Factors associated with hospitalization of adolescents with COVID-19 in Eswatini, March 2020 to January 2022

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Declaration

I, Musawenkhosi Mzamo Mbuli declare that this research report is my own work. It is being submitted for the award of a Master of Science degree in Epidemiology in the field of Field Epidemiology to the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination of degree at this or any other University.

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Dedication

To my family and friends, for the love and support they have shown throughout my life. A special feeling of gratitude is extended to my mother, Mrs. Thulisile Mbuli, who has been a source of love and inspiration in my life. To my Bestie Phumelele, thank you Mkhulandle for the unwavering support you demonstrated through your love, inspiration, patience and words of encouragement.

Abstract

Background

Coronavirus disease (COVID-19) was amongst the leading global public health threats with high morbidity and mortality. During the COVID-19 pandemic adolescents were not spared from the effects of the COVID-19 infection. This study was aimed at assessing the factors associated with the hospitalization of adolescents with COVID-19 in Eswatini.

Methods

A cross-sectional study that utilized secondary data was conducted. Data used was from the Eswatini national COVID-19 database collected from March 2020 to January 2022. The data analyzed was of adolescents aged 10-19 years diagnosed with COVID-19 and hospitalized in health facilities in Eswatini. Descriptive statistics of demographic and clinical characteristics were presented using frequency tables and graphs. Differences in means were assessed using a Student's t-test while differences in proportions were assessed using the Chi-square and Fisher's exact test as necessary. The univariate and multivariate logistic regression analyses were used to determine the factors associated with COVID-19 related hospitalization.

Results

Of the 9277 adolescents diagnosed with COVID-19, 3.43% (n=318) were hospitalized. The mean±(standard deviation) age of the adolescents was 15.36, ±2.7 years. A total of 57.21% (n=5307) of the study participants were females. A majority, 76.73% (n=7118) of the adolescents had mild disease severity at diagnosis. Findings from the study revealed that after adjusting for other factors, being symptomatic increased the odds of COVID-19 hospitalization by 2.48 times (aOR=2.48; 95%CI: 1.43-4.28; p<0.001) compared to those without symptoms. Likewise compared to those living without, living with comorbidities was associated

with 4-fold increased odds of COVID-19 hospitalization (aOR=4.04; 95%CI: 1.91-8.52; p<0.001).

Conclusion

The findings from this study highlights the need for targeted interventions for adolescents as underscored by the risk factors found to be associated with hospitalization of adolescents with COVID-19 in Eswatini. COVID-19 patient management approaches like access to healthcare services such as vaccination even for marginalized populations should be targeted in resource-limited settings as they are crucial to managing COVID-19 infection.

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Abbreviations and Acronyms

aOR: Adjusted Odds Ratio

BMI: Body Mass Index

CI: Confidence Interval

CKD: Chronic Kidney Disease

COPD: Chronic Obstructive Pulmonary Disease

COR: Crude Odds Ratio

COVID-19: Coronavirus disease

DKA: Diabetic Ketoacidosis

DM: Diabetes Mellitus

EDCU: Epidemiology and Disease Control Unit

EHHRRB: Eswatini Human Health Research Review Board

EUA: Emergency Use Authorisations

ICU: Intensive Care Unit

IMS: Incident Management System

IMT: Incident Management Team

IQR: Interquartile Range

mAbs: monoclonal Antibodies

NCDs: Non-Communicable Diseases

OR: Odds Ratio

PCR: Polymerase Chain Reaction

PID: Primary Immunodeficiency

QGIS: Quantum Geographic Information System

RDT: Rapid Diagnostic Antigen Tests

SAFETP: South African Field Epidemiology Training Programme

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

SCD: Sickle Cell Disease

SD: Standard Deviation

SITREP: Situational Report

UK: United Kingdom

UNICEF: United Nations International Children Emergency Fund

USA: United States of America

Wits HREC: Wits Human Research Ethics Committee (Medical)

WHO: World Health Organization

CHAPTER ONE: INTRODUCTION

This chapter provided a brief background of the study, focused on the coronavirus disease (COVID-19) burden and hospitalization among adolescents globally, in Africa and sub-Saharan Africa region. The chapter also highlighted the gaps that existed in the literature, and the importance of why this study was conducted in Eswatini. The study's aims and objectives were laid out in this chapter.

1.1. Background

1.1.1. Global Burden of COVID-19

Globally, COVID-19 was among the leading public health threats with a high morbidity and mortality rate. As of 30 January 2022, globally a total of 373 819 859 confirmed cases and 5 662 449 deaths were due to COVID-19.[1] According to the World Health Organization (WHO) regions, as of 30 January 2022, Europe had the highest number of confirmed cases 144 557 762, followed by Americas with a total of 135 579 447 confirmed cases.[1] The South-East Asia region had 47 566 934 confirmed cases, followed by the Western Pacific region with 20 673 455 confirmed cases and the Eastern Mediterranean region with 18 831 779 confirmed cases.[1]

Deaths due to COVID-19 as of 30 January 2022 were mostly from the Americas region with 2 519 501 deaths, followed by Europe with 1 805 827 deaths, South-East Asia had 591 477 deaths, Eastern Mediterranean had 321 492 deaths and Western Pacific with 312 716 deaths.[1] There is a limitation to get specific age-disaggregated global COVID-19 statistics, including those specific to adolescents.

1.1.2. Burden of COVID-19 in the African region

In Africa, as of 30 January 2022, 8 098 432 cumulative confirmed cases and 164 111 deaths were reported to the World Health Organization, and South Africa in the sub-Saharan Africa region had reported 3 605 222 cumulative confirmed cases and 95 093 deaths.[1] However, these statistics underestimated the true impact of COVID-19 due to factors like underreporting and the region's pre-existing healthcare capacity issues.[7]

Public health initiatives at the height of the pandemic such as lockdowns, hygiene practices, and vaccine campaigns helped to slow the spread, but difficulties such as disinformation and delays in key health services hampered response efforts.[7] The emergence of more transmissible variants, such as the delta and omicron variants, contributed to an increase in the number of cases and deaths, notably in 2021.[7] Sero-prevalence studies suggested that true COVID-19 infection rates were substantially higher than reported, indicating a much wider disease burden across Africa.[7]

The virus's transmission and severity in Africa were influenced by socioeconomic factors such as population density and hygiene, as well as biophysical factors such as the prevalence of comorbidities for instance hypertension, diabetes, and HIV.[7] There were limited studies done in Africa that looked at the factors associated with COVID-19 hospitalization among adolescents; hence, the focus of this study.

1.1.3. COVID-19 situation in Eswatini

In Eswatini, the first reported case to be diagnosed with COVID-19 was seen on the 14th of March 2020, and thereafter the number people infected increased exponentially.[8] As of 31 January 2022, there were 68 367 cumulative confirmed cases with COVID-19 and 1375 total deaths as shown in Table 1.[1,8,9] Eswatini experienced five waves of COVID-19 from the first reported person, Figure 1. The first wave was between March 2020 and December 2020 during which the country recorded a total of 6633 confirmed cases and 126 deaths.[8,9] The second wave was declared on the 11th of December 2020 with 10 313 cumulative confirmed cases recorded. The third wave was declared on the 7th of July 2021, and cumulative confirmed cases recorded were 45 971.[8,9]

Table 1: Summary of total cases confirmed with COVID-19 and deaths in Eswatini, March 2020 - January 2022

Region	Cumulative cases confirmed with COVID-19 (n)	Cumulative deaths (n)	Case fatality rate (%)
Hhohho	23 113	419	1.8
Lubombo	24 486	535	2.2
Manzini	11 974	156	1.3
Shiselweni	8 793	265	3.0
Total	**68 367**	**1375**	**2.0**

(Adapted from the Eswatini COVID-19 SITREP).[8,9]

The fourth wave was from the 28th of November 2021 and confirmed cases recorded were 19 581 and 83 deaths (with the highest daily confirmed cases of 1642 recorded in December 2021).[8,9] The fifth wave started on the 14th of April 2022 and ended on the 30th of June 2022 and confirmed cases recorded were over 4886 and 32 deaths.[8,9] Children and adolescents accounted for 15% of the total cumulative confirmed cases in Eswatini.[8,9]

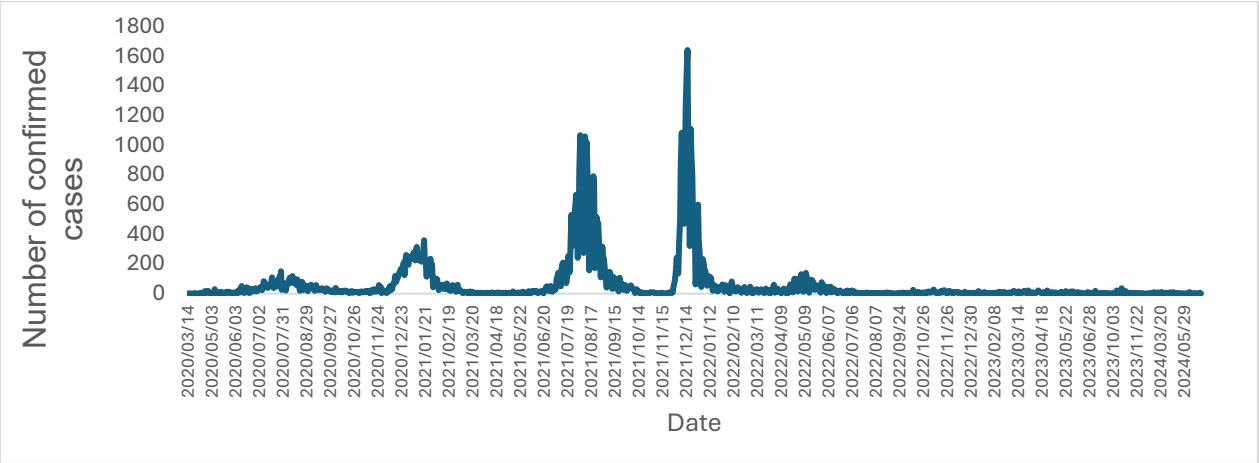

Figure 1: Distribution of COVID-19 confirmed cases from 2020 to 2024 in Eswatini

(Adapted from the Eswatini COVID-19 SITREP).[8,9]

COVID-19 was declared a state of national emergency by His Excellency the Right Honourable Prime Minister on 17th of March 2020, with a focus on banning mass gatherings, closing schools and tertiary institutions as well as non-essential businesses.[8,10] The Ministry of Health activated the Incident Management System (IMS), and a COVID-19 Incident Management Team (IMT) was established for the coordination of response activities.[8]

The management of COVID-19 respiratory infection depended on the severity of the disease, and hospitalization was not indicated for all patients, but severe individuals were prioritized for hospital admission.[8,10,11] The treatment plans included home care for asymptomatic and mild individuals, and hospital admission for severe and critical individuals.[8,10–12] Two national COVID-19 treatment centres were established, one in the Manzini region and the other in the Lubombo region. COVID-19 patients were admitted in the treatment centres and also in the regional hospitals in all four regions, including hospitals under private health facilities.[8,10–12]

1.1.4. COVID-19 among children and adolescents

A child, as defined by UNICEF, is any person less than 18 years and an adolescent as a person aged 10 to 19 years in the stage between childhood and adulthood.[13] Adolescents are a subset of children and few studies had focused solely on this sub-population in trying to understand COVID-19 in adolescents.[14–16] An adult is defined as “a person older than 19 years of age unless national law delimits an earlier age”.[17]

UNICEF reported that among the 4.4 million COVID-19 deaths globally as of December 2023, 0.4% (17 400) deaths occurred in children and adolescents, and of the 17 400 deaths, 53% occurred among adolescents 10 to 19 years.[18] A study in the United States of America (USA) found that in 2021 and 2022 COVID-19 was amongst the leading causes of mortality among children and adolescents, caused about 2% of deaths with an overall death rate of 1.0 per 100 000.[19]

Despite the availability of vaccines for children aged 5 and up in USA, vaccination rates in 2022 had fallen behind standard paediatric immunisation rates.[2] While 55% of adolescents aged 12-17 years were fully vaccinated received all the recommended doses by early 2022, only 22% of children aged 5-11 had gotten full vaccination, leaving a sizable section of the paediatric population at risk.[2] In South Africa, between March 2020 to 4 December 2024, children and adolescents made up 12.5% of the cumulative cases, 5% COVID-19-associated admissions and 0.7% COVID-19-associated hospital deaths.[20] Tracking the clinical characteristics, hospitalization rates, intensive care unit (ICU) admissions and outcomes was critical to the characterization of the burden of disease and deaths due to COVID-19 among adolescents.[21]

1.1.5. Risk factors

COVID-19 infection affected all age groups. In light of dynamic risk factors involved in each age group, children were likely to have fewer symptoms and mild disease compared to adults.[22] Symptoms commonly reported were fatigue, dyspnoea and myalgia, and they were associated with being over 11 years old.[25] Critically ill hospitalized paediatric patients had symptoms for a long duration and were significantly more hypoxic, thrombocytopenic and inflamed.[26]

Several risk factors for hospitalization among adolescents identified, included; "diabetes, chronic kidney disease (CKD), immunocompromising conditions, sickle cell disease (SCD), cardiovascular disease, elevated body mass index, chronic lung diseases, pregnancy, neurodevelopmental disorders, and medical- related technology dependence".[2] COVID-19 infection was associated with new-onset diabetes mellitus and glucose dysregulation, as observed in adolescents admitted with diabetic ketoacidosis (DKA) with no previous diabetes diagnosis.[27]

1.2. Problem Statement

Children and adolescents accounted for 15% of the total cumulative confirmed cases in Eswatini.[8,9] Despite the availability of vaccinations for eligible adolescents from the age 12 and up in Eswatini, those less than 12 years were not eligible for vaccination leaving a greater proportion still at risk. There is limited data in Eswatini regarding risk factors for hospitalization in children and adolescents diagnosed with COVID-19. While information from other studies conducted in different settings such as high-income, upper-middle-income, lower-middle-income and low-income countries is valuable, it is hard to separate the proportion of adolescents since these studies

included children from birth who were a completely different age group with unique risk factors.[27,29–31]

There was a limited number of studies focusing solely on adolescents, which were those in the age group of 10-19 years.[2,27,28,32–35] Thus, there is a need for a special focus on the adolescent group to understand the risk factors and prevent future hospitalizations due to disease severity and prevent mortalities for future pandemics of this nature. Therefore, it was important to understand the risk factors that might potentially get adolescents hospitalized due to severe disease.

1.3. Justification

There is limited published data on the hospitalization of adolescents in Eswatini. While studies assessing risk factors for COVID-19 hospitalization among adolescents were well documented, such studies had not been undertaken in Eswatini.[27,29,36–40] Therefore, there was a need for this study to understand factors associated with hospitalization of adolescents in Eswatini. Findings from this study will add data to the body of knowledge on such risk factors from a low-income country with a dual burden of infectious diseases and non-communicable diseases (NCDs) to inform targeted interventions.

1.4. Research Question

What factors were associated with COVID-19-related hospitalization of adolescents in Eswatini in the first four COVID-19 waves between March 2020 and January 2022?

1.5. Aim

To determine factors associated with the hospitalization of adolescents with COVID-19 in Eswatini in the first four COVID-19 waves, from March 2020 to January 2022.

1.6. Objectives

1. To describe the socio-demographic and clinical characteristics of adolescents with COVID-19 in Eswatini from March 2020 to January 2022.
2. To determine factors associated with the hospitalization of adolescents with COVID-19 in Eswatini from March 2020 to January 2022.

CHAPTER TWO: LITERATURE REVIEW

This chapter covered concepts in detail introduced in the first chapter and elaborated further on the risk factors associated with hospitalization in adolescents and children as highlighted in the literature. The chapter described each risk factor in detail and provided background information on the factors included in the analyses of this study.

2.1. COVID-19 and its effects

Globally, COVID-19 brought a significant amount of disruption and disturbances for individuals of all ages. While the pandemic affected all sectors of society, the burden of COVID-19 disease had adverse health outcomes directly associated with the infection with the virus and secondary effects, including increased unemployment, loss of jobs, and economic struggles, among other effects to name a few.[14,38]

COVID-19 presented mostly with mild disease among children and adolescents compared to adults, although severe disease also occurred among adolescents and required hospitalization and admission to intensive care units.[23,41] Adolescents were vulnerable to COVID-19 severe disease, 4.1% of adolescents aged 11-15 years had severe disease and were critical, and 3.0% of adolescents greater than 15 years old had severe disease.[42] Manifestation of COVID-19 in adolescents exhibited similar signs and symptoms just as described in adults, while the multisystem inflammatory syndrome was most common in children. [24] The common signs and symptoms included: fever, cough, respiratory distress, muscle pain, loss of smell, dizziness, headache, abdominal pain, vomiting, and nausea.[43]

2.2. Hospitalization due to COVID-19 among adolescents

Hospitalizations among children were high amongst those with comorbidities.[23] Severe COVID-19 occurred in about 30% of hospitalized children and about 12.0 per 100,000 children in the USA.[39] In other studies in the USA, the adolescent

hospitalization rates were 49.9 per 100 000 from March 2020 to April 2021 and 49.7 per 100 000 between March to August 2021.[15,44] In Italy, the hospitalization rate for children was 13.3% between February and May 2020.[36]

A study that was conducted in Germany, reported that hospitalization due to COVID-19 was at 3.35 per 10 000 among children and adolescents between July to October 2021.[30] In USA, it was reported that COVID-19 hospitalization rates amongst adolescents were above historical hospitalization rates for seasonal influenza during similar periods and were 2.5 to 3.0 times higher than previous hospitalization rates for seasonal-influenza.[15,45] Weekly hospitalization rates for adolescents increased, ranging from 10-25%, and admission to the ICU was required by one-third of hospitalized adolescents.[15,41]

Among the adolescents hospitalized, 34.6% required admission into the ICU or supplementation of oxygen, and of those admitted to the ICU, 21.2% required invasive ventilation.[28] When compared to other sub-Saharan African countries, the Southern Africa region had the highest number of children and adolescents requiring ICU admission at 52.4%.[28,46] While monthly hospitalization rates were 6 times greater in unvaccinated adolescents compared to adolescents fully vaccinated aged 12 -17 years.[47] During the period (July to 18 December 2021) predominated by the Delta variant, the number of hospitalized adolescents who were fully vaccinated was lower compared to the period (December 19 to 31 December 2021) Omicron predominated.[47] A higher number of unvaccinated adolescents were admitted to the ICU (30.3%) when compared to vaccinated adolescents (15.5%).[47]

2.3. Factors associated with COVID-19 hospitalization.

Hospitalization due to COVID-19 is associated with several risk factors ranging from socio-demographic and clinical characteristics (Table 2). The U.S.A Food and Drug Administration's Emergency Use Authorisations (EUAs) for monoclonal antibodies (mAbs) identified several risk factors for hospitalization among adolescents.[2]

Table 2: Factors associated with COVID-19 hospitalization by type among adolescents, March 2020 to January 2022

Type	Factors
Socio-demographic	Age Sex Socio-economic (educational level, place of residence)
Clinical- comorbidities	Obesity Diabetes Mellitus Hypertension Cardiovascular disease Chronic obstructive pulmonary disease (COPD) Chronic kidney disease

2.3.1. Sex and COVID-19

Biological factors in COVID-19 infection may pose a risk for hospitalization. A meta-analysis conducted looking at gender differences associated with the severity of coronavirus disease 2019 infection, found that when compared to females, males were more likely to suffer severe COVID-19 infection.[48] Several studies conducted, also found that being male was a risk factor at hospital entrance that predicted severe COVID-19 disease.[49,50]

2.3.2. Age and COVID-19

A study conducted in Brazil found that infants and adolescents aged 12 to 19 had an increased risk of death compared to children aged 2 to 11 years.[51] Another study conducted in Brazil, also found that the age group of adolescents was an associated

factor for COVID-19 mortality.[32,35] A study in Italy found that a lower risk of COVID-19 disease was associated with increasing age.[36]

2.3.3. Obesity and COVID-19

Obesity was found to be a risk factor for severe COVID-19 and obesity among adolescents with COVID was among the factors associated with hospitalization.[53,54] Adjustments in dietary behaviours fuelled food intake and unhealthy food choices were noted during the COVID-19 pandemic.[54] A study conducted in the USA, outlined that during the summer holidays, adolescents gained weight and the rate of childhood obesity was estimated to increase due to the number of months when schools were closed during the COVID-19 pandemic.[55] A study in the USA found that a total of 1.27 million childhood obesity cases were in 2020.[54,55] Metabolic changes associated with obesity increase the risk of having non-communicable diseases.[53] COVID-19 restrictions posed a factor in increased obesity rates as physical activity and movements were restricted, and obesity posed a risk factor associated with hospitalization of adolescents with COVID-19.[54] Organ changes because of obesity increased the risk of ventilatory support, thromboembolism, altered glomerular filtration rate, changes in immune response and chronic inflammatory response.[56]

2.3.4. Diabetes Mellitus and COVID-19

Diabetes mellitus (DM) has the following 3 main types: type 1 DM, type 2 DM and gestational diabetes.[57,58] Type 1 DM is defined as “when the body produces very little or no insulin, type 2 DM referred to when the body does not make maximal use of the insulin that it produces”.[57,58] Gestational diabetes is defined as “a type of DM that consists of high blood glucose during pregnancy and is associated with complications for both mother and children”.[57,58] Fluctuating glucose levels in the blood and the presence of complications due to DM make it challenging to manage and treat people living with DM when they develop a viral infection.[59,60] There is increased

susceptibility among individuals living with DM to have respiratory infections, mostly influenza and pneumonia.[61] Poor prognosis has been reported among people living with DM ever since the start of the COVID-19 pandemic.[61,62] Individuals with DM co-infected with COVID-19 due to the concurring effect of multiple factors have been reported to have worse prognosis.[63,64] DM is associated with increased odds of poor prognosis in COVID-19 patients.[65] The prevalence of DM as a comorbidity among patients diagnosed with COVID-19 ranges between 7 and 30%.[66]

DM incidence increased for the general population even for adolescents during the COVID-19 pandemic.[67] Diabetes mellitus whether type 1 or 2 was the frequently found endocrine condition in children and adolescents hospitalized with COVID-19.[67] A tertiary care children's hospital in New York City conducted a study and reported that from March to October 2020, a history of DM and shortness of breath was predominantly significant among the hospitalized compared to the non-hospitalized.[27] The presence of type 1 DM, and cardiac and circulatory congenital anomalies in children increased the risk of both hospitalization and severe illness when hospitalized.[68]

2.3.5. Cardiovascular Disease and COVID-19

COVID-19 affected mainly the respiratory system, but its effects were not restricted to one system, atypical presentations in children and adolescents were reported.[69] Another crucial system that was affected by COVID-19 was the cardiovascular system.[70] COVID-19 severe outcomes were associated with congenital heart disease and hypertension.[71] In the USA, 1 out of 25 adolescents aged between 12 to 19 years had hypertension and 1 out of 10 adolescents had elevated blood pressure.[73] A study in the USA revealed that adolescents with obesity had high blood pressure common among them.[73] Adolescents during the COVID-19 pandemic had an

increased risk of having hypertension compared to the pre-pandemic period among adolescents.[74] The prevalence of hypertension among children and adolescents increased from 7.1% to 12.5% during the COVID-19 pandemic.[74] Hypertension increases the susceptibility to developing severe COVID-19 disease because of underlying endothelial dysfunctions and coagulopathy.[75,76] Delayed COVID-19 clearance and exacerbated lung inflammation due to abnormal immune response and airway inflammation were seen in individuals with hypertension.[71]

Congenital heart disease (CHD) is defined as “a range of birth defects that affect the structure of the heart and the normal way the heart works.”[77,78] ICU admissions due to COVID-19 were associated with several heart biomarkers.[79] Poor COVID-19 outcomes among hospitalized adolescents with CHD were due to the damaging effect of COVID-19 on the heart.[80]

2.3.6. Sickle cell disease and COVID-19

Nearly all organs and systems are affected by sickle cell disease (SCD) and individuals with SCD have an amplified risk of complications from influenza illness.[82] Adolescents with SCD required hospitalization and SCD was found as a risk factor for severe COVID-19 disease.[83] Adolescents with comorbidities like sickle cell disease were considered to be at risk for hospitalization and severe disease.[84] History of pain, SCD-related heart, lung and renal comorbidities were risk factors associated for worse COVID-19 outcomes in adolescents.[85]

2.3.7. Asthma and COVID-19

Asthma was reported as the most common comorbidity among adolescents with COVID-19 and was also listed as a risk factor for severe COVID-19 disease.[29,87] Asthma and COVID-19 relationship in children was not clearly understood, as data about this relationship was mostly from adults.[88] A study in the USA outlined that

there were subgroups with higher morbidity risk by COVID-19 among patients with severe asthma.[89] There was limited information on whether childhood asthma was a risk factor for COVID-19 severity and some studies on the other hand reported that asthma was not related to an increased risk of hospitalization.[86,88,90]

2.3.8. Neurologic conditions and COVID-19

Due to structural, biochemical or electrical abnormalities in the brain, spinal cord or nerves it may result in a range of symptoms including paralysis, muscle weakness, poor coordination, loss of sensation, seizures, confusion, pain and altered levels of consciousness.[91] In the USA, about 22% of hospitalized adolescents with COVID-19 had neurological involvement.[92] Children and adolescents who had a broad range of neurologic symptoms involving seizures, headache, and fatigue were associated with COVID-19 varied by age.[92] A study in the United Kingdom (UK) about hospitalized children and adolescents with neurological and COVID-19 infection reported that 3.8 per 100 hospitalized had neurological disorders.[93]

Epilepsy was one of the neurological disorders that were commonly found in hospitalized patients with COVID-19.[94] Epilepsy is a “common brain disorder characterized by two or more unprovoked seizures”.[95] Adolescents with epilepsy were reported to be at increased risk of severe COVID-19 disease when hospitalized.[44] Data about epilepsy and COVID-19 was rare, however, a recent study outlined an increased risk of mortality among patients with epilepsy and COVID-19.[44]

CHAPTER THREE: METHODS

This chapter described in detail the design used in the analysis, the data sources, the setting and population used in the study as well as the criteria used to include and exclude participants in the secondary data analysis. It also provided the details of the processes conducted for data management to ensure robust and accurate analysis. Finally, a detailed description of the analysis plan followed to transform the data into meaningful results.

3.1. Study design

The study adopted a quantitative approach using an analytic cross-sectional design.

3.2. Study setting

The Kingdom of Eswatini is a landlocked monarchy with four administrative regions, namely; Hhohho, Lubombo, Manzini and Shiselweni region. The country is bordered by South Africa and Mozambique. According to the 2017 census data, the total population in Eswatini was approximately 1 093 238, and adolescents (aged 10-19 years) accounted for 18.8% (205 507) of the total population.[96]

Eswatini's health care system consists of both formal and informal service sectors which has both public and private service providers. [97,98] The health system has three levels of primary health care: primary, secondary and tertiary.[97] At the primary level there are clinics, outreach services and community health workers. There are health centres at the secondary level, that offer outpatients and inpatient services and serve as a referral point for the primary level facilities.[97,98] The tertiary level comprises regional hospitals, specialised hospitals and national referral hospitals.[97,98] In total, there are 327 health facilities in the country: 18 hospitals of which 9 are private hospitals, 5 health centres, 7 public health units, and 297 clinics (public and private clinics).[97,98] Secondary and tertiary-level facilities provide inpatient admission

services. There were 17 health facilities (hospitals and health centres) that provided COVID-19 hospital admissions/inpatient services (Figure 2).

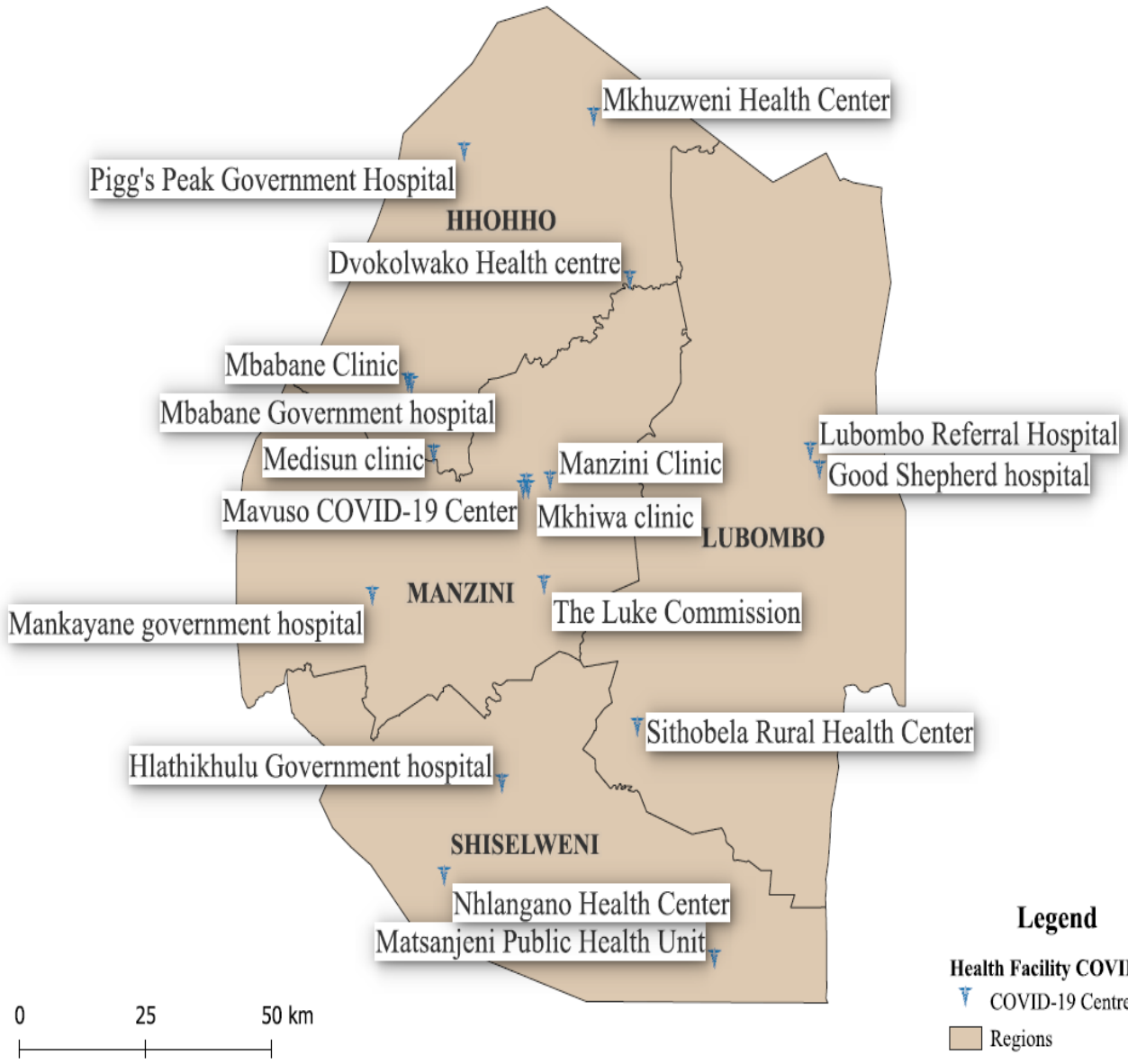

Figure 2: COVID-19 admitting Health Facilities in Eswatini, March 2020 to January 2022

(Created using Quantum Geographic Information System -QGIS)

3.3. Study population

The study population included all adolescents (aged 10-19 years) who were diagnosed with COVID-19 at health facilities in Eswatini from March 2020 to January 2022.

3.4. Data Source

The Kingdom of Eswatini's national-level data was collected from health facilities from March 2020 to January 2022. The Eswatini national COVID-19 database secondary data routinely captured for COVID-19 morbidity and mortality tracking was utilized in the study. The data was used for continual monitoring of COVID-19 trends in the country. The Ministry of Health houses the national COVID-19 dataset for all COVID-19 cases and deaths reported in Eswatini from all sources. The case management team generated and assigned unique case numbers for all the reported cases and deaths. The team also followed up on all the cases and recorded additional data including hospitalizations. An online password-protected database was generated and documented all COVID-19 cases.

3.5. Sampling

There was no sampling done in this study but the whole dataset was used. A power analysis was conducted to determine if the study is powered enough.

3.5.1. Power Calculation

A post hoc power calculation based on the secondary data was conducted using the Chi-square test for two independent proportions. The final sample size of 9277 was adolescents with 3.4% hospitalized. A 12% prevalence from a study conducted in South Africa looking at the changing epidemiology of COVID-19, 2020 to 2022, was used. [33] Power was computed at different percentages at an alpha level of 0.05 at a 95% confidence interval. Given the sample size, the study had sufficient power at 100% to detect a difference in risk for hospitalization at an alpha level of 0.05.

3.5.2. Inclusion criteria

The study included all adolescents in Eswatini who were aged 10 to 19 years and were diagnosed with COVID-19 from March 2020 to January 2022 and whose data was available in the database.

3.5.3. Exclusion criteria

All records for which the date of diagnosis of COVID-19 diagnosis and/or hospitalization variable was not available in the dataset were excluded.

3.6. Operational Definitions

Adolescent: An adolescent was defined as a person aged 10-19 years at the time of hospitalization.

COVID-19 confirmed case: A COVID-19 confirmed case was an adolescent with a confirmed COVID-19 laboratory diagnosis using rapid diagnostic antigen tests (RDT) and or Polymerase Chain Reaction (PCR) testing in the period of March 2020 to January 2022.

COVID-19 Hospitalization: COVID-19 hospitalization was defined as any inpatient overnight stay admission of an adolescent with a positive COVID-19 laboratory diagnosis regardless of the reason for admission in the period of March 2020 to January 2022.

3.7. Data collection and management

Data was obtained from the Ministry of Health in an Excel spreadsheet and was exported to Stata 17.0 for management and analysis. Data cleaning and coding was performed, where duplicates were checked using the unique case numbers, age, sex, region and date of diagnosis. String variables were converted to numeric format to enable analysis. Most variables except for age were categorical, and age was analysed as a continuous variable. The outcome variable was hospitalization, a binary variable with yes and no categories. The yes category meant those adolescents who tested positive for COVID-19 and were hospitalized, and the no category meant those adolescents who tested positive for COVID-19 and were not hospitalized in any health facility. Definitions and categories of the exploratory variables (demographic and clinical) are provided in Table 3.

Table 3: Extracted Variables from the Eswatini COVID-19 dataset and their definitions, March 2020 to January 2022

Variable	Definition	Data type
Age (years)	The reported age of the adolescents or age calculated from the date of birth to the date of diagnosis.	Continuous
Sex	Biological make-up of the adolescents	Categorical (Male, Female)
Date of diagnosis	Date of COVID-19 diagnosis	Numeric
Status at Diagnosis	Living status of the adolescent at diagnosis	Categorical (Alive, Dead)
Severity at notification	Disease severity based on clinical presentation at the time of diagnosis	Categorical (Asymptomatic, Mild, Moderate, Severe)
Hospitalization	Hospital admission due to COVID-19	Categorical (Yes, No)
Symptomatic	Clinical status of COVID-19-related symptoms (fever, sore throat, cough, runny nose, shortness of breath, chest pains, loss of taste and smell) the adolescent presented with at the time of diagnosis	Categorical (Yes, No)
Presence of comorbidities	Comorbidities (hypertension, diabetes mellitus, cardiovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, obesity, asthma, TB, HIV, cancer) the adolescent presented with at the time of diagnosis	Categorical (Yes, No)

3.8. Data analysis

Categorical variables were summarized using frequencies and proportions. A histogram was used to test for normality and age as the only continuous variables did not violate normality assumptions and as such was summarized using means and standard deviations (SD).

The Chi-square test was used to test for differences in the proportions for categorical variables. The unpaired Student's t-test was used to assess differences in means for age. Fisher's exact test was used as appropriate for categorical variables which had expected values of less than 5 cases per cell. The symptoms and comorbidities variables in this study had few observations due to missing data and thus only included in the descriptive analysis and not in the inferential analysis. Univariate logistic analysis was used to assess associations between the hospitalization and the exposure variables, and crude odds ratios (COR) were estimated, 95% confidence interval (CI) and p-values were reported. Statistical significance for the univariate analysis was considered at $p< 0.05$.

Multivariable logistic regression analysis was performed to identify factors associated with hospitalization using hospitalization as the outcome variable and the following explanatory variables tested at univariate: age, sex, region, COVID-19 severity, symptomatic and comorbidities. Model building was done through the manual selection of variables from the univariate logistic analysis with odds ratios that had $p<0.2$ in the univariate analyses, which were included in the multivariable model. Statistical significance for the univariate analysis was considered at $p\leq0.2$ to avoid losing variables to include in the model.[99] Due to prior knowledge showing a significant association with hospitalization, age and sex were included in the final model regardless of their p-values in the univariate analysis.[27] Also, region, being symptomatic and the presence of comorbidities were included in the final model based on statistical significance at the univariate analysis. Adjusted odds ratios (aORs), p-values and 95% CI from the multivariable model were reported. The study adopted and reported a 5% significance level as such a $p<0.05$ was deemed statistically significant.

Multicollinearity was checked by examining correlation coefficients for all independent variables to determine correlation. Variables in the final model with correlation coefficients above 0.6 were not included. The Hosmer-Lemeshow goodness of fit test was used to assess how good the model was, for prediction of the factors associated with hospitalization by the independent variables, considering that the model was considered fit when the expected p-value was $p>0.05$.

3.9. Ethical considerations

Ethical clearance for the study was sought from the University of Witwatersrand Human Research Ethics Committee (Medical) (certificate number M230244 M230830-A-0001) and Eswatini Human Health Research Review Board (certificate number EHHRRB 071/2023) (Appendix 3 and 4). Permission for data use was obtained from the Ministry of Health (Appendix 5). Data was received with no names but with case numbers and data was analysed at population rather than individual level with no possibility to link findings with any individual who participated in this study.

CHAPTER FOUR: RESULTS

This chapter covered the results according to the two study objectives and their interpretations. Both descriptive and inferential analyses were presented in the form of tables and graphs. Tests for associations using univariate and multivariable logistic regression analysis were presented in tables.

4.1. Descriptive Analysis

The study focused on adolescents diagnosed with COVID-19 in Eswatini from the 14th of March 2020 to the 31st of January 2022. As of the 31st of January 2022, there were 68 367 cumulative people diagnosed with COVID-19 and of those, 9314 were adolescents. Of these adolescents, 96.60% (n=9277) had an outcome variable (hospitalization) specified. Hospitalized adolescents accounted for 3.41% (n=318) of the adolescents with COVID-19 (Figure 3).

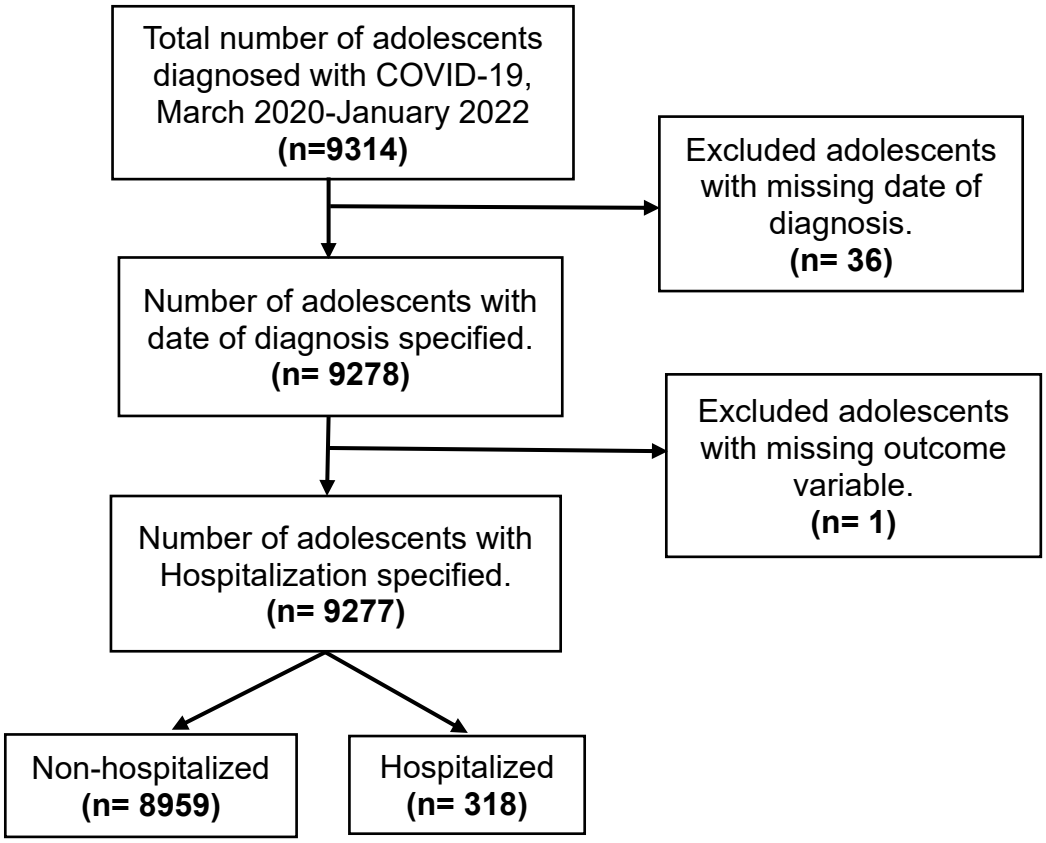

Figure 3: Flow chart of data management of adolescents with COVID-19 in Eswatini, March 2020- January 2022

Table 4 shows the demographic and clinical characteristics of the adolescents. Most of the adolescents were females, 57.21% (n=5307) and the overall mean age was 15.36 SD± 2.70 years. When disaggregated by regions most of the adolescents 33.83% (n=3138) were from the Hhohho region and the Manzini region 32.42% (n=3008). The majority of the adolescents 76.73% (n=7118) had mild disease at diagnosis and only 3.43% (n=318) were hospitalized.

Table 4: Demographic and clinical characteristics of adolescents with COVID-19 in Eswatini, March 2020- January 2022 (N=9277)

Variable	Frequency(n)	Percentage (%)
Sex		
Female	5307	57.21
Male	3970	42.79
Age, mean (SD)	15.36 (2.70)	
Region		
Hhohho	3138	33.83
Manzini	3008	32.42
Lubombo	1736	18.71
Shiselweni	1392	15.00
Not stated	3	0.03
COVID-19 severity		
Asymptomatic	1149	12.39
Mild	7118	76.73
Moderate	979	10.18
Severe	62	0.67
Not stated	4	0.04
Symptomatic		
No	405	4.37
Yes	300	3.23
Not stated	8572	92.40
Comorbidities		
No	817	8.81
Yes	65	0.70
Not stated	8395	90.49
Hospitalized		
No	8959	96.57
Yes	318	3.43
Hospitalization Outcome		
Died	9	0.10
Discharged	9268	99.90

Of those adolescents who were symptomatic 3.23% (n=300), the common symptoms reported were displayed in Figure 4. Cough (17.33%; n=52) was the most reported symptom with the least reported being chest pains (5.00%; n=15). Some adolescents presented with one or more symptoms and a majority had symptom specification not stated.

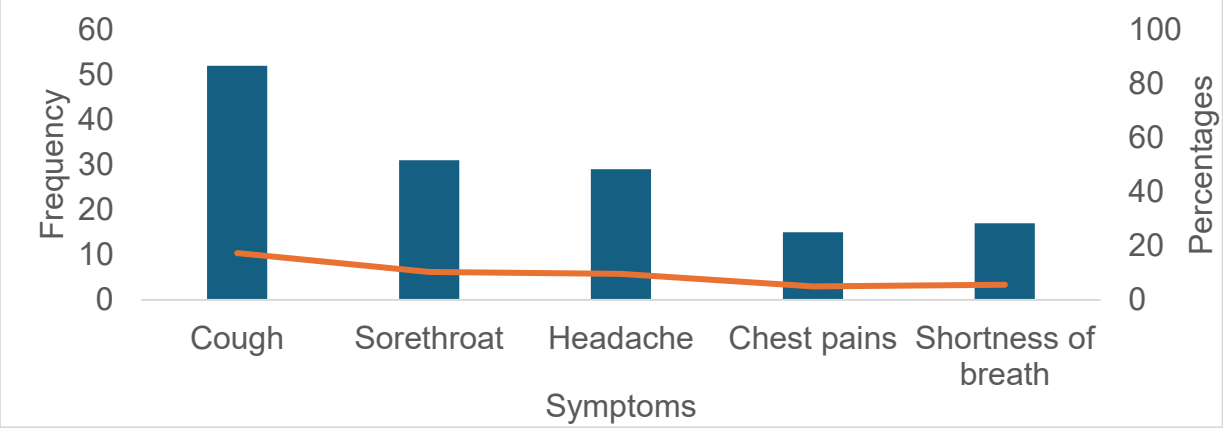

Figure 4:Common symptoms reported by adolescents with COVID-19 in Eswatini, March 2020- January 2022

A total of 0.70% (n=65) adolescents had comorbidities, of those who had comorbidities just over half reported to have had asthma (53.85%, n=35) and the least reported diabetes mellitus and hypertension at 4.62% (n=3) respectively (Figure 5).

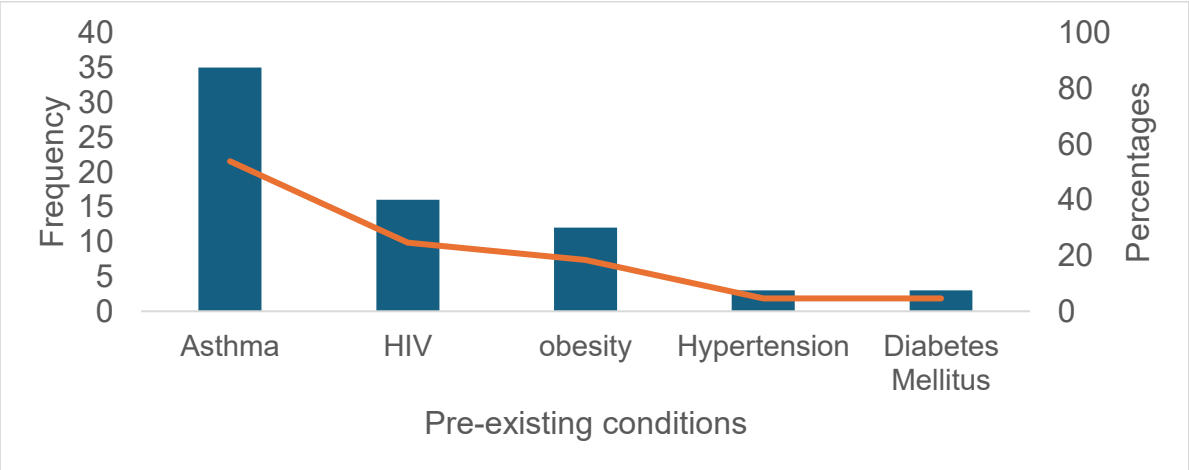

Figure 5:Common Comorbidities reported in adolescents with COVID-19 in Eswatini, March 2020- January 2022

4.2. Inferential analysis

4.2.1 Demographic and clinical factors by COVID-19 hospitalization

Table 5 shows the association of demographic and clinical factors with hospitalization status. A higher proportion of females (3.62%, n=192) were hospitalized compared to 3.17%, n=126 for males but the difference was not significant at (p=0.245). The Manzini region had the highest proportion of hospitalization (5.32%) and the regional difference in hospitalization varied significantly, p<0.001. Adolescents who presented with moderate symptoms had the highest proportion (32.73%) among the hospitalized adolescents and the differences in severity varied significantly, p<0.001.

Table 5: Demographic and clinical characteristics of adolescents by COVID-19 hospitalization in Eswatini, March 2020- January 2022 (N=9277)

Variable	Not hospitalized n (%)	Hospitalized n (%)	P-value
Sex			0.245
Female	5115 (96.38)	192 (3.62)	
Male	3844 (96.93)	126 (3.17)	
Mean age (SD), years	15.35 (2.70)	15.60 (2.62)	0.107
Region**			<0.001
Hhohho	3059 (97.48)	79 (2.52)	
Lubombo	1706 (98.27)	30 (1.73)	
Manzini	2848 (94.68)	160 (5.32)	
Shiselweni	1343 (96.48)	49 (3.52)	
COVID-19 severity**			<0.001*
Asymptomatic	1149 (100.00)	0 (0.00)	
Mild	7117 (99.99)	1 (0.01)	
Moderate	635 (67.27)	309 (32.73)	
Severe	54 (87.10)	8 (12.90)	
Symptomatic**			<0.001
No	382 (94.32)	23 (5.68)	
Yes	255 (85.00)	45 (15.00)	
Comorbidities**			<0.001
No	541 (66.22)	276 (33.78)	
Yes	30 (46.15)	35 (53.85)	

P values are chi-square (χ^2) unless noted, * Fisher's exact p-value,
**Variables with missing information

A high proportion (53.85%) of the hospitalized adolescents had comorbidities, and the differences were significant, p<0.001. There were differences in hospitalization by region, and the difference was significant at p<0.001. There was also a significant difference in severity at diagnosis by hospitalization (p<0.001). There were no differences in hospitalization by age and sex at p>0.05.

4.2.2 Factors associated with COVID-19 hospitalization

The univariate and multivariable logistic regression analysis results are presented in Table 6.

Table 6: Univariate and multivariable logistic regression models for COVID-19 hospitalization of adolescents in Eswatini, March 2020- January 2022 (N=9277)

Variable	Total (n)	Univariate OR (95% CI)	P-value	Multivariable aOR (95% CI)	P-value
Sex					
Female	5307	Ref		Ref	
Male	3970	0.87 (0.69-1.10)	0.245	0.99 (0.58-1.68)	0.965
Age (years)		1.04 (0.99-1.08)	0.108	1.09 (0.99-1.20)	0.085
Region**					
Lubombo	1736	Ref		Ref	
Hhohho	3138	1.47 (0.96- 2.25)	0.076	0.22 (0.09-0.57)	0.002*
Manzini	3008	3.19 (2.15-4.74)	<0.001	0.45 (0.20- 1.01)	0.053
Shiselweni	1392	2.07 (1.31- 3.28)	0.002	0.62 (0.23-1.66)	0.339
COVID-19 severity **					
Asymptomatic	1149	Ref			
Mild	7118	0.001 (0.00-0.01)	<0.001		
Moderate	979	3.28 (1.54-6.99)	0.002		
Severe	62	1 (omitted)			
Symptomatic**					
No	405	Ref		Ref	
Yes	300	2.93 (1.73 - 4.96)	<0.001	2.48 (1.43-4.28)	<0.001*
Comorbidities**					
No	817	Ref		Ref	
Yes	65	2.29 (1.37- 3.80)	<0.001	4.04 (1.91-8.52)	<0.001*

OR= Odds Ratio, aOR=adjusted Odds Ratio
*statistically significant at p<0.05, **variables with missing information

Adolescents from the Manzini region had 3.19 times the odds of hospitalization compared to those from the Lubombo region (OR= 3.19; 95% CI: 2.15-4.74), the association was significant. Compared to those from the Lubombo region, adolescents from the Shiselweni region were 2.07 times as likely to be hospitalized, and the association was significant (OR= 2.07; 95% CI: 1.31- 3.28).

Compared to those with no symptoms, presenting with mild disease at diagnosis was associated with hospitalization (OR= 0.001; 95% CI: 0.00-0.01) and the association was significant. Being symptomatic had 2.93 times the odds of hospitalization compared to those without symptoms (OR=2.93; 95%CI: 1.73- 4.96) and the association was significant. Adolescents who had the presence of comorbidities had 2.29 times the odds of hospitalization compared to those who did not have comorbidities (OR= 2.29; 95% CI: 1.37- 3.80) and the association was significant. The following variables: Age, Sex and being from the Hhohho region were not significantly associated with hospitalization at univariate analysis

The following variables were included in the final model in multivariable model: sex, age, region, symptomatic and comorbidities. Severity at diagnosis was not included in the final model as it was strongly correlated to hospitalization r=0.615. After adjusting for sex, age, symptomatic, and comorbidities in the final model, only adolescents from the Hhohho region were significantly associated with hospitalization (aOR=0.22; 95% CI: 0.09-0.57) when compared to the Lubombo region. Symptomatic adolescents had 2.48 times the odds of hospitalization when compared to those without symptoms and the association was statistically significant (aOR= 2.48; 95% CI: 1.43 - 4.28).

Adolescents who had the presence of comorbidities had 4.04 times as likely the odds of hospitalization compared to those without have comorbidities, and this association was significant (aOR= 4.04; 95% CI: 1. 91- 8.52). The final model showed that being from the Hhohho region, being symptomatic and having the presence of comorbidities were risk factors associated with hospitalization ($p<0.05$). Age, Sex and region being from Manzini and Shiselweni were not significantly associated with hospitalization in the final model. The model fit was found to be good enough to predict the factors after conducting the Hosmer-Lemeshow goodness of fit test with p-value of 0.764.

CHAPTER 5: DISCUSSION

The aim of this study was to investigate factors associated with the hospitalization of adolescents with COVID-19 in Eswatini in the first four COVID-19 waves, from March 2020 to January 2022. Adolescents and children were both used throughout the discussion section as reference was also taken from studies that were looking at both children and adolescents.

This study found that a minority (3.43%, n=318) of the adolescents were hospitalized. This finding suggested that adolescents had minimal contribution to the hospitalization burden due to COVID-19. Most of the hospitalized adolescents presented with moderate disease severity at diagnosis and most (8.81%, n=817) had no comorbidities at diagnosis. These findings are comparable to a study in Germany that found that COVID-19 infections in children and adolescents were associated with low hospitalization and more than 50% of the children and adolescents were not admitted to hospital due to COVID-19 but rather due to other reasons.[23]

In this study, a majority of the adolescents diagnosed with COVID-19 were females and of the hospitalized adolescents a high number were also females. Sex in this study was not associated with hospitalization and this suggested that there were no differences in outcomes due to sex when it came to COVID-19 hospitalization among adolescents. This finding was comparable and consistent with a study conducted in the USA, that found a majority of adolescents were females and that there were no detected differences in biological sex.[27] Another study conducted in Texas concurred with the findings of this study as it found that most of the adolescents were females.[3] On the other hand, a study conducted in Italy, found the majority of adolescents to be

males.[36] The mean age for this study was 15.36 years (±2.70), and age was found not to be statistically associated with hospitalization. This suggested that being between the age of 10 to 19 years was not associated with being hospitalized. When comparing to other studies, this study reported the mean with its standard deviation while other studies reported median age with its interquartile ranges. A study conducted in the USA found that the overall median age to be 16.8 (IQR: 7.3-20.2) years and the median age was statistically significant.[27] A study conducted in Brazil found the overall median age of hospitalized adolescents diagnosed with COVID-19 to be 14.7 (IQR: 10.1-17.9) years, and the median age was statistically significant.[32]

Additionally, in this study a high number of adolescents were from the Hhohho region and of the hospitalized adolescents, a high number were from the Manzini region. Residing in the Hhohho region was associated with being hospitalized. This finding implies that region-specific variances that reflect variations in healthcare availability and access, population density, or local epidemic dynamics, increasing hospitalization risks. The Hhohho region harboured national referral hospital and 5 other COVID-19 admitting centres which might have attributed to the ease of access of health services in this region, which could have contributed to the regional variations. Adolescents from other regions might have also been transferred to hospitals in the Hhohho region as the region has the tertiary level hospital. Our findings agree with a study in Brazil found that poor clinical outcomes were attributable to several reasons including significant socioeconomic gaps and economic differences even within the same location.[51]

With regards to COVID-19 severity, a high number of adolescents had mild disease, and a minority had severe disease. This suggested that most adolescents suffered

mild COVID-19 disease severity, this could have been as a result of multiple factors such as strong immune system for the adolescents. This finding was consistent with results from a study in Germany that found that COVID-19 infections are usually mild among adolescents.[23] Also supporting this finding, a study in Canada found that severe outcomes were rare among children.[38]

The findings in this study also showed that only a small proportion (0.70%, n=65) of the adolescents had already existing comorbidities. Among the hospitalized, the presence of comorbidities increased the risk of hospitalization and thus adolescents with comorbidities needed special attention to manage them. When studying the presence of comorbidities in literature, it was found that the risk for severe disease among hospitalized children was higher among children with greater than one underlying medical condition.[39] Comorbidities such as immunocompromising disorders, obesity, diabetes, neurologic disease, and pulmonary disease except mild asthma were related to hospitalization at or following COVID-19 diagnosis in a study conducted in the USA.[2] In this study, however, specific comorbidities were not run in the final model due to the limitation of having too few observations to be taken for inferential analysis.

In this study, mortality amongst adolescents was found to be very low (0.10%,n=9). This finding was similar to what was found in a study conducted in the USA that 0.5% of those aged below 18 years (children and adolescents) died during hospitalization.[39] This finding was also comparable to findings of a meta-analysis study conducted, that found mortality among children and adolescents to be at 0.28%.[100] This finding implied that there was a very low proportion of adolescents who died due to being hospitalized with COVID-19.

5.1. Limitations

The study presented factors associated with COVID-19 related hospitalization among adolescents. However, the study had some limitations, and they were discussed as follows: Due to the use of secondary data for the study, there was no control and influence on the data capturing system to align with the interests of our analyses. The number of variables captured in the line list was a limitation in restricting in-depth analysis. The results of the study are subject to potential reporting bias as data in the line list depended on if health facilities were reporting the adolescents diagnosed with COVID-19.

A majority of the variables included in the analysis had missing information, data not stated and thus limiting our ability to carry out inferential analysis and potentially introducing bias in data analysis. The symptomatic and presence of comorbidities variables had 92.40%, (n=8572) and 90.49%, (n=8395) missing data respectively, resulting in data gaps due to missing information and thus were not included in the inferential analysis. Thus, this limited the results of the study in how possibly such variables excluded could have potentially played a part in the associations of being risk factors for hospitalization among the adolescents. As all the hospitalized adolescents were tested for COVID-19 and that might have resulted in opportunistic diagnoses going undiagnosed and the underlying reason for hospitalization might have been unrelated to COVID-19.The results of this study cannot be generalized due to small numbers of hospitalized adolescents, the limited number of variables in the dataset with missing information.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

This chapter detailed the conclusion of this study by summarizing the key findings of the study in line with the study objectives and research question. The chapter highlighted the major limitations of the study and further suggested recommendations.

In conclusion, the study found that a majority of the adolescents diagnosed with COVID-19 were females and the hospitalization rate of the adolescents was low (3.43%, n=318) in the period of the study. Being symptomatic, residing in the Hhohho region and living with comorbidities were factors associated with the hospitalization of adolescents with COVID-19 in Eswatini. These factors should be considered when developing interventions for example, those with symptoms should be prioritized to prevent unintended outcomes. However, with the data quality limitations in this study, more can still be explored on the inferential analysis of the risk factors. Thus, preventive measures and strategies for COVID-19 and similar nature pandemics should be inclusive of and target adolescents as they are not spared from the effects of COVID-19.

Based on the findings from this study, the following recommendations are proposed:

- Strengthening surveillance systems with robust data collection and management systems during pandemics. Such systems should ride on existing platforms to ensure good data quality which will be useful in guiding response interventions.
- Promote data use and research particularly during emergencies to provide data and support prompt data improvement to inform response direction.

- Studies of similar nature be conducted with improvements in considering number of variables to be included in the analysis, quality data with high completeness of data in the variables to perform inferential statistics to identify the risk factors.
- Policy makers should design region specific interventions as regional variations might be useful in addressing regional differences.
- Policy makers should consider adolescents as one of the priority groups when designing COVID-19 response programs.

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Appendix 1: Plagiarism Declaration

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Musawenkhosi Mzamo Mbuli (Student number: 2571730) am a student registered for the degree of Master of Science Epidemiology in Field Epidemiology in the academic year 2025.

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: 29 September 2025

Appendix 2: Turn it in page

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30 September 2025

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Appendix 3: University of Witwatersrand Human Research Ethics Committee (Medical) Ethics Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Mr Musawenkhosi Mzamo Mbuli

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M230244 M230830-A-0001

NAME: (**Principal Investigator**)	Mr Musawenkhosi Mzamo Mbuli
DEPARTMENT:	Epidemiology and Biostatistics Ministry of Health Epidemiology and Disease Control Unit, The Kingdom of Eswatini
PROJECT TITLE:	Factors associated with hospitalization of adolescents with coronavirus disease in Eswatini, March 2020 to January 2022
DATE CONSIDERED:	24-Feb-2023
DECISION:	Approved unconditionally
CONDITIONS:	N/A
NOTE:	Application Number: MED23-01-107
SUPERVISOR:	Mr V. Lokotfwako, Dr N. Ndlovu and Miss T. Zwane

APPROVED BY: Prof P. Ruff, Chairperson, HREC (Medical)

DATE OF APPROVAL: 30-Aug-2023 **EXPIRY DATE:** 30-Aug-2028

This clearance certificate is valid for 5 years from data of approval. Extension may be applied for.

DECLARATION OF INVESTIGATOR(S)

I/we fully understand the conditions under which I am/we are authorized to carry out the abovementioned 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 resubmit the application to the Committee. **I agree to submit a yearly progress report** in the month date of convened meeting each year until study is closed. Failure to submit annual report will result in ethics clearance certificate suspension. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. Unreported changes to the application may invalidate the clearance given by the HREC (Medical). Email a signed copy of ethics clearance certificate to HREC-Medical.ResearchOffice@wits.ac.za

Signature of Principal Investigator Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 4: Eswatini Human Health Research Review Board Ethics Certificate

ESWATINI HEALTH AND HUMAN RESEARCH REVIEW BOARD
MBANDZENI HOUSE, 3RD FLOOR, CHURCH STREET
P.O. BOX 5, MBABANE, ESWATINI

ONE YEAR RESEARCH PROTOCOL APPROVAL CERTIFICATE

BOARD REGISTRATION NUMBER	FWA 00026661/IRB 00011253							
PROTOCOL REFERENCE NUMBER	**EHHRRB 071/2023**							
Type of review	Expedited	**X**		Full Board				
Name of Organization	**Masters Student**							
Title of study	Factors associated with hospitalization of adolescents with Coronavirus disease in Eswatini, March 2020 to January 2022							
Protocol version	1.0							
Nature of application	New		Amendment		Renewal		Extension	CT updates
	X							
List of study sites	Eswatini							
Name of Principal Investigator	**Mr. Mbuli Musawenkhosi Mzamo**							
Names of Co- Investigators	Dr. Ntombizodwa Ndlovu, Mr. Lokotfwako Vusie and Ms. Zwane, Thembekile							
Names of steering committee members in the case of clinical trials	N/A							
Names of Data and Safety Committee members in the case of clinical trials	N/A							
Level of risk (Tick appropriate box)	Minimal		**More than minimal**		High			
	X							
Initial study Approval information	**Approved**	X	**Study completion date**	31/12/2023	**Certificate expiry Date**	04/07/2024		
	Approval date	05/07/2023						
Study renewal approval information	**Renewal date**				**End date**			
Study amendment approval information	**Amendment date**							
Study extension approval information	**Extension date**				**End date**			
Signature of Chairperson								
Signing date	**05/07/2023**							
Secretariat Contact Details	Name of contact officers		**Babazile Shongwe**					
	Email address		es@ehhrrb.org.sz					
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ESWATINI HEALTH & HUMAN RESEARCH REVIEW BOARD
06 JUL 2023
P.O. BOX 5, MBABANE, H250
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ESWATINI

Appendix 5: Ministry of Health permission letter

Telegrams:
Telex:
Tele: (+268 404 2431)
Fax: (+268 404 2092)

Ministry of Health
P.O. Box 5
Mbabane
Eswatini

THE KINGDOM OF ESWATINI

20th April 2022

Our Ref: MH/738

Musawenkhosi Mzamo Mbuli
P O Box 8831
Mbabane

Dear Musawenkhosi

RE: PERMISSION TO USE ESWATINI HEALTH DATA IN THE MASTER OF SCIENCE IN EPIDEMIOLOGY TRAINING UNDER THE SOUTH AFRICAN FIELD EPIDEMIOLOGY TRAINING PROGRAM (SAFETP) BASED AT THE UNIVERSIRTY OF THE WITWATERSRAND, SOUTH AFRICA.

Eswatini like other developing countries bear the brunt of communicable diseases (CDs) which has resulted in increased morbidity and mortality. Surveillance data also indicates that non-communicable diseases (NCDs) are increasing particularly on the younger population. The emergence COVID-19 and other CDs like leprosy further exacerbates the situation.

This therefore calls for in-depth epidemiological analysis to fully understand the risk factors and predictors for infection. The International Health Regulations (IHR 2005), Joint External Evaluation (JEE) indicated the need for Field Epidemiology Training Program to strengthen epidemiological expertise. In 2020, the NICD-SAFETP partnered with the Eswatini Ministry of Health to train heath workers towards attainment of a Master of science in Epidemiology tenable at the University of Pretoria and the University of the Witwatersrand in South Africa.

It is against this background that I grant you permission to use and analyse the ministry's datasets for academic purposes. We hope that findings from your work will assist the country in coming up with recommendations aimed at improving health outcomes.

Sincerely yours

DR SIMON M. ZWANE
PRINCIPAL SECRETARY

MINISTRY OF HEALTH
PRINCIPAL SECRETARY'S OFFICE
22 APR 2022
P.O. BOX 5
MBABANE H100
ESWATINI