese, Not obese, Unknown |
| | Admission Ward | Medical ward (incl. isolation), High care, ICU |
| | Oxygen Therapy | No oxygen, Oxygen therapy, Intubated |

| | | |
|---|---|---|
| | Comorbidities Present | None, 1 comorbidity, ≥2 comorbidities |
| **2.7.2.3. Binary Variables** | Sex | Male, Female |
| | Sector Admitted | Public, Private |
| | In-hospital Outcome | Alive (discharged, still hospitalized, transferred), Dead (SARS-CoV-2-related, SARS-CoV-2 positive but not primary cause) |
| | Provinces | Gauteng, KwaZulu-Natal |

## 2.8. Statistical analysis (refer to Table 4)

### 2.8.1. Bivariate Analysis:

A Pearson Chi-squared test was utilized to identify factors significantly associated with severe SARS-CoV-2 disease in children, focusing on risk factors and comorbidities. Statistically significant associations, defined as p values of <0.05, were assessed between disease severity and variables such as age, HIV status, race, hypertension, diabetes mellitus, cardiac disease, chronic kidney failure, previous tuberculosis, obesity, discharge status, province, and type of healthcare sector. Following this, bivariate logistic regression was then conducted.

### 2.8.2. Multivariable Analysis:

A multivariable logistic regression model was used to evaluate the association between disease severity and possible risk factors. Variables with a p-value of <0.2 on univariate analysis were considered for inclusion in the multivariable model.

For the model selection, backward elimination was applied, retaining variables with a p-value <0.05, indicating statistical significance. Confounders such as age, sex, and race were checked and adjusted for in the analysis. Additionally, variables not statistically significant were included in the model if deemed epidemiologically important, such as race, sex, the province and the hospital sector in which the participants were admitted. Children aged 1–4 years, female sex, other race, care in the private sector, residence in KwaZulu-Natal province, and absence of documented comorbidities were specified as the reference categories, as these groups represented the most common or clinically relevant baseline populations against which comparisons were made.

Continuous variables were summarized using interquartile ranges (IQR). Odds ratios (OR) and 95% confidence intervals (CI) are reported. Percentages for comorbidities were calculated from cases with known status only. NS indicates results that were not statistically significant. The multivariable logistic regression model was adjusted for all covariates listed; adjusted odds ratios (aORs) reflect the odds of severe disease compared with the reference category within each variable. Variables such as ward of admission, oxygen use, and outcomes resulting in death secondary to COVID-19 were not included as separate variables, as they were incorporated into the classification of severe and non-severe disease.

The final logistic regression model was assessed for goodness of fit using the Hosmer–Lemeshow test. Model results included odds ratios (OR), adjusted odds ratios (aOR), and corresponding p-values for each variable. The Hosmer–Lemeshow test indicated an

adequate model fit, with no significant difference between observed and predicted outcomes ($p > 0.05$).

#### 2.8.3. Subgroup Analysis:

The analysis was conducted with data from both provinces combined. In addition, separate analyses were conducted for each province to identify province-specific risk factors. An sub-analysis was also done to assess the risk factors for mortality, with in hospital outcome as the outcome variable.

## 2.9. Data management

The statistical software STATA version 18 was used to manage and analyse the data. Once ethics was approved, the dataset was made available by NICD. The dataset was cleaned, checked for validity and duplicates were removed. The variables were coded and recoded according to the available data. The data was stored and locked in a password-protected device. Participant's ages were filtered to align with the inclusion criteria, specifically ranging from 0 days to under 18 years. Subsequently, hospital admission dates were constrained to the period between April 1, 2020, and March 31, 2022.

## 2.10. Ethical considerations

Patient data were de-identified and assigned unique identification numbers before being shared for analysis. Ethical clearance for the research report was obtained through the University of the Witwatersrand. The primary DATCOV study received ethical approval as

a national surveillance program from the University of the Witwatersrand's Human Research Ethics Committee (Medical), under reference number M160667 (41). Ethics approval for this specific research report was granted in April 2024, with the reference number M240146. Refer to appendix 2.

# CHAPTER 3

## Results

The results are presented according to the specific objectives. First by looking at the summary of the data, the demographics and clinical characteristics, then the univariate and multivariate analysis; and finally, the multivariate analysis of risk factors for mortality.

As shown in Figure 1, the total number of admissions was 13,630. After excluding 53 duplicate cases, 13,577 participants were included in the analysis. Of these, 5,013 (37%) were admitted in KwaZulu-Natal Province and 8,564 (63%) in Gauteng Province. In KwaZulu-Natal, 4,559 (91%) participants presented with non-severe disease, while 454 (9%) had severe disease. Gauteng had 7,449 (87%) participants with non-severe disease, and 1,115 (13%) had severe disease.

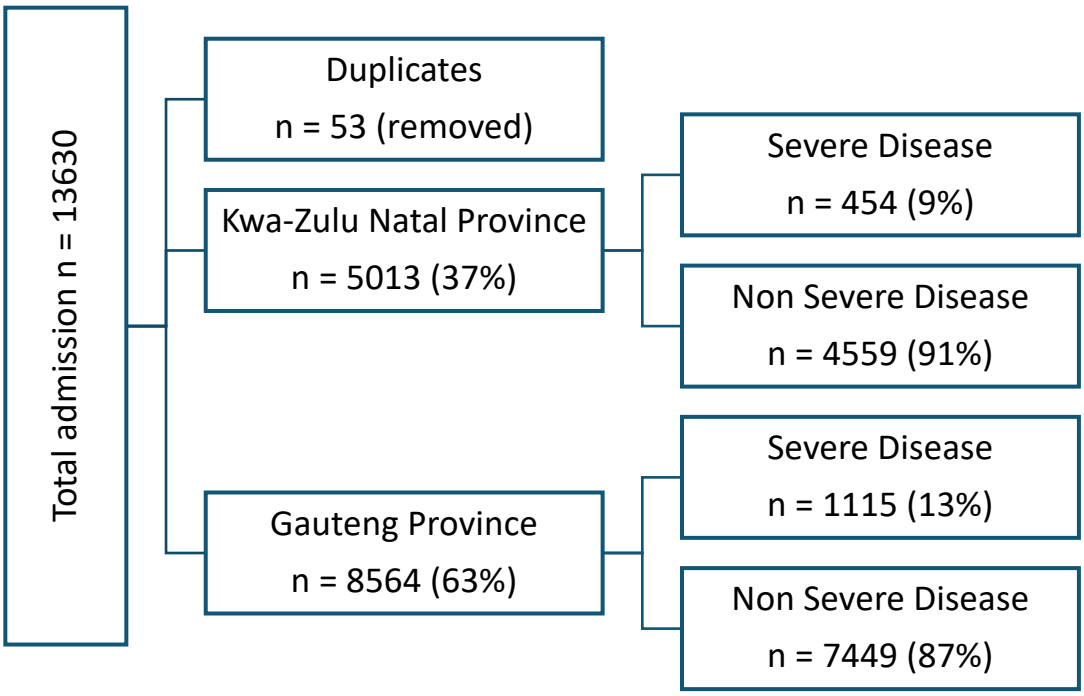


***Figure 1:*** *A flow diagram demonstrating severe and non-severe COVID-19 in KwaZulu-Natal and Gauteng provinces in paediatric patients admitted from April 2020 to March 2022.*

Table 3 presents the demographic, clinical, and hospital-related characteristics of the study population (N = 13,577). The table provides an overview of patient distribution based on age, sex, race, hospital admission details, comorbidities, oxygen therapy requirements, and in-hospital outcomes and their associated Pearson chi squared test.

**Table 3:** *Demographic, clinical, in-hospital management, and outcomes of children under 18 years with COVID-19–related admissions by severity status, pooled data from KwaZulu-Natal and Gauteng, April 2020–March 2022*

| Variable | Disease severity | | | |
|---|---|---|---|---|
| | **Non-Severe** | **Severe** | **Total** | **p-value** |
| **N** | 12,008 (88.4%) | 1,569 (11.6%) | 13,577 (100.0%) | |
| **Age (in years)** Median (IQR) | 4 (0 – 12) | 3 (0 -12) | 4 (0 – 12) | 0.578 |
| **Age in groups** | | | | |
| newborns | 565 (4.7%) | 201 (12.8%) | 766 (5.6%) | <0.001 |
| 1 month to 11 months | 2,551 (21.2%) | 366 (23.3%) | 2,917 (21.5%) | |
| 1 year to 4 years | 3,306 (27.5%) | 258 (16.4%) | 3,564 (26.3%) | |
| 5 years to 12 years | 2,866 (23.9%) | 421 (26.8%) | 3,287 (24.2%) | |
| 13 years to 17 years | 2,720 (22.7%) | 323 (20.6%) | 3,043 (22.4%) | |
| **Sex** | | | | |
| Female | 5,850 (48.7%) | 674 (43.0%) | 6,524 (48.1%) | <0.001 |
| Male | 6,131 (51.1%) | 879 (56.0%) | 7,010 (51.6%) | |
| Unknown / Missing | 27 (0.2%) | 16 (1.0%) | 43 (0.3%) | |
| **Ethnicity** | | | | |
| Black African | 6,977 (58.1%) | 1,080 (68.8%) | 8,057 (59.3%) | <0.001 |
| Other | 797 (6.6%) | 104 (6.6%) | 901 (6.6%) | |
| Unknown/ Missing | 4,234 (35.3%) | 385 (24.5%) | 4,619 (34.0%) | |
| **Comorbidity present** | | | | |
| No comorbidities / Unknown | 11,235 (93.6%) | 1,403 (89.4%) | 12,638 (93.1%) | <0.001 |
| 1 comorbidity | 690 (5.7%) | 141 (9.0%) | 831 (6.1%) | |
| 2 or more comorbidities | 83 (0.7%) | 25 (1.6%) | 108 (0.8%) | |
| **Province** | | | | |
| Gauteng | 7,449 (62.0%) | 1,115 (71.1%) | 8,564 (63.1%) | <0.001 |
| KwaZulu-Natal | 4,559 (38.0%) | 454 (28.9%) | 5,013 (36.9%) | |
| **Hospital Sector** | | | | |
| Private | 6,477 (53.9%) | 625 (39.8%) | 7,102 (52.3%) | <0.001 |
| Public | 5,531 (46.1%) | 944 (60.2%) | 6,475 (47.7%) | |
| **Ward admitted** | | | | |
| Medical/ Isolation Ward | 12,008 (100.0%) | 299 (19.1%) | 12,307 (90.6%) | <0.001 |
| High Care | 0 (0.0%) | 741 (47.2%) | 741 (5.5%) | |
| Intensive Care Unit | 0 (0.0%) | 529 (33.7%) | 529 (3.9%) | |
| **HIV Status** | | | | |
| Negative | 6,794 (56.6%) | 705 (44.9%) | 7,499 (55.2%) | <0.001 |

| | | | | |
|---|---|---|---|---|
| Positive | 157 (1.3%) | 37 (2.4%) | 194 (1.4%) | |
| Unknown / Missing | 5,057 (42.1%) | 827 (52.7%) | 5,884 (43.3%) | |
| **Hypertension** | | | | |
| No | 7,097 (59.1%) | 731 (46.6%) | 7,828 (57.7%) | <0.001 |
| Yes | 115 (1.0%) | 25 (1.6%) | 140 (1.0%) | |
| Unknown / Missing | 4,796 (39.9%) | 813 (51.8%) | 5,609 (41.3%) | |
| **Diabetes Mellitus** | | | | |
| No | 7,052 (58.7%) | 710 (45.3%) | 7,762 (57.2%) | <0.001 |
| Yes | 133 (1.1%) | 52 (3.3%) | 185 (1.4%) | |
| Unknown / Missing | 4,823 (40.2%) | 807 (51.4%) | 5,630 (41.5%) | |
| **Asthma** | | | | |
| No | 6,873 (57.2%) | 718 (45.8%) | 7,591 (55.9%) | <0.001 |
| Yes | 209 (1.7%) | 24 (1.5%) | 233 (1.7%) | |
| Unknown / Missing | 4,926 (41.0%) | 827 (52.7%) | 5,753 (42.4%) | |
| **Cardiac Disease** | | | | |
| No | 6,981 (58.1%) | 727 (46.3%) | 7,708 (56.8%) | <0.001 |
| Yes | 62 (0.5%) | 19 (1.2%) | 81 (0.6%) | |
| Unknown / Missing | 4,965 (41.3%) | 823 (52.5%) | 5,788 (42.6%) | |
| **Chronic Lung Disease** | | | | |
| No | 6,986 (58.2%) | 735 (46.8%) | 7,721 (56.9%) | <0.001 |
| Yes | 39 (0.3%) | 6 (0.4%) | 45 (0.3%) | |
| Unknown / Missing | 4,983 (41.5%) | 828 (52.8%) | 5,811 (42.8%) | |
| **Chronic Renal Failure** | | | | |
| No | 6,969 (58.0%) | 726 (46.3%) | 7,695 (56.7%) | <0.001 |
| Yes | 25 (0.2%) | 14 (0.9%) | 39 (0.3%) | |
| Unknown / Missing | 5,014 (41.8%) | 829 (52.8%) | 5,843 (43.0%) | |
| **Cancer** | | | | |
| No | 6,975 (58.1%) | 736 (46.9%) | 7,711 (56.8%) | <0.001 |
| Yes | 48 (0.4%) | 4 (0.3%) | 52 (0.4%) | |
| Unknown / Missing | 4,985 (41.5%) | 829 (52.8%) | 5,814 (42.8%) | |
| **Tuberculosis** | | | | |
| No TB | 6,726 (56.0%) | 691 (44.0%) | 7,417 (54.6%) | <0.001 |
| TB: Current/Past | 63 (0.5%) | 10 (0.6%) | 73 (0.5%) | |
| Unknown / Missing | 5,219 (43.5%) | 868 (55.3%) | 6,087 (44.8%) | |
| **Obesity** | | | | |
| No | 1,972 (16.4%) | 299 (19.1%) | 2,271 (16.7%) | 0.013 |
| Yes | 26 (0.2%) | 6 (0.4%) | 32 (0.2%) | |
| Unknown / Missing | 10,010 (83.4%) | 1,264 (80.6%) | 11,274 (83.0%) | |
| **Oxygen therapy** | | | | |
| No Oxygen Therapy | 12,008 (100.0%) | 1,460 (93.1%) | 13,468 (99.2%) | <0.001 |
| Supplementary oxygen | 0 (0.0%) | 101 (6.4%) | 101 (0.7%) | |

| | | | | |
|---|---|---|---|---|
| Ventilated | 0 (0.0%) | 8 (0.5%) | 8 (0.1%) | |
| Unknown / Missing | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | |
| **Length of hospital stay (in days)** Median (IQR) | 4 (2 – 7) | 6 (2 – 12) | 4 (2 – 8) | 0.026 |
| **Length of hospital stay** | | | | |
| 7 or less days admitted | 9,135 (76.1%) | 932 (59.4%) | 10,067 (74.1%) | <0.001 |
| 8 to 14 days admitted | 1,712 (14.3%) | 317 (20.2%) | 2,029 (14.9%) | |
| 15 or more days admitted | 1,161 (9.7%) | 320 (20.4%) | 1,481 (10.9%) | |
| **In-hospital outcome** | | | | |
| Alive | 12,008 (100.0%) | 1,249 (79.6%) | 13,257 (97.6%) | <0.001 |
| Dead | 0 (0.0%) | 320 (20.4%) | 320 (2.4%) | |

**Note:**
*IQR: interquartile ranges
Note: Percentages may not sum to 100% due to rounding. Unknown categories were included where they represented a substantial proportion of the data.

The median age of the population was 4 years (interquartile range [IQR]: 0–12 years). The median age was similar among patients with non-severe disease, 4 years (IQR: 0–12) and severe disease, 3 years (IQR: 0–12). Among participants with non-severe disease, 565 (4.7%) were newborns, 2,551 (21.2%) were infants aged 1 to 11 months, 3,306 (27.5%) were 1 to 4 years old, 2,866 (23.9%) were 5 to 12 years old, and 2,720 (22.7%) were 13 to 17 years old. Among those with severe disease, 421 (26.8%) were 5 to 12 years old, followed by 366 (23.3%) in the 1- to 11-month age group, and then the 13- to 17-year age group.

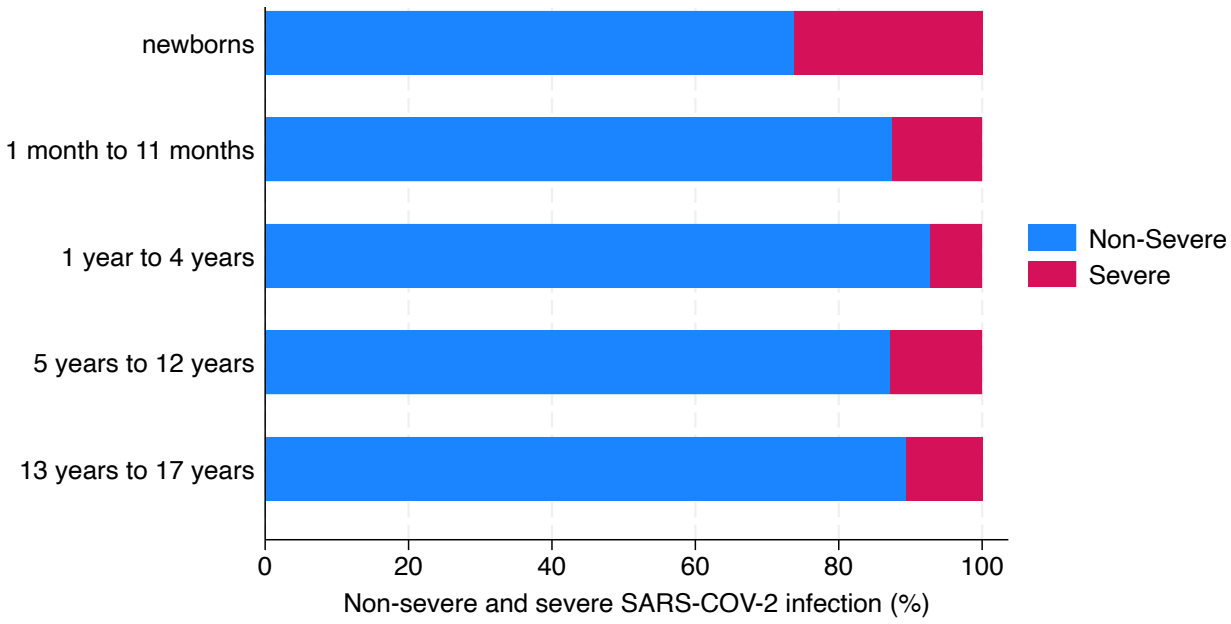


**Figure 2:** Distribution of disease severity across age groups in admitted participants with SARS-COV-2 infection in children < 18 years in KwaZulu-Natal Province and Gauteng Province from April 2020 to March 2022

In Figure 2, the proportion of severe disease was highest among newborns (201, 26%), followed by the 5 to 12 year age group (421, 12.8%), then the 1 to 11 month age group (366, 12.5%). The 13 to 17 year age group had 323 cases (11%), and lastly, 7.2% of cases among those aged 1 to 4 years old had severe disease.

Overall, the sex distribution was relatively balanced, with majority being male 51.6% (n = 7,010). Similarly, among non-severe and severe cases majority were males, 51% (n = 6131) and 56% (n = 878), respectively. Regarding race, most (n= 8057, 59.3%) participants were classified as Black African (Table 2).

Most patients were admitted to a medical ward or isolation ward (90.6%, n = 12,307). A smaller proportion required higher levels of care, with 5.5% (n = 741) in high-care units and 3.9% (n = 529) in the intensive care unit (ICU).

Most of the participants were admitted to private sector facilities, accounting for 52.3% (n = 7,102) of the total admissions. The geographic distribution showed that approximately two thirds of cases were in Gauteng Province (63.1%, n = 8,564).

Most of the study population (93.1%, n = 12,638) had no documented or had unknown status for pre-existing comorbidities. A total of 6.1% (n = 831) had one comorbidity, while 0.8% (n = 108) had two or more comorbidities.

The most reported conditions among participants were asthma (1.7%, n = 233), diabetes mellitus (1.4%, n = 185), and HIV infection (1.4%, n = 193). Other notable conditions included hypertension (1.0%, n = 140), tuberculosis (current or previous) (0.5%, n = 73), chronic lung disease (0.3%, n = 45), cardiac disease (0.6%, n = 81), malignancy (0.4%, n = 52), and obesity (0.2%, n = 32).

Most participants (99.2%, n = 13,468) did not require supplemental oxygen. A small subset received nasal prong oxygen ($NPO_2$) or high-flow nasal prong oxygen ($HFNPO_2$) (0.7%, n = 101), while 0.1% (n = 8) required invasive mechanical ventilation.

Among severe cases, 93% (n = 1456) received no oxygen therapy, 6.5% (n = 101) required non-invasive positive-pressure oxygen therapy ($NPO_2$/$HFNPO_2$), while 0.5% (n = 8) required invasive ventilation.

The median length of hospital stay was 4 days (IQR: 2–8 days). Most patients (74.0%, n = 10,067) had a short stay (≤7 days), while 15.0% (n = 2,029) remained hospitalized for 8 to 14 days, and 11.0% (n = 1,481) stayed for ≥15 days.

The overall in-hospital case fatality rate was 2.4% (n = 320). From this cohort, 11.5% had severe disease.

*Table 4: Risk factors for COVID-19 associated severity among children aged <18 years with severe vs non-severe COVID-19 related illnesses in KwaZulu-Natal Province and Gauteng Province between April 2020 to March 2022*

| Characteristic | Non severe disease n = 12008 | Severe Disease n = 1,569 | Univariate OR (95% CI) | p-value | aOR (95% CI) | p-value |
|---|---|---|---|---|---|---|
| **Age** | | | | | | |
| Median (IQR), years | 4 (0–12) | 3 (0–12) | 1.00 (0.99–1.01) | 0.578 | - | - |
| **Age Groups** | | | | | | |
| Newborns | 565/766 (74%) | 201/766 (26%) | 4.6 (3.7–5.6) | <0.001 | 4.7 (3.4 – 6.5) | <0.001 |
| 1–11 months | 2551/2917 (87%) | 366/2917 (13%) | 1.8 (1.5–2.2) | <0.001 | 2.0 (1.6 – 2.5) | <0.001 |
| 1–4 years | 3306/3564 (93%) | 258/3564 (7%) | Reference | - | Reference | - |
| 5–12 years | 2866/3287 (87%) | 421/3287 (13%) | 1.9 (1.6–2.2) | <0.001 | 1.7 (1.3 – 2.0) | <0.001 |
| 13–17 years | 2720/3043 (89%) | 323/3043 (11%) | 1.5 (1.3–1.8) | <0.001 | 1.7 (1.3 – 2.2) | <0.001 |
| **Sex** | | | | | | |
| Female | 5850/6524 (90%) | 674/6524 (10%) | Reference | - | Reference | - |
| Male | 6131/7010 (87%) | 879/7010 (13%) | 1.2 (1.1–1.4) | <0.001 | 1.2 (1.1 – 1.4) | 0.013 |
| Unknown / Missing | 27/43 (63%) | 16/43 (37%) | 5.2 (2.8–9.6) | <0.001 | N/S | - |
| **Race** | | | | | | |
| Black African | 6977/8057 (87%) | 1080/8057 (13%) | 1.2 (0.96 – 1.5) | 0.118 | 1.0 (0.7 – 1.4) | 0.995 |
| Other | 797/901 (88%) | 104/901 (12%) | Reference | - | Reference | - |
| Unknown / Missing | 4234/4619 (92%) | 385/4619 (8%) | 0.7 (0.6–0.9) | 0.002 | 1.1 (0.8 – 1.5) | 0.757 |
| **Healthcare Sector** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Public | 5531/6475 (85%) | 944/6475 (15%) | 1.8 (1.6–2.0) | <0.001 | 1.2 (1.0 – 1.3) | 0.06 |
| Private | 6477/7102 (91%) | 625/7102 (9%) | Reference | - | | |
| **Province** | | | | | | |
| Gauteng | 7449/8564 (87%) | 1115/8564 (13%) | 1.5 (1.3 – 1.7) | <0.001 | 1.5 (1.3 – 1.7) | <0.001 |
| KwaZulu-Natal | 4559/5013 (91%) | 454/5013 (9%) | Reference | - | Reference | - |
| **Comorbidities** | | | | | | |
| None | 11235/12638 (89%) | 1403/12638 (11%) | Reference | - | Reference | - |
| 1 comorbidity | 690/831 (83%) | 141/831 (17%) | 1.6 (1.4–2.0) | <0.001 | 1.6 (1.3 – 1.9) | <0.001 |
| ≥2 comorbidities | 83/108 (77%) | 25/108 (23%) | 2.4 (1.5–3.8) | <0.001 | 1.8 (1.1 – 2.9) | <0.001 |
| **Specific Comorbidities†** | | | | | | |
| Chronic lung disease | 39/45 (87%) | 6/45 (13%) | 1.5 (0.6–3.5) | 0.388 | N/S | - |
| Asthma | 209/233 (90%) | 24/233 (10%) | 1.1 (0.7–1.7) | 0.666 | N/S | - |
| Cardiac disease | 62/81 (77%) | 19/81 (23%) | 2.9 (1.8–4.9) | <0.001 | 1.8 (1.0 – 3.3) | 0.064 |
| Diabetes mellitus | 133/185 (72%) | 52/185 (28%) | 3.9 (2.8–5.4) | <0.001 | 3.6 (2.3 – 5.5) | <0.001 |
| Hypertension | 115/140 (82%) | 25/140 (18%) | 2.1 (1.4–3.3) | 0.001 | N/S | - |
| Chronic renal failure | 25/39 (64%) | 14/39 (36%) | 5.4 (2.8–10.4) | <0.001 | N/S | - |
| Tuberculosis (Past or Current) | 63/73 (86%) | 10/73 (14%) | 1.5 (0.8–3.0) | 0.204 | N/S | - |
| HIV positive | 157/194 (81%) | 37/194 (19%) | 2.3 (1.6–3.3) | <0.001 | 1.6 (1.0 – 2.6) | 0.043 |
| Cancer | 48/52 (92%) | 4/52 (8%) | 0.8 (0.2–2.2) | 0.651 | N/S | |
| **Length of hospital stay** | | | | | | |
| ≤7 days | 9135/10067 (91%) | 932/10067 (9%) | Reference | - | Reference | - |
| 8–14 days | 1712/2029 (84%) | 317/2029 (16%) | 1.8 (1.6–2.1) | <0.001 | 2.6 (2.1 – 3.3) | <0.001 |
| ≥15 days | 1161/1481 (78%) | 320/1481 (22%) | 2.7 (2.3–3.1) | <0.001 | 6.0 (4.8 – 7.6) | <0.001 |

Data from the table 4 are presented as quotient (%), unless otherwise specified, with comparisons made between severe and non-severe disease groups. The findings provide insight into factors associated with severe disease, which helped in the identification of at-risk populations.

### 3.1 Univariate analysis of factors associated with severe disease

Table 4 identifies key risk factors associated with severe SARS-CoV-2 disease. Newborns had a significantly higher risk of severe diseese (OR: 4.6) compared to children aged 1–4 years. Male participants (OR: 1.2) were also at higher risk than females, as were those of unknown sex (OR: 5.2). Black African children (OR: 1.7), compared to other racial groups, and those admitted to public healthcare facilities (OR: 1.8), compared to those in private facilities, also had increased odds of severe disease.

Comorbidities were strongly associated with severity, with one comorbidity increasing risk (OR: 1.6) and two or more further elevating the odds of severe disease (OR: 2.4). Specific conditions such as cardiac disease (OR: 3.0), diabetes (OR: 3.9), hypertension (OR: 2.1), chronic kidney failure (OR: 5.4), HIV (OR: 2.3), and prior tuberculosis (OR: 2.9) were significantly associated with severe outcomes. In contrast, chronic lung disease, asthma, and tuberculosis were not statistically significant risk factors.

Longer hospital stay was also associated with disease severity, with those hospitalized for 8–14 days (OR: 1.8) and ≥15 days (OR: 2.7) being at higher risk. These findings highlight vulnerable populations and key clinical factors contributing to severe COVID-19 outcomes.

### 3.2. Multivariate analysis associated with disease severity

Table 4 also presents the factors associated with disease severity in children admitted with SARS-CoV-2 infection between April 2020 and March 2022.

Regarding age group, newborns had the highest odds of severe disease as compared to children aged 1–4 years., with an aOR of 4.7 (95% CI: 3.4–6.5, p < 0.001), indicating a significantly greater likelihood of severe outcomes. Elevated risks were also observed among children aged 1–11 months (aOR = 2.0, 95% CI: 1.6–2.5, p < 0.001), 5–12 years (aOR = 1.7, 95% CI: 1.5–2.0, p < 0.001), and 13–17 years (aOR = 1.7, 95% CI: 1.3–2.2, p < 0.001), although these risks were lower than those in newborns. Race was not significantly associated with disease severity, although Black African and other racial groups were retained in the model a priori. Males were more likely to develop severe disease compared to females (aOR = 1.2, 95% CI: 1.1–1.4, p = 0.013).

Children admitted in Gauteng had higher odds of severe disease than those in KwaZulu-Natal (aOR = 1.5, 95% CI: 1.3–1.7, p < 0.001). Although the point estimate for public sector admission suggested increased severity, this association was not statistically significant (aOR = 1.2, 95% CI: 0.99–1.3, p = 0.06). Longer hospital stay was strongly associated with disease severity: children hospitalized for 8–14 days had higher odds of severe disease (aOR = 2.6, 95% CI: 2.1–3.3, p < 0.001), while those hospitalized for ≥15 days had even greater risk (aOR = 6.0, 95% CI: 4.8–7.6, p < 0.001), compared to those admitted for ≤7 days.

Comorbidities also influenced severity. Children with one comorbidity had an aOR of 1.6 (95% CI: 1.3–1.9, p < 0.001), and those with ≥2 comorbidities had an aOR of 1.8 (95% CI: 1.1–2.9, p < 0.001) compared to children without or with unknown comorbidities. However, due to collinearity (as this variable was derived from specific comorbidities), it could not be included in the final model. Among individual conditions, diabetes mellitus

was strongly associated with severe disease (aOR = 3.6, 95% CI: 2.3–5.5, p < 0.001), followed by chronic renal failure (aOR = 2.3, 95% CI: 1.1–4.7, p = 0.020). Cardiac disease showed a trend towards increased severity (aOR = 1.8, 95% CI: 0.99–3.3, p = 0.06), though this was not statistically significant. HIV-positive status was significantly associated with severe disease (aOR = 1.6, 95% CI: 1.0–2.6, p = 0.043).

In conclusion, several factors such as younger age (particularly being a newborn), male sex, prolonged hospital stays, and the presence of comorbidities, especially diabetes and HIV, were strongly associated with increased risk of disease severity in children with SARS-CoV-2 infection. However, factors such as race and the hospital sector did not show strong associations, indicating that these may not be significant determinants of severity in this cohort.

***Table 5:*** *The demographics and clinical characteristics of children <18 years with COVID-19 related admission (Severe vs Non-Severe disease) in Gauteng province between April 2020 to March 2022*

| | **Disease severity** | | | |
|---|---|---|---|---|
| | **Non-Severe** | **Severe** | **Total** | **P value** |
| N | 7,449 (87.0%) | 1,115 (13.0%) | 8,564 (100.0%) | |
| **Age** Median (IQR) | 3 (0 – 11) | 3 (0 – 11) | 3 (0 – 11) | 0.720 |
| **Age in groups** | | | | |
| newborns | 382 (5.1%) | 148 (13.3%) | 530 (6.2%) | <0.001 |
| 1 month to 11 months | 1,646 (22.1%) | 264 (23.7%) | 1,910 (22.3%) | |
| 1 year to 4 years | 2,145 (28.8%) | 192 (17.2%) | 2,337 (27.3%) | |
| 5 years to 12 years | 1,744 (23.4%) | 291 (26.1%) | 2,035 (23.8%) | |
| 13 years to 17 years | 1,532 (20.6%) | 220 (19.7%) | 1,752 (20.5%) | |
| **Sex** | | | | |
| Female | 3,595 (48.3%) | 484 (43.4%) | 4,079 (47.6%) | <0.001 |
| Male | 3,843 (51.6%) | 617 (55.3%) | 4,460 (52.1%) | |
| Unknown / Missing | 11 (0.1%) | 14 (1.3%) | 25 (0.3%) | |
| **Race** | | | | |
| Black African | 3,951 (53.0%) | 752 (67.4%) | 4,703 (54.9%) | <0.001 |
| Other | 509 (6.8%) | 57 (5.1%) | 566 (6.6%) | |
| Unknown / Missing | 2,989 (40.1%) | 306 (27.4%) | 3,295 (38.5%) | |
| **Comorbidities** | | | | |

| | | | | |
|---|---|---|---|---|
| Unknown/ No comorbidities | 7,026 (94.3%) | 1,013 (90.9%) | 8,039 (93.9%) | <0.001 |
| 1 comorbidity | 385 (5.2%) | 86 (7.7%) | 471 (5.5%) | |
| 2 or more comorbidities | 38 (0.5%) | 16 (1.4%) | 54 (0.6%) | |
| **Healthcare Sector** | | | | |
| Private | 4,142 (55.6%) | 468 (42.0%) | 4,610 (53.8%) | <0.001 |
| Public | 3,307 (44.4%) | 647 (58.0%) | 3,954 (46.2%) | |
| **Ward** | | | | |
| Medical/ Isolation Ward | 7,449 (100.0%) | 208 (18.7%) | 7,657 (89.4%) | <0.001 |
| High Care | 0 (0.0%) | 497 (44.6%) | 497 (5.8%) | |
| Intensive Care Unit | 0 (0.0%) | 410 (36.8%) | 410 (4.8%) | |
| **Oxygen therapy** | | | | |
| No Oxygen Therapy | 7,449 (100.0%) | 1,026 (92.0%) | 8,475 (99.0%) | <0.001 |
| Supplementary oxygen | 0 (0.0%) | 83 (7.4%) | 83 (1.0%) | |
| Ventilated | 0 (0.0%) | 6 (0.5%) | 6 (0.1%) | |
| **HIV Status** | | | | |
| Negative | 3,946 (53.0%) | 455 (40.8%) | 4,401 (51.4%) | <0.001 |
| Positive | 57 (0.8%) | 15 (1.3%) | 72 (0.8%) | |
| Unknown / Missing | 3,446 (46.3%) | 645 (57.8%) | 4,091 (47.8%) | |
| **Hypertension** | | | | |
| No | 4,083 (54.8%) | 464 (41.6%) | 4,547 (53.1%) | <0.001 |
| Yes | 63 (0.8%) | 17 (1.5%) | 80 (0.9%) | |
| Unknown / Missing | 3,303 (44.3%) | 634 (56.9%) | 3,937 (46.0%) | |
| **Diabetes Mellitus** | | | | |
| No | 4,062 (54.5%) | 448 (40.2%) | 4,510 (52.7%) | <0.001 |
| Yes | 83 (1.1%) | 42 (3.8%) | 125 (1.5%) | |
| Unknown /Missing | 3,304 (44.4%) | 625 (56.1%) | 3,929 (45.9%) | |
| **Asthma** | | | | |
| No | 3,967 (53.3%) | 461 (41.3%) | 4,428 (51.7%) | <0.001 |
| Yes | 136 (1.8%) | 10 (0.9%) | 146 (1.7%) | |
| Unknown /Missing | 3,346 (44.9%) | 644 (57.8%) | 3,990 (46.6%) | |
| **Cardiac Disease** | | | | |
| No | 4,035 (54.2%) | 460 (41.3%) | 4,495 (52.5%) | <0.001 |
| Yes | 40 (0.5%) | 14 (1.3%) | 54 (0.6%) | |
| Unknown / Missing | 3,374 (45.3%) | 641 (57.5%) | 4,015 (46.9%) | |
| **Chronic Lung Disease** | | | | |
| No | 4,057 (54.5%) | 466 (41.8%) | 4,523 (52.8%) | <0.001 |
| Yes | 12 (0.2%) | 5 (0.4%) | 17 (0.2%) | |
| Unknown / Missing | 3,380 (45.4%) | 644 (57.8%) | 4,024 (47.0%) | |
| **Chronic Renal Failure** | | | | |
| No | 4,047 (54.3%) | 461 (41.3%) | 4,508 (52.6%) | <0.001 |
| Yes | 16 (0.2%) | 9 (0.8%) | 25 (0.3%) | |
| Unknown / Missing | 3,386 (45.5%) | 645 (57.8%) | 4,031 (47.1%) | |
| **Cancer** | | | | |
| No | 4,041 (54.2%) | 466 (41.8%) | 4,507 (52.6%) | <0.001 |
| Yes | 28 (0.4%) | 3 (0.3%) | 31 (0.4%) | |
| Unknown / Missing | 3,380 (45.4%) | 646 (57.9%) | 4,026 (47.0%) | |
| **Tuberculosis** | | | | |
| No TB | 3,904 (52.4%) | 437 (39.2%) | 4,341 (50.7%) | <0.001 |

| | | | | |
|---|---|---|---|---|
| TB: Current/Past | 23 (0.3%) | 3 (0.3%) | 26 (0.3%) | |
| Unknown / Missing | 3,522 (47.3%) | 675 (60.5%) | 4,197 (49.0%) | |
| **Obesity** | | | | |
| No | 812 (10.9%) | 131 (11.7%) | 943 (11.0%) | 0.683 |
| Yes | 16 (0.2%) | 2 (0.2%) | 18 (0.2%) | |
| Unknown | 6,621 (88.9%) | 982 (88.1%) | 7,603 (88.8%) | |
| **Length of Stay** Median (IQR) | 3 (2 – 7) | 6 (2 – 12) | 4 (2 – 8) | 0.049 |
| **Length of Stay** | | | | |
| 7 or less days admitted | 5,701 (76.5%) | 646 (57.9%) | 6,347 (74.1%) | <0.001 |
| 8 to 14 days admitted | 879 (11.8%) | 228 (20.4%) | 1,107 (12.9%) | |
| 15 or more days admitted | 869 (11.7%) | 241 (21.6%) | 1,110 (13.0%) | |
| **Outcome** | | | | |
| Alive | 7,449 (100.0%) | 910 (81.6%) | 8,359 (97.6%) | <0.001 |
| Dead | 0 (0.0%) | 205 (18.4%) | 205 (2.4%) | |

Table 5 describes the demographics and clinical characteristics of 8,564 children under 18 years admitted with COVID-19 in Gauteng between April 2020 and March 2022. Of these, 13.0% (n=1,115) had severe disease. The median age was 3 years across both severity groups. Among children with severe disease, the proportion was highest in newborns (148/530, 28%), followed by children aged 5 to 12 years (291/2035, 14%). Among those with non-severe disease, the highest proportion was in children under 1 year (2028/2449, 27%), followed by those aged 1 to 4 years (1161/4559, 25.5%), 5 to 12 years (1122/4559, 24.6%), and over 13 years (1188/1227, 24.6%). Among severe cases, males (55.3%) and Black African children (67.4%) were more prevalent.

Children with comorbidities, particularly those with one or more chronic conditions, were significantly more likely to experience severe disease ($p<0.001$). Severe cases were more frequently managed in the public sector. Respiratory support was 7.9% of the participants requiring oxygen therapy or ventilation. Several comorbidities—including HIV, hypertension, diabetes, asthma, cardiac and renal disease, TB, and cancer—were more

prevalent in the severe group (all p<0.001), although obesity was not significantly associated with severity. Median length of hospital stay was longer among severe cases (6 vs. 3 days, p=0.049), and a greater proportion of these children were admitted for more than 7 days (42% vs. 23.5%, p<0.001).

***Table 6:*** *The demographics and clinical characteristics of children <18 years with COVID-19 related admission (Severe vs Non-Severe disease) in KwaZulu-Natal between April 2020 to March 2022*

| | Disease severity | | | |
|---|---|---|---|---|
| | **Non-Severe** | **Severe** | **Total** | **P value** |
| N | 4,559 (90.9%) | 454 (9.1%) | 5,013 (100.0%) | |
| **Age** Median (IQR) | 5 (1 – 13) | 6 (0 – 12) | 5 (1 – 13) | 0.655 |
| **Age in groups** | | | | |
| newborns | 183 (4.0%) | 53 (11.7%) | 236 (4.7%) | <0.001 |
| 1 month to 11 months | 905 (19.9%) | 102 (22.5%) | 1,007 (20.1%) | |
| 1 year to 4 years | 1,161 (25.5%) | 66 (14.5%) | 1,227 (24.5%) | |
| 5 years to 12 years | 1,122 (24.6%) | 130 (28.6%) | 1,252 (25.0%) | |
| 13 years to 17 years | 1,188 (26.1%) | 103 (22.7%) | 1,291 (25.8%) | |
| **Sex** | | | | |
| Female | 2,255 (49.5%) | 190 (41.9%) | 2,445 (48.8%) | 0.008 |
| Male | 2,288 (50.2%) | 262 (57.7%) | 2,550 (50.9%) | |
| Unknown / Missing | 16 (0.4%) | 2 (0.4%) | 18 (0.4%) | |
| **Race** | | | | |
| Black African | 3,026 (66.4%) | 328 (72.2%) | 3,354 (66.9%) | <0.001 |
| Other | 288 (6.3%) | 47 (10.4%) | 335 (6.7%) | |
| Unknown / Missing | 1,245 (27.3%) | 79 (17.4%) | 1,324 (26.4%) | |
| **Comorbidities** | | | | |
| Unknown/ No comorbidities | 4,209 (92.3%) | 390 (85.9%) | 4,599 (91.7%) | <0.001 |
| 1 comorbidity | 305 (6.7%) | 55 (12.1%) | 360 (7.2%) | |
| 2 or more comorbidities | 45 (1.0%) | 9 (2.0%) | 54 (1.1%) | |
| **Healthcare Sector** | | | | |
| Private | 2,335 (51.2%) | 157 (34.6%) | 2,492 (49.7%) | <0.001 |
| Public | 2,224 (48.8%) | 297 (65.4%) | 2,521 (50.3%) | |
| **Ward** | | | | |
| Medical/ Isolation Ward | 4,559 (100.0%) | 91 (20.0%) | 4,650 (92.8%) | <0.001 |
| High Care | 0 (0.0%) | 244 (53.7%) | 244 (4.9%) | |
| Intensive Care Unit | 0 (0.0%) | 119 (26.2%) | 119 (2.4%) | |
| **Oxygen therapy** | | | | |
| No Oxygen Therapy | 4,559 (100.0%) | 434 (95.6%) | 4,993 (99.6%) | <0.001 |
| Supplementary oxygen | 0 (0.0%) | 18 (4.0%) | 18 (0.4%) | |
| Ventilated | 0 (0.0%) | 2 (0.4%) | 2 (0.0%) | |
| **HIV Status** | | | | |
| Negative | 2,848 (62.5%) | 250 (55.1%) | 3,098 (61.8%) | <0.001 |
| Positive | 100 (2.2%) | 22 (4.8%) | 122 (2.4%) | |

| | | | | |
|---|---|---|---|---|
| Unknown / Missing | 1,611 (35.3%) | 182 (40.1%) | 1,793 (35.8%) | |
| **Hypertension** | | | | |
| No | 3,014 (66.1%) | 267 (58.8%) | 3,281 (65.4%) | 0.006 |
| Yes | 52 (1.1%) | 8 (1.8%) | 60 (1.2%) | |
| Unknown / Missing | 1,493 (32.7%) | 179 (39.4%) | 1,672 (33.4%) | |
| **Diabetes Mellitus** | | | | |
| No | 2,990 (65.6%) | 262 (57.7%) | 3,252 (64.9%) | 0.001 |
| Yes | 50 (1.1%) | 10 (2.2%) | 60 (1.2%) | |
| Unknown /Missing | 1,519 (33.3%) | 182 (40.1%) | 1,701 (33.9%) | |
| **Asthma** | | | | |
| No | 2,906 (63.7%) | 257 (56.6%) | 3,163 (63.1%) | 0.002 |
| Yes | 73 (1.6%) | 14 (3.1%) | 87 (1.7%) | |
| Unknown /Missing | 1,580 (34.7%) | 183 (40.3%) | 1,763 (35.2%) | |
| **Cardiac Disease** | | | | |
| No | 2,946 (64.6%) | 267 (58.8%) | 3,213 (64.1%) | 0.016 |
| Yes | 22 (0.5%) | 5 (1.1%) | 27 (0.5%) | |
| Unknown / Missing | 1,591 (34.9%) | 182 (40.1%) | 1,773 (35.4%) | |
| **Chronic Lung Disease** | | | | |
| No | 2,929 (64.2%) | 269 (59.3%) | 3,198 (63.8%) | 0.050 |
| Yes | 27 (0.6%) | 1 (0.2%) | 28 (0.6%) | |
| Unknown / Missing | 1,603 (35.2%) | 184 (40.5%) | 1,787 (35.6%) | |
| **Chronic Renal Failure** | | | | |
| No | 2,922 (64.1%) | 265 (58.4%) | 3,187 (63.6%) | <0.001 |
| Yes | 9 (0.2%) | 5 (1.1%) | 14 (0.3%) | |
| Unknown / Missing | 1,628 (35.7%) | 184 (40.5%) | 1,812 (36.1%) | |
| **Cancer** | | | | |
| No | 2,934 (64.4%) | 270 (59.5%) | 3,204 (63.9%) | 0.081 |
| Yes | 20 (0.4%) | 1 (0.2%) | 21 (0.4%) | |
| Unknown / Missing | 1,605 (35.2%) | 183 (40.3%) | 1,788 (35.7%) | |
| **Tuberculosis** | | | | |
| No TB | 2,822 (61.9%) | 254 (55.9%) | 3,076 (61.4%) | 0.025 |
| TB: Current/Past | 40 (0.9%) | 7 (1.5%) | 47 (0.9%) | |
| Unknown / Missing | 1,697 (37.2%) | 193 (42.5%) | 1,890 (37.7%) | |
| **Obesity** | | | | |
| No | 1,160 (25.4%) | 168 (37.0%) | 1,328 (26.5%) | <0.001 |
| Yes | 10 (0.2%) | 4 (0.9%) | 14 (0.3%) | |
| Unknown | 3,389 (74.3%) | 282 (62.1%) | 3,671 (73.2%) | |
| **Length of Stay** Median (IQR) | 4 (2 – 7) | 5 (3 – 10) | 4 (2 – 8) | 0.775 |
| **Length of Stay** | | | | |
| 7 or less days admitted | 3,434 (75.3%) | 286 (63.0%) | 3,720 (74.2%) | <0.001 |
| 8 to 14 days admitted | 833 (18.3%) | 89 (19.6%) | 922 (18.4%) | |
| 15 or more days admitted | 292 (6.4%) | 79 (17.4%) | 371 (7.4%) | |
| **Outcome** | | | | |
| Alive | 4,559 (100.0%) | 339 (74.7%) | 4,898 (97.7%) | <0.001 |
| Dead | 0 (0.0%) | 115 (25.3%) | 115 (2.3%) | |

Table 6 describes severe and non-severe cases from KZN. Of these, 454 (9.1%) experienced severe disease. The proportion of children under 1 year was higher among severe cases, with 53/454 (11.7%) being newborns and 102/454 (22.5%) aged 1–11 months. In contrast, non-severe cases were more common in children aged ≥1 year, with 1–4 years (1161/4559, 25.5%), 5–12 years (1122/4559, 24.6%), and ≥13 years (1188/1227, 24.6%). Amongst severe disease 72% (328/454) were Black African. The presence of comorbidities was significantly associated with severe disease: 14.1% of severe cases had at least one comorbidity compared to 7.7% of non-severe cases. Severe cases were also more commonly admitted to public hospitals (65.4%).

Amongst those with severe disease, those with asthma was (14/87, 16%), HIV (22/122, 18%) and diabetes mellitus (10/60, 17%) was the most prevalent. A higher proportion of severe cases had hospital stays longer than 14 days, with 17.4% of those with severe disease compared to 6.4% of those with non-severe disease.

***Table 7:*** *Factors associated with severe COVID-19 among hospitalized children by demographic and Clinical Characteristics in Gauteng vs KwaZulu-Natal provinces*

| | Gauteng Province | | | KwaZulu-Natal | | |
|---|---|---|---|---|---|---|
| **Characteristics** | **OR (95% CI)** | **aOR (95% CI)** | **p-value** | **OR (95% CI)** | **aOR (95% CI)** | **p-value** |
| **Age Groups** | | | | | | |
| Newborns | 5.9 (3.6 – 9.7) | 5.2 (3.5 – 7.8) | <0.001 | 6.2 (3.2 – 12.1) | 3.7 (2.2 – 6.2) | <0.001 |
| 1–11 months | 2.2 (1.4 – 3.4) | 1.9 (1.4 – 2.6) | <0.001 | 2.0 (1.1 – 3.7) | 1.8 (1.2 – 2.8) | <0.001 |
| 1–4 years | Reference | | - | Reference | | - |
| 5–12 years | 1.5 (0.9 – 2.5) | 1.9 (1.4 – 2.6) | <0.001 | 0.9 (0.5 – 1.8) | 1.1 (0.7 – 1.6) | 0.755 |
| 13–17 years | 2.0 (1.2 – 3.2) | 2.0 (1.4 – 2.7) | <0.001 | 2.0 (1.1 – 3.6) | 1.1 (0.7 – 1.6) | 0.788 |
| **Sex** | | | | | | |
| Female | Reference | | - | Reference | | - |
| Male | 0.9 (0.6 – 1.1) | 1.2 (1.1–1.4) | <0.001 | 0.9 (0.6 – 1.1) | 1.3 (0.95 – 1.6) | 0.106 |
| Unknown / Missing | 3.3 (0.8 – 14.1) | - | - | - | N/S | - |
| **Race** | | | | | | |
| Black African | 3.0 (1.4 – 6.3) | 1.3 (0.8 – 2.0) | 0.018 | 1.7 (0.7 – 3.9) | 0.97 (0.6 – 3.4) | 0.901 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Other | Reference | | - | Reference | | - |
| Unknown / Missing | 0.7 (0.3 – 1.7) | 1.7 (1.1 – 2.6) | 0.025 | 0.3 (0.1 – 0.9) | 0.4 (0.2 – 0.7) | 0.002 |
| **Healthcare Sector** | | | | | | |
| Public | 7.4 (5.0 – 10.9) | N/S | - | 6.3 (3.7 -10.8) | N/S | - |
| Private | Reference | | - | Reference | | - |
| **Comorbidities** | | | | | | |
| None | Reference | | - | Reference | | - |
| 1 comorbidity | 2.8 (1.8 – 4.2) | N/S | - | 2.9 (1.8 – 4.8) | N/S | - |
| ≥2 comorbidities | 5.7 (2.4 – 13.5) | N/S | - | 5.1 (2.0 – 13.1) | N/S | - |
| **Specific Comorbidities†** | | | | | | |
| Chronic lung disease | 10.8 (2.4 – 48.5) | N/S | - | 1.6 (0.2 – 12.1) | N/S | - |
| Asthma | N/S | N/S | - | 1.0 (0.2 – 4.2) | 3.3 (1.7 – 6.4) | <0.001 |
| Cardiac disease | 8.4 (3.2 – 21.9) | 2.3 (1.1 – 4.7) | 0.028 | 3.5 (0.8 – 15.0) | N/S | - |
| Diabetes mellitus | 7.2 (3.6 – 14.4) | 4.0 (2.4 – 6.6) | <0.001 | 4.2 (1.6 – 10.8) | 2.2 (0.9 – 5.4) | 0.089 |
| Hypertension | 3.0 (0.9 – 9.7) | N/S | - | 1.5 (0.4 – 6.4) | N/S | - |
| Chronic renal failure | 15.7 (5.2 – 47.3) | N/S | - | 7.4 (1.6 – 33.8) | N/S | - |
| Tuberculosis (Past or Current) | 6.9 (2.2 – 4.2) | N/S | - | 8.8 (3.8 – 20.4) | N/S | - |
| HIV positive | 3.1 (2.3 – 4.3) | N/S | - | 4.9 (2.5 – 9.6) | 2.2 (1.2 – 3.8) | 0.008 |
| Cancer | 2.7 (0.4 – 20.1) | N/S | - | 2.1 (0.3 – 16.0) | N/S | |
| **Length of hospital stay** | | | | | | |
| ≤7 days | Reference | | - | Reference | | - |
| 8–14 days | 1.7 (1.1 – 2.4) | 4.3 (3.3 – 5.7) | <0.001 | 1.1 (0.7 – 1.8) | 1.4 (0.99 – 2.0) | 0.052 |
| ≥15 days | 2.0 (1.4 – 2.8) | 6.5 (4.9 – 8.6) | <0.001 | 2.0 (1.1 – 3.5) | 6.0 (3.9 – 9.0)) | <0.001 |

Note:
† Specific comorbidities were included as individual variables in the multivariable logistic regression model.
N/S = Not significant (p > 0.1) or not retained in the final model; OR= Odds Ratio; aOR = Adjusted Odds Ratio; CI = Confidence Interval.
*Multivariable logistic regression model adjusted for all covariates listed. Adjusted odds ratios (aORs) indicate the odds of severe disease compared to the reference category within each variable. *Variables such as ward admitted, oxygen and outcome resulting in death second to COVID-19 were not included as separate variables as they were used for classification of severe and non-severe disease*.

Table 7 summarizes the adjusted odds ratios (aORs) for severe SARS-CoV-2 disease among hospitalized children in Gauteng and KwaZulu-Natal provinces, based on multivariable logistic regression analysis. In both provinces, younger age was significantly associated with increased odds of severe disease. Newborns had the highest risk (Gauteng: aOR 5.2, 95% CI 3.5–7.8; KwaZulu-Natal: aOR 3.7, 95% CI 2.2–6.2; both $p < 0.001$), followed by infants aged 1–11 months (Gauteng: aOR 1.9, 95% CI 1.4–2.6; KwaZulu-Natal: aOR 1.8, 95% CI 1.2–2.8; both $p < 0.001$), compared to the reference

group of children aged 1–4 years. In Gauteng, children aged 5–12 and 13–17 years also had significantly elevated odds of severe disease (aORs ~2.0), whereas no significant associations were observed in these age groups in KwaZulu-Natal. Male sex was independently associated with higher odds of severe disease in Gauteng (aOR 1.2, 95% CI 1.1–1.4, $p < 0.001$), but not in KwaZulu-Natal. Race was not statistically significant in the model for either province but was included a priori.

The healthcare sector (public vs. private) was not significantly associated with disease severity in either province and was excluded from the final model due to lack of model improvement. While the presence of comorbidities overall was not significantly associated with severity, several specific conditions were. Asthma was strongly associated with increased severity in KwaZulu-Natal (aOR 3.3, 95% CI 1.7–6.4, $p < 0.001$), and in Gauteng, cardiac disease (aOR 2.3, 95% CI 1.1–4.7, $p = 0.028$) and diabetes mellitus (aOR 4.0, 95% CI 2.4–6.6, $p < 0.001$) were significant predictors. HIV infection was associated with increased severity in KwaZulu-Natal (aOR 2.2, 95% CI 1.2–3.8, $p = 0.008$). Length of hospital stay was a strong marker of disease severity in both provinces, with children hospitalized for ≥15 days demonstrating substantially higher odds of severe disease (Gauteng aOR 6.5, 95% CI 4.9–8.6; KwaZulu-Natal aOR 6.0, 95% CI 3.9–9.0; both $p < 0.001$), relative to those admitted for ≤7 days.

***Table 8:*** *Risk factors associated with paediatric deaths among patients who tested positive for SARS-CoV-2 at time of admission in KwaZulu-Natal and Gauteng Province between April 2020 to March 2022.*

| Category | Total deaths = 320 n/N (%) | aOR (95% CI) | p Value |
|---|---|---|---|
| **Age group** | | | |
| Newborns | 57/ 320 (17.8%) | 3.2 (2.1 - 4.8) | <0.001 |
| 1-11 months | 81/ 320 (25.3%) | 1.7 (1.2 - 2.5) | 0.003 |
| 1-4 years | 47/ 320 (14.7%) | Reference | - |
| 5-12 years | 56/ 320 (17.5%) | 1.01 (0.7- 1.5) | 0.968 |
| 13-17 years | 79/ 320 (24.7%) | 1.6 (1.1 - 2.3) | 0.016 |
| **Race** | | | |
| Black African | 270/ 320 (84.4%) | 1.5 (0.8 - 2.7) | 0.174 |
| Other | 13/ 320 (4.1%) | Reference | - |
| Unknown | 37/ 320 (11.6%) | 1.6 (0.8 - 3.2) | 0.195 |
| **Sex** | | | |
| Female | 154/ 320 (48.1%) | Reference | |
| Male | 164/ 320 (51.2%) | 1.1 (0.9 - 1.4) | 0.444 |
| Unknown | 2/ 320 (0.6%) | 0.8 (0.2 - 3.3) | 0.728 |
| **Comorbidity** | | | |
| No/ unknown comorbidities | 262/320 (81.9%) | Reference | - |
| 1 comorbidity | 47/320 (14.7%) | 2.3 (1.7 - 3.3) | <0.001 |
| 2 or more comorbidities | 11/320 (3.4%) | 3.2 (1.6 - 6.2) | 0.001 |
| **Hospital sector** | | | |
| Public | 45/320 (14.1%) | 7.1 (4.5 - 11) | <0.001 |
| Private | 275/320 (85.9%) | Reference | |
| **Ward category** | | | |
| Medical ward | 220/320 (68.8%) | Reference | - |
| High Care | 42/ 320 (13.1%) | 2.4 (1.7 - 3.4) | <0.001 |
| Intensive Care Unit | 58/ 320 (18.1%) | 8.2 (5.9 - 11.5) | <0.001 |
| **Length of hospital stay** | | | |
| ≤ 7 days | 204/320 (63.7%) | Reference | - |
| 8-14 days | 58/320 (18.1%) | 0.7 (0.5 - 0.9) | 0.011 |
| 15+ days | 58/320 (18.1%) | 1.0 (0.7 - 1.4) | 0.903 |

Table 8 summarizes the demographic and clinical characteristics of participants who died, totaling 320 deaths. It presents demographic variables and risk factors, along with

adjusted odds ratios (aORs), 95% confidence intervals (CIs), and corresponding p-values.

Infants under one year accounted for the highest proportion of deaths (43.1%, n = 138/ 320), including 81 deaths (25.3%) among children aged 1–11 months and 57 deaths (17.8%) among newborns. Adolescents aged 13–17 years represented the second-largest group, with 79 deaths (24.7%), followed by children aged 5–12 years (56 deaths, 17.5%) and those aged 1–4 years (47 deaths, 14.7%). Newborns had the highest risk of death, with an aOR of 3.2 (2.1 – 4.8, $p < 0.001$), compared to children aged 1–4 years, who served as the reference group. Elevated risks were also observed among infants aged 1–11 months (aOR 1.7, $p = 0.003$) and adolescents aged 13–17 years (aOR 1.6, $p = 0.016$), whereas children aged 5–12 years did not show a significant difference ($p = 0.968$) compared to children aged 1-4 years.

In terms of racial distribution, the majority of deaths occurred among Black African children, accounting for 270 (84.4%) cases, while 17 (4.0%) were from other racial groups and 37 (11.6%) had unknown race. However, the association between race and mortality was not statistically significant ($p = 0.174$). Sex distribution was relatively balanced, with slightly more males than females: 164 (51.3%) males compared to 154 (48.1%) females, while 2 (0.6%) cases had undocumented sex. Similarly, the association between sex and mortality was not statistically significant ($p = 0.444$).

With respect to comorbidities, most children (262, 81.9%) had either no documented comorbid conditions or unknown comorbidity status. Among those with comorbidities, 47 (14.7%) had one comorbid condition, while 11 (3.4%) had two or more. Children with one

comorbidity had an adjusted odds ratio (aOR) of 2.3 (95% CI: 1.7 – 3.3; $p < 0.001$), while those with two or more comorbidities had an aOR of 3.2 (95% CI: 1.6 – 6.2; $p = 0.001$), compared to children without or with unknown comorbidity status.

# CHAPTER 4

# Discussion and conclusion

## 4.1. Discussion

As demonstrated in the results, this study reported several significant factors associated with the severity among children admitted with COVID-19, presenting important implications for clinical practice and healthcare delivery. We will now discuss each risk factor individually as observed in Gauteng and KwaZulu-Natal provinces, including demographics, the presence or absence of comorbidities, and clinical factors.

**Age and severe COVID-19:**

The association between age, specifically newborns, and severe disease represents one of the most significant findings of this analysis with an aOR of 4.7 (95% CI: 3.4 – 6.5, $p < 0.001$), indicating a critical need for enhanced monitoring and preventive strategies in neonatal care units. In a study conducted in Brazil by Hendler et al., newborns were found to be at the highest risk of developing severe disease, with a statistically significant aOR (2.3, 95% CI: 3.0 – 30.1) (15). Although gestational age was not specified in this dataset, prematurity has been documented to increase the risk of severe SARS-CoV-2 infection in children under 2 years compared to term infants, with a RR of 2.00; 95% CI, 1.63 – 2.46. Poor outcomes and increased risk of critical care were also observed in children born prematurely (13, 42). A US study demonstrated that infants <6 months had the highest admission rates in the paediatric population, comparable to high-risk adult groups. Maternal vaccination proved to be a critical intervention in reducing hospitalization rates,

ICU admissions, and mortality among infants under 6 months. Notably, infants of vaccinated mothers not only presented to hospitals at an older age with SARS-CoV-2 infection but also demonstrated less severe disease (19).

In the systematic review by Choi et al., younger children, particularly those under the age of 2, were identified as having a higher risk for severe COVID-19. This group tends to experience more significant respiratory complications and is more likely to require hospitalization compared to older children. Children between 5 to 17 years were generally less likely to experience severe COVID-19 compared to infants and toddlers. However, the severity can increase in those with underlying comorbidities or other risk factors (42) which was also observed in our study.

The risk of severe disease and need for critical care admission however gradually decreased across paediatric age groups but remained significant, indicating that age-specific interventions should be considered across the paediatric care spectrum. The risk pattern observed across other paediatric age groups suggests age-dependent susceptibility, potentially attributable to their immature immune systems and unique physiological characteristics. possibly reflecting developmental variations in immune response and ACE2 receptor expression patterns (22, 43).

Children have been described as having higher ACE2 expression compared to adults, which increases cellular susceptibility to SARS-CoV-2 infection but also has protective effects, improving inflammation regulation and promoting tissue repair. This could explain their ability to better regulate inflammation and avoid severe disease, despite their cells

being equally susceptible to infection. These two factors highlight the complexity of ACE2 in severe SARS-CoV-2 infections (43).

**Race, ethnicity and severe COVID-19:**

The racial disparities identified in our analysis should be interpreted with caution. Although race was not statistically significant, it was retained in the final model due to its epidemiological relevance. This highlights the need to consider additional underlying factors—such as socioeconomic status, access to healthcare, cultural practices, and potential biological differences—that may contribute to observed disparities and warrant further investigation (44). In future studies, incorporating more granular data on these variables could help clarify the role of race in disease severity.

However, in a study done in the Unites States, Black, American Indian/ Alaska Native and Hispanic/ Latino children were more likely to be admitted secondary to COVID-19 and have severe disease. These were likely due to systematic issues and social determinants of health, and not from biological or genetic differences (45). A South African study by Jassat et al. showed that African Black and other non-white individuals had a higher risk of hospitalization, severe disease, and mortality. The study highlighted social determinants of health, such as access to healthcare, as contributing factors (44).

**Presence of comorbidities and severe COVID-19:**

The analysis of comorbidities revealed complex patterns of disease interaction. The significant association between single comorbidities and severe disease (aOR=1.6, $p<0.05$) underscores the importance of underlying health conditions. This increased even further with the presence of $\geq 2$ comorbidities as evidenced by the aOR of 1.8.

The strong association with diabetes mellitus (aOR=3.6, 95% CI: 2.3 – 5.5, $p<0.001$) aligns with global observations and may reflect the impact of metabolic dysfunction on COVID-19 pathophysiology. The pathogenesis of SARS-CoV-2 infection and diabetes mellitus includes ACE2 receptors, which are expressed in pancreatic β-cells. These receptors serve as an entry point for SARS-CoV-2. Once the virus binds to ACE2, it can lead to the destruction of β-cells, potentially triggering acute diabetes or exacerbating pre-existing diabetes (46).

HIV seropositivity showed a significant association with increased risk (aOR = 1.6, 95% CI: 1.0 – 2.6, p value 0.043), and important in our setting with high prevalence in the adult population. Studies examining tuberculosis as a risk factor are limited, highlighting the need for further research. Additionally, TB is challenging to diagnose in children, making misclassification a possibility. While this study did not demonstrate statistically significant associations between obesity, chronic respiratory disease, chronic kidney failure or cardiac disease and severe outcomes, these associations have been documented in other published literature (11, 13, 14, 16, 20, 21, 33, 47).

Asthma was not a significant risk factor in the overall dataset but was identified as a risk factor for severe disease in KwaZulu-Natal, consistent with risk factors previously described in existing studies. (16, 21).

**Length of hospital stay & hospital sector admitted:**

Although a higher risk of severe disease was observed among participants admitted to public sector hospitals (aOR = 1.2, 95% CI: 0.99–1.3, p = 0.06), this association was not statistically significant in our model. However, it warrants further investigation in future studies. Notably, a larger proportion of participants in this study were admitted to private sector facilities, despite over 70% of the general population relying on public healthcare services (48).

An increased risk of severe disease was observed among children admitted to Gauteng province compared to KwaZulu-Natal (aOR = 1.5, 95% CI: 1.3–1.7, p <0.001). Notably, 63% (8,564/13,577) of admissions across the two provinces occurred in Gauteng.

There was a significant association between length of hospital stay and disease severity which suggests a complex relationship between hospitalization duration and outcomes. This analysis showed that the longer you stayed in hospital, the higher the likelihood of severe disease. While this could reflect the severity of underlying conditions, it might also indicate potential risks associated with prolonged hospitalization, emphasizing the importance of efficient patient management and timely discharge planning.

**Sex and severe COVID-19:**

With regards to sex, the analysis indicated higher risk amongst males (OR=1.2, 95% CI: 1.1 – 1.4, p 0.013), which align with previous research (21, 34) showing sex-based differences in health outcomes. This finding suggests the need for sex-sensitive approaches in healthcare delivery and risk assessment.

**Severe disease by province:**

This sub-analysis examined each province individually to identify province-specific risk factors. When stratified by province, a strong association was also observed between younger age and severe SARS-CoV-2 infection among hospitalized children. Newborns were still at the highest risk, with odds of severe disease in Gauteng having an aOR 5.2, 95% CI 3.5–7.8, and in KwaZulu-Natal having an aOR 3.7, 95% CI 2.2–6.2) compared with children aged 1–4 years. Infants aged 1–11 months also had significantly elevated odds (Gauteng: aOR 1.9, 95% CI 1.4–2.6; KwaZulu-Natal: aOR 1.8, 95% CI 1.2–2.8), emphasizing the particular vulnerability of children under one year of age. In Gauteng, older children (5–12 years: aOR 2.0, 95% CI 1.4–2.7; 13–17 years: aOR 2.0, 95% CI 1.3–3.0) also demonstrated increased risk, suggesting provincial differences in age-related susceptibility or health system factors. Male sex was independently associated with greater severity in Gauteng (aOR 1.2, 95% CI 1.1–1.4), though this association was not observed in KwaZulu-Natal.

Comorbidities were also important predictor. In Gauteng, cardiac disease (aOR 2.3, 95% CI 1.1–4.7) and diabetes mellitus (aOR 4.0, 95% CI 2.4–6.6) significantly increased the

risk of severe disease, while in KwaZulu-Natal, asthma (aOR 3.3, 95% CI 1.7–6.4) and HIV infection (aOR 2.2, 95% CI 1.2–3.8) were associated with higher risk of severe disease. These findings highlight the need for province-specific strategies to identify and protect high-risk children. Race and healthcare sector were not independently associated with severity.

Length of hospitalization was a consistent marker of disease severity across both provinces. Children admitted for ≥15 days had markedly higher odds of severe disease (Gauteng: aOR 6.5, 95% CI 4.9–8.6; KwaZulu-Natal: aOR 6.0, 95% CI 3.9–9.0) compared with those admitted for ≤7 days, reflecting both the clinical complexity and prolonged recovery of the most severely affected patients.

**Severe COVID-19 resulting in mortality:**

The overall case fatality rate was 2.4%. This study also highlighted key demographic and risk factors associated with paediatric COVID-19 mortality. Age was a significant predictor of death, where over 40% of deaths occurred under the age of 1 years. Newborns, infants (1-11 months), and adolescents (13-17 years) had a higher risk compared to children aged 1-4 years. Although Black African children accounted for the 84% of deaths, race was not independently associated with mortality. Similarly, there was no significant difference in mortality risk between males and females. The presence of comorbidities markedly increased the likelihood of death, with a higher risk observed in children with multiple underlying conditions. Healthcare sector and level of care were also critical factors, with children admitted to public hospitals experiencing a significantly higher mortality risk, were 85% of deaths occurred in public hospitals, as compared to those

admitted in private facilities. ICU admission was strongly associated with increased mortality, which reflected the severity of illness in critically ill children.

Length of hospital stay also influenced outcomes, as children who died within the first week had a higher risk, whereas those who survived beyond 8-14 days had a lower mortality risk. These findings underscore the importance of early identification and management of high-risk paediatric patients, particularly newborns infants, and those with comorbidities, to improve survival outcomes. Strengthening healthcare capacity especially in public hospitals and enhancing critical care resources may help reduce mortality in this vulnerable population.

## 4.2. Strengths:

The use of the DATCOV national surveillance dataset is a major strength. It enabled the identification of paediatric patients admitted with laboratory-confirmed SARS-CoV-2 infection across multiple provinces and hospitals in South Africa. As it was a surveilance system during the pandemic, it allowed for reliable tracking of admission trends in hospitals represented, the burden of disease, and identification of groups most at risk of severe illness and death. The large sample size and representativeness of the dataset increase the generalisability of the findings, while its real-time data collection during the pandemic provided timely insights that informed both clinical and public health responses.

## 4.3. Limitations:

A key limitation of this study is that it is based on secondary data analysis, which means that not all relevant data needed for the research were originally collected. As a result, there were gaps in certain critical variables, including missing data. Specifically, important information pertinent to the paediatric population, such as HIV exposure, nutritional status, immunization status, and clinical presentation was unavailable. These factors could potentially influence the severity of SARS-CoV-2 disease in children, and their absence may limit the comprehensiveness of the findings. There were several other challenges which affected our final model such as the use of oxygen, whether the newborns had underlying comorbidities such as prematurity and those with low birth weights. As the majority of participants who experienced severe disease did not receive oxygen (1,460/1,569, 93%), as expected, they were likely admitted due to underlying comorbidities, which may have influenced their in-hospital outcomes, along with the impact of limited resources. Additionally, the incomplete data on these key variables may introduce bias or affect the generalizability of the study's conclusions. Additionally, the absence of data for some demographic groups represents a gap that future research should address. This data was collected during the pandemic by frontline clinicians, and some hospitals may have been under-resourced, making it challenging to collect complete data.

## 4.4. Recommendations:

Some recommendation includes women being prioritized for the COVID-19 vaccination to provide passive immunity and protect infants, particularly during the first six months of

life when they are at highest risk and currently ineligible for vaccination (19). Children identified as being at increased risk of severe COVID-19 and those with underlying comorbidities, and who meet eligibility criteria should receive the COVID-19 vaccine (49).

Ongoing monitoring of COVID-19 in children, especially those under five years, is needed to assess the impact of maternal vaccination, disease severity patterns, and new variants which may arise. Paediatric and neonatal services should maintain readiness to manage severe cases, particularly during future waves.

## 4.5. Conclusion:

Prospective studies examining the impact of targeted interventions for high-risk groups, especially newborns and patients with comorbidities such as diabetes mellitus, HIV seropositivity, cardiac disease, and asthma, would be extremely valuable. These interventions include COVID-19 vaccination for vulnerable populations, including pregnant women and children with underlying conditions. In addition, research into the factors contributing to public–private sector disparities could guide strategies for health system strengthening.

The findings from this study have several important implications for clinical practice and health policy. First, enhanced surveillance and preventive measures are needed for identified high-risk groups, particularly newborns and patients with comorbidities such as HIV, diabetes mellitus, asthma, and cardiac disease. Second, disparities between healthcare sectors highlight the need for targeted interventions to strengthen public healthcare delivery and to prioritize resources. Finally, addressing these challenges will

not only improve equity in current care but also build resilience in preparation for future pandemics.

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# APPENDIX 1

Senate plagiarism policy


**PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS**

SENATE PLAGIARISM POLICY: APPENDIX ONE

I **Dr Dominique Adrienne Tapamo** (Student number: **2372534**) am a student registered for the degree of a **MSc in Epidemiology and Biostatistics** in the academic year __3_____.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: **09 October 2025**

# APPENDIX 2

Ethics certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr DA Tapamo

## HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
## CLEARANCE CERTIFICATE NO. M240146

**NAME:** Dr DA Tapamo **DEGREE:** MSc
**Principal Investigator**

**DEPARTMENT:** School of Public Health
Division of Epidemiology and Biostatistics
Medical School
University

**PROJECT TITLE:** *Factors associated with disease severity amongst children admitted with SARS-COV-2 infection in Gauteng Province, 2020 to 2022*

**DATE CONSIDERED:** 26 January 2024

**DECISION:** Approved unconditionally

**CONDITIONS:**

**NOTE:** If contact information regarding student study participants is required, please contact the Registrar's office <Nicoleen.Potgieter@wits.ac.za>

**SUPERVISOR:** Dr S Walaza

**APPROVED BY:**
Professor P Ruff, Chairperson, HREC (Medical)

**DATE OF APPROVAL:** 23 April 2024 **EXPIRY DATE:** 22 April 2029

**This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.**

**DECLARATION OF INVESTIGATORS**

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report** in the format available at https://wits.ac.za/research/researcher-support/research-ethics/ethics-committees/. This report is due annually, for the duration of the Clearance Certificate, beginning on the first anniversary of Date of Approval above. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator Date