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COVID-19 BREAKTHROUGH OUTCOMES AMONG HEALTH WORKERS IN MARONDERA DISTRICT, MASHONALAND EAST PROVINCE, ZIMBABWE 2021

BY

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Abstract

Coronavirus disease (COVID-19) was pronounced a global pandemic after it spread across the globe causing a lot of health and economic burden. This pandemic had an impact on health workers as they were on the frontline fighting against the disease. Several vaccines were produced to lessen the burden of COVID-19. However, breakthrough infections among the health workers were recorded. Health workers in Marondera District, Zimbabwe were also affected by these breakthrough infections. Breakthrough infections amongst health workers challenged the efforts towards reducing the burden of the disease in the district. In Marondera District, outcomes for breakthrough infections among health care workers had not been studied before. The aim of the study was to determine the outcomes of COVID-19 breakthrough infections and the factors associated with severe illness amongst health care professionals working in Marondera District. The study used a retrospective cohort design using secondary data set analysis. The study population comprised of the records of all the health workers in Marondera District who tested positive to SARS-CoV-2 between 1 April and 31 December 2021 and total population sampling was used. Three hundred and four (304) records were used for the study. The researcher used the line list of COVID-19 cases in the district together with vaccination and admission records. The data was analysed using Epi Info version 7.2.2. Univariate, bivariate and multivariate analysis of the data was done. The unvaccinated were 144 (47.4%) whilst the vaccinated (breakthrough infections) were 160 (52.6%). Most of the individuals with breakthrough infections (86.9%) and unvaccinated (88.9%) health workers were aged below 50 years. The median age for health workers with breakthrough infections was 38 years. Vaccinated health workers who were involved in clinical work were 68.1% and the unvaccinated who were involved in clinical work were 54.2%. Amongst health workers with breakthrough infections 30.6% had comorbidities while 32.6% of those unvaccinated had comorbidities. Among the breakthrough infections, 26.3% had hypertension and 7.5% had diabetes and among the unvaccinated 23.6% had hypertension and 4.2% had diabetes. 35.0% of the breakthrough infections were asymptomatic while 8.3% of those unvaccinated were asymptomatic. Among health workers with breakthrough infections, 6.2% were hospitalised and 1.9% were admitted in the ICU. All of the breakthrough infections recovered and only one death was recorded amongst the unvaccinated. Factors significantly associated with severe disease were; having comorbidities (RR=4.2; 95% CI: 2.3-7.6; $p<0.01$), hypertension (RR=2.6; 95% CI: 1.5- 4.5; $p<0.01$), diabetes (RR=5.1; 95% CI: 3.0- 8.7; $p<0.01$) and having five more or symptoms at baseline (RR= 50.4; 95% CI: 7.0- 362.2; $p<0.01$). Being vaccinated was protective against severe disease (RR=0.2; 95% CI: 0.1- 0.5; $p<0.01$) including being aged below 50 years (RR= 0.26; 95% CI: 0.2- 0.5; $p<0.01$). From the findings of the study, it can be concluded COVID-19 vaccines were protective against severe illness. The researcher recommends that all health workers should receive a COVID-19 vaccine so as to prevent severe illness after infection.

Key words: breakthrough, COVID-19, health workers, severity

Declaration Page

I declare that this dissertation is my original work except where sources have been cited and acknowledged. The work has never been submitted, nor will it be submitted to another university for the award of a degree.

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Dedication

The dissertation is in honour of my two sons, Munenyasha Sean and Kunashe Daryl Nyabiko who have been my constant source of motivation.

List of acronyms and abbreviations

Ag-RDTs	Antigen detecting rapid diagnostic test
AUREC	Africa University Research Ethics Committee
CDC	Centres for Disease Control and Prevention
COVID-19	Corona virus disease of 2019
ICU	Intensive care unit
IgG	Immunoglobulin G
MOHCC	Ministry of health and Child Care
mRNA	Messenger ribonucleic acid
PCR	Polymerase Chain Reaction
PMD	Provincial Medical Director
RDT	Rapid Diagnostic Test
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
UK	United Kingdom
WHO	World Health Organisation

Definition of terms

COVID-19 breakthrough infections	The detection of SARS-CoV-2 from a person at least 14 days after they have completed all recommended doses of a vaccine.
Presence of SARS-COV-2 infection	Nasopharyngeal swab positive to SARS-CoV-2 by Ag-RDT or PCR.
Severe disease	Illness requiring hospitalisation, or with high likelihood to result in death

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CHAPTER 1 INTRODUCTION

1.1 Introduction

Several cases of a new respiratory illness were reported in Wuhan City, China in December 2019 (Dzinamarira *et al.,* 2020). The patients presented with pneumonia symptoms and initially the media called the disease Wuhan pneumonia because of the location (Liu, Kuo, & Shih, 2020). After extensive investigation and genome sequencing, it was determined in January 2020 that the illness was caused by a novel coronavirus known as SARS-CoV-2, and the condition was given the name corona virus disease of 2019, C0VID-19 (Uddin *et al*., 2020; Liu *et al*., 2020).

The virus is spread via droplets inhaled when people talk, cough, or sneeze, and by fomite mediated transmission when people touch their faces, noses, and eyes with hands that have contacted contaminated surfaces (Uddin *et al*., 2020). Everyone is susceptible to SARS-CoV-2 with the elderly and those with underlying diseases more likely to have severe illness (Li, Liu, Yu, Tang, & Tang, 2020). COVID-19 has a clinical spectrum of mild to moderate disease (80%), severe disease (15%), and critical illness (5%) with an overall case fatality rate (CFR) of 0.5–2.8% with much higher rates (3.7–14.8%) in those aged above eighty years (Balkhair, 2020).

Since the COVID-19 was identified in China it spread across the globe rapidly, respecting no boarders. On 11 March 2020, it was stated a global pandemic and upon that declaration 114 countries had recorded more than 100,000 cases and 4,291 people had lost their lives due to the disease (World Health Organisation [WHO], 2020a). As at date, 10 September 2021 there were 223,022,538 confirmed cases of COVID-19, including 4,602,882 deaths, reported to WHO (WHO, 2021a) and there

were 126,056 confirmed cases of COVID-19 with 4,521 deaths, reported to WHO in Zimbabwe (WHO, 2021b).

To combat COVID-19, a number of vaccines have been developed. Vaccines offer individual protection and herd immunity. It has been beneficial to introduce herd immunity by mass immunization through the prevention of the spread of infectious diseases among vulnerable population groups (Frederiksen, Zhang, Foged, & Thakur, 2020; Brosh-Nissimov, *et al.,* 2021).

Health workers are people engaged in the conservation, promotion and enhancement of the health of the people (Dal Poz, Kinfu, Dräger and Kunjumen, 2007). They have been the mainstay in the fight against COVID-19. They are among the people with the greatest likelihood of contracting COVID-19 due to occupational exposure (WHO, 2021c). The prevalence of COVID-19 among health workers in a meta-analysis study by Gómez-Ochoa *et al.* (2021) ranged from 0.4% to 57.06%. According to the report on 27 August 2021, 5 366 health workers in Zimbabwe had contracted COVID-19 contributing to 4.3% of the total number of cases in the country (Ministry of Health and Child Care [MOHCC], 2021a). COVID-19 vaccines have been prioritised for health workers. However, breakthrough infections among this population have been reported.

The researcher carried out a retrospective cohort design on health workers who tested positive to SARS-CoV-2 in Marondera District. This aim of the study was to establish the outcomes and factors associated with severe breakthrough infections among health workers in Marondera District, Mashonaland Province, Zimbabwe 2021. The results of the study helped to identify health care workers at higher risk of

severe breakthrough infections so that appropriate monitoring can be done to prevent severe disease.

1.2 Background to the Study

On March 20, 2020, Zimbabwe reported its initial COVID-19 case as an imported case from a Victoria Falls resident who had returned from the United Kingdom (UK) (Murewanhema *et al.,* 2020). In reaction to COVID-19 cases recorded in the country in the country, the Government of Zimbabwe on March 30, 2020 introduced public health measures to control the spread of the disease in the country which included several lockdowns (Dzobo, Chitungo, and Dzinamarira, 2020). However, despite the measures set up the disease managed to spread in the country. As at date 10 September 2021 were 126,056 confirmed cases of COVID-19 with 4,521 deaths, reported to WHO in Zimbabwe (WHO, 2021b). Given the high contagiousness of SARS-CoV-2, various vaccinations have been developed worldwide and are the most essential public health tool for reducing the burden from COVID-19 (Amanat, & Krammer, 2020).

Zimbabwe rolled out its vaccination programme on 18 February 2021 and the vaccines were prioritised for frontline workers, the elderly and those with underlying conditions (Dzinamarira *et al.*, 2021). Vaccination was then expanded to include all those aged above 12 years as more vaccines had been procured. As at date 10 September 2021, 2,824,596 individuals had been given the first dose and 1,831,231 had received the second dose (MOHCC, 2021b). Vaccines being rolled out in Zimbabwe include the Sinovac-CoronaVac-19 and the Sinopharm COVID-19 vaccines.

Mashonaland East Province, Zimbabwe has not been spared from the scourge of COVID-19. As at date 6 September 2021 the COVID-19 cases reported in the province since the beginning of the pandemic were 13212. A total of 333 deaths had been reported with a CFR of 2.5%. The province launched the COVID-19 vaccine programme on the 22nd of February 2021. As at date 6 September 2021 a cumulative figure of 277,654 people had been given the first dose and 179, 872 had received the second dose of COVID-19 vaccination giving a 17% coverage in the province (MOHCC, 2021c).

Marondera District was the mostly affected district in Mashonaland East Province with 3388 cases reported as at date 6 September 2021 with 6.1% of these cases being health workers. However, there were reports of several breakthrough infections among health care workers who received the vaccines. As at date 6 September 2021, 34.9% of the COVID-19 total cases recorded in the district were among health workers were vaccinated against COVID-19 (MOHCC, 2021c).

1.3 Statement of the Problem

Healthcare workers form the backbone towards COVID-19 control and response efforts as they are on the frontline providing services for the prevention, identification, management of COVID-19 cases and continuity of essential healthcare. As at date 6 September 2021, 6.1% of Marondera district cases were among health workers. Thus, 22.6% of the total health workers in the district had been affected by the disease. The disease had been a huge global public health burden highlighting the necessity of a vaccine. However, despite the high efficacy levels of the vaccines developed, there were several breakthrough infections recorded. 34.9% of the total cases recorded in Marondera District amongst health

workers were breakthrough infections. Severe illness was reported in 6.8% of those with breakthrough infections. Breakthrough infections among health workers challenge the efforts towards reducing the burden of the disease in the district and on the healthcare system. The clinical manifestations and outcomes among health care workers with breakthrough infections compared with similar controls had not been studied. Thus, it was against this backdrop that we set to carry out this study.

1.4 Research Objectives

1.4.1 Broad objective

To determine outcomes of COVID-19 breakthrough infections and the factors associated with severe illness among health care workers in Marondera District, 2021

1.4.2 Specific Objectives

1. To determine the socio demographic characteristics of health workers with COVID-19 breakthrough infections in Marondera District 2021.
2. To identify the clinical characteristics of health workers with COVID-19 breakthrough infections in Marondera District, 2021
3. To assess the clinical presentation and outcomes of health workers with COVID-19 breakthrough infections in Marondera District, 2021
4. To analyse factors associated with severe disease in health workers with COVID-19 breakthrough infections in Marondera District, 2021

1.5 Research Questions

1. Which socio demographic characteristics were associated with health workers with COVID-19 breakthrough infections in Marondera District 2021?

2. What were the clinical characteristics of health workers with COVID-19 breakthrough infections in Marondera District, 2021?
3. How did health workers with COVID-19 breakthrough infections in Marondera District, 2021 present clinically?
4. Which factors were associated with severe disease in health workers with COVID-19 breakthrough infections in Marondera District, 2021?

1.6 Assumptions

The researcher made an assumption that the records that were going to be used were available and had complete information on the variables collected. The researcher also assumed that the individuals who got vaccinated developed immunity to the coronavirus. The researcher also assumed that the unvaccinated individuals had no prior infection resulting in some immunity towards the virus.

1.7 Significance of the Study

The COVID-19 pandemic has been a major burden to the health system and greatly affected the economy of the country. COVID-19 vaccines have been important in alleviating the burden from the pandemic. However, having breakthrough infections might limit the progress towards reduction of the burden. The study helped to evaluate outcomes associated with breakthrough infections among health care workers in Marondera District and determine those at the greatest risk of severe breakthrough infections, hospitalisation and death since health workers are prime to the fight against the pandemic. In order to fully comprehend the vaccine's benefits, it's also necessary to evaluate the severity of the sickness in those who get a breakthrough infection. There was paucity of such information in the country.

Findings from the study will help the MOHCC to promote targeted interventions and ensure appropriate monitoring of vulnerable populations among health workers in order to prevent severe disease and improve outcomes. Thus, the results of the study will help to decrease the burden of the pandemic on the health system through retaining vaccinated health workers. The findings of the study contribute to literature on COVID-19 breakthrough infections in Zimbabwe. Future researchers may explore on other areas associated with breakthrough infections and immunity against the different SARS-CoV-2 variants.

1.8 Delimitation of the Study

The current study was limited to the records of health workers who had tested positive to SARS CoV-2 in Marondera District, 2021 as the researcher only had access to data from Marondera District. Thus the study results might not be representative of the entire province and country. The study population was limited to records of health workers on the district's line list who were recorded from public health facilities, COVID-19 cases from private health facilities might have not been included. Different variants of SARS CoV-2 virus have been identified however, the study did not assess the variants associated with the breakthrough infections. The study included those who were tested by PCR and Ag-RDTs however, some cases might have been missed by using the Ag-RDTs for testing as Ag-RDT's are mostly accurate when the viral load is still high and a lot of false negatives might be reported in patients who get tested after the acute stage of the disease when the viral load decreases (Peeling, Olliaro, Boeras, & Fongwen, 2021).

1.9 Limitations of the study

The researcher used secondary data and had no control over the contents of the data. Asymptomatic cases who were not tested were missed from the study.

1.10 Chapter summary

COVID-19 was declared a global pandemic by the WHO on 11 March 2020. It has a clinical spectrum of mild disease to severe and critical illness. Health workers are the pillar to the fight against COVID-19. Health workers in Marondera District, Mashonaland East Province, Zimbabwe were not spared from the scourge of COVID-19. On February 22, 2021, the district began its COVID-19 vaccination programme however, health workers with breakthrough infections were reported in the district. The broad objective of this study was to determine the outcomes of COVID-19 breakthrough infections and their associated factors among health workers in Marondera District as breakthrough infections challenge the efforts towards reducing the burden of the disease. Clinical presentation and outcomes for breakthrough infections compared with similar controls among health workers in the district had not been studied. Findings obtained from the study will promote targeted interventions on vulnerable health workers in order to prevent severe disease. The study results will also contribute to literature on COVID-19 breakthrough infections in Zimbabwe in future researches. The study was limited to the records of health workers who tested positive to SARS CoV-2 in Marondera District, 2021 however, asymptomatic cases who were not tested might have been omitted from the study. Since the researcher was using secondary data, she had no control over the contents of the data.

CHAPTER 2 REVIEW OF RELATED LITERATURE

2.1 Introduction

This chapter gives a review of related literature. Reviewing literature gave an extensive understanding of what was done in accordance with COVID-19 breakthrough infections outcomes. The objectives guided the literature review. Similar studies were reviewed in order to observing similarities and distinctions in the findings of these studies in order to come up with inferences to inform this study. The literature review focused on clinical features of COVID-19, vaccine efficacy and effectiveness, breakthrough infections, approaches used by other researchers, outcomes of breakthrough infections. The section also looked at the conceptual framework used.

2.2 Conceptual Framework

Conceptual frameworks are part of the crucial aspects of a research. According to Onsaloo and Grant (2016) they serve as a blue print to the research and guide the research process. The conceptual framework used for this research is shown below (Figure 2.1). It shows the socio-demographic characteristics and clinical characteristics associated with COVID-19 breakthrough infections. It also shows the clinical course that follows when one is diagnosed with a breakthrough infection, some will be asymptomatic while some show symptoms and some might require hospitalisation due to severe disease. Ultimately individuals diagnosed with breakthrough infections either recover or die from the disease.

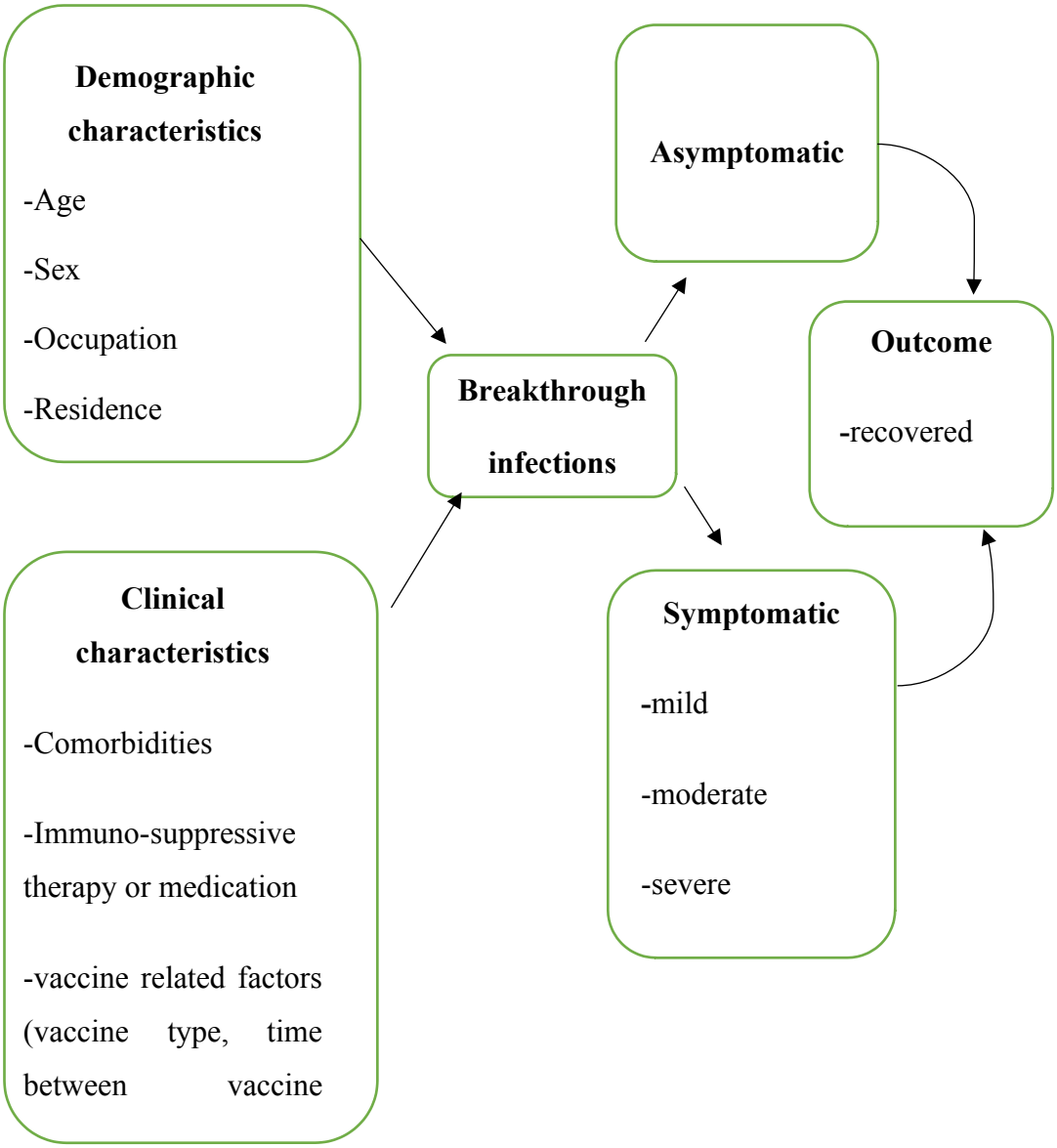


Figure 1.1: Conceptual framework

2.3 Relevance of the Conceptual Framework to the Study

A conceptual framework provides explicitness to the research process and gives direction to the research design (Leshem and Trafford, 2007). The conceptual framework was adapted from a study by Van Goethem *et al*. (2021). It helped to identify research variables and also defined the relationship among the different variables. Demographic, clinical and outcome variables were identified from the

framework. The conceptual framework guided the researcher on what to focus on during the study.

2.4 Vaccine efficacy and effectiveness

SARS-CoV-2 is highly contagious and has presented a great burden globally. Because of the COVID-19 impact worldwide several vaccines were produced. SARS-CoV-2 vaccines have been considered to be the most effective action in the battle against the COVID-19 pandemic. Several studies demonstrated their effectiveness in decreasing new infections, severity of illness and death (Dzinamarira *et al*., 2022). Understanding how effectively vaccines work is important to a number of professionals including public health epidemiologists, clinicians, policy makers and researchers (Crowcroft and Klein, 2018). Although the vaccines are an effective vital tool, there is none that is 100% effective in the prevention of COVID-19 illness (Vasireddy, Vanaparthy, Mohan, Malayala and Atluri, 2021).

Marondera District public health facilities have been rolling out the Sinovac and Sinopharm vaccines from China. The Sinovac-CoronaVac-19 is manufactured by a Beijing based pharmaceutical company (WHO, 2021d), while the Sinopharm vaccine is developed by Beijing Bio-Institute of Biological Products Co Ltd (WHO, 2021f). Both vaccines are suitable for low resource settings as they have easy storage requirements. The vaccines have a two-dose schedule.

According to WHO (2021e) the efficacy of the Sinopharm vaccine against symptomatic disease and hospitalisation was about 79%. According to Mallapathy (2021) the Sinopharm vaccine's effectiveness in preventing infection after 2

vaccination doses was 79-86% and it was 100% effective in averting deaths among immunised individuals.

According to Halim, Halim and Tjhin (2021) they found that the Sinovac vaccine was 100% effective in preventing moderate infections and 77.9% of mild cases. However, according to WHO (2021d) efficacy results of the Sinovac vaccine revealed that the vaccine prevented symptomatic illness in 51% of vaccinated people and prevented severe disease in 100% of those studied.

In Brazil, Sinovac (2021) reported that the efficacy against hospitalisation, severe illness and death was 100% and the efficacy against symptomatic cases who reported medical treatment was 83.7%. Sinovac (2021) also reported that efficacy against symptomatic COVID-19 cases was 91.25% in Turkey. However, in another study done in Brazil, adjusted effectiveness against symptomatic COVID-19 was 46.8% and vaccine effectiveness against symptomatic COVID-19 was seen to deteriorate with increasing age at 14 or more days after the second dose (Rannzani *et al.*, 2021).

Studies on other vaccines have been done to determine the efficacy of the vaccines. For example a study by Polack *et al*. (2021) showed that the BNT162b2 vaccine was 95% effective in the prevention of COVID-19 and vaccine efficacy was observed across different subgroups defined by sex, age, body mass index, ethnicity, race, and the presence of comorbidities. In a study by Glatman-Freedman, Bromberg, Dichtiar, Hershkovitz and Keinan-Boker (2021) they found out that the BNT162b2 vaccine was effective in the prevention of new cases and effectiveness developed more slowly among those aged 80 years and older. They also found out that the vaccine reduced complications and death in breakthrough cases. The moderna vaccine (mRNA-1273) also showed a high efficacy of 94.1% (Baden *et al*., 2021). However,

new SARS-CoV-2 mutations may have an impact on vaccine efficacy (Prévost and Finzi, 2021).

There are limited studies on vaccine effectiveness and efficacy in Africa. The uneven development of clinical facilities in Africa has resulted in a lack of efficacy research. (Makoni, 2021). However, most of the published work on vaccine efficacy and effectiveness in Africa were done in South Africa where they focused on the efficacy of different vaccines against the SARS-CoV-2 variants that were identified in the country. There are no published articles done for vaccine efficacy and effectiveness in Zimbabwe.

In a study by Thomas *et al.* (2021) to evaluate the BNT162b2 vaccine efficacy against COVID-19 in South Africa after the second dose, it was reported that the vaccine had 91.1% efficacy against COVID-19 and had 97% efficacy against severe disease. However, due to diminishing immunity, Thomas *et al*. (2021) observed that there was a gradual deterioration in efficacy to 83.7% from 4 to 6 months after receiving the second dose.

Madhi *et al.* (2021) did a study to determine the efficacy of the COVID-19 vaccine (ChAdOx1 nCoV-190 against a SARS-CoV-2 variant (B.1.351) and they found that the vaccine efficacy was 21.9% for mild to moderate COVID-19 at least 14 days after the second dose. There were no cases of severe disease which required hospitalisation in the study.

Efficacy studies are also needed in Africa as Africans represent a genetically diverse population living in distinct climatic conditions, and there are several comorbidities,

such as tuberculosis and human immunodeficiency virus (HIV), that are more prevalent among Africans.

Despite the efficacy of the vaccines produced, breakthrough infections among people who have received the full vaccine doses have been reported.

2.5 The definition of SARS-CoV-2 breakthrough infections

Vaccine breakthrough infections are a subject of concern however, in the real world setting adequate data on the infections are unavailable (Tyagi *et al*., 2021). Vaccine breakthrough infections occur in individuals who have been fully vaccinated against a disease. Several breakthrough infections for different diseases have been reported after receiving a vaccine. Some of the diseases where breakthrough infections have been reported include invasive pneumococcal disease (Adebanjo *et al.*, 2020), varicella (Leung, Broder & Marin, 2017) and rotavirus (Adlhoch *et al.*, 2013).

According to CDC (2021a) a COVID-19 vaccine breakthrough infection is defined as the identification of SARS-CoV-2 from a person at least 14 days after they have completed all doses of a vaccine. According to clinical data, about 2-3 days after receiving the first dose, partial protection against symptomatic infection begins and receiving all the doses will give optimal protection against COVID-19 (Barrett *et al*., 2021). The study by Glatman-Freedman *et al*. (2021) showed that high level of protection was provided after receiving the full vaccine doses. Because no vaccine is guaranteed to be 100% effective, breakthrough infections are expected. There is shortage of published studies on breakthrough infections in Zimbabwe and Africa at large.

After getting both doses of the vaccine, immunocompromised people may not always develop sufficient levels of protection (CDC, 2021b). Older age groups also have a greater risk of having breakthrough infections than those younger (WHO, 2021f; Butt, Khan, *et al*., 2021). Factors which may also contribute to SARS-CoV-2 breakthrough infections include waning immunity and immune escape variants (Shrotri *et al*., 2021). Vaccinated people in contact with confirmed cases have an increased likelihood of breakthrough infections (Alishaq *et al*., 2021) and these include health workers who are constantly in contact with COVID-19 patients. Vaccinated populations should continue practicing preventative measures which include masking, head hygiene and practicing social distancing. According to CDC (2021c) unvaccinated people have 6.1 times greater risk of testing positive for COVID-19 compared to the individuals fully vaccinated.

In this research the researcher adapted the CDC definition of COVID-19 breakthrough infections. The researcher carried out the study on health workers who had a positive test of SARS-CoV-2, 14 or more days after receiving the full doses of the vaccines given in Marondera District.

2.6 Clinical features of COVID-19

The symptoms of COVID-19 range from asymptomatic to death. Based on the cases studied by the WHO in China signs and symptoms of COVID-19 included fever, sore throat, dry cough, sputum production, fatigue, shortness of breath, nasal congestion, headache, nausea or vomiting, diarrhea, myalgia or arthralgia, chills and conjunctival congestion (WHO, 2020b). In their review, Jiang *et al.* (2020) also recorded the same symptoms. According to WHO (2020d) approximately 80% of the cases studied had mild to moderate disease, 13.8% had severe disease and 6.1% had

critical illness. Oran and Topol (2020) reported that asymptomatic cases were around 40% to 45% of the infections.

A meta-analysis of COVID-19 patients in Africa reported that fever, cough, headache, rhinorrhea, breathing problems and diarrhea as the most prevalent signs and common symptoms observed (Olumade and Uzairue, 2021).

The most frequently observed complications in people who had COVID-19 infection included sepsis, acute respiratory distress syndrome, respiratory failure, heart failure and septic shock (Zhou *et al.,* 2020). According to Harapan and Yoo (2021) complications reported in COVID-19 patients included cerebrovascular disease (stroke, cerebral venous thrombosis), Guillain–Barré syndrome, epilepsy, seizures, acute myelitis, meningitis, encephalitis, meningoencephalitis, Miller Fisher syndrome and posterior reversible encephalopathy syndrome.

2.6.1 Clinical features of COVID-19 breakthrough infections

The presentation of COVID-19 in people who were vaccinated are similar to those in unvaccinated individuals however, it might differ in severity. In Bergwerk *et al.* (2021) study 67% of the health workers who had breakthrough infections reported mild symptoms and the rest were asymptomatic. In the study upper respiratory congestion was reported by most (36%) of the patients followed by myalgia, anosmia, ageusia and fever. In the same study 31% of the individuals with breakthrough infections reported residual symptoms 2 weeks after the diagnosis was made and 19% reported having symptoms after 6 weeks of their diagnosis. These symptoms included weakness, persistent cough, loss of smell and dyspnea.

Tyagi *et al.* (2021) in their study reported that symptomatic infections in the individuals with breakthrough infections occurred in only 13.3% of the cases. All of

the symptomatic cases had fever. Other symptoms reported included cough, sore throat, diarrhea, ageusia, anosmia and pneumonia in one case who was hospitalised. In the study symptoms only lasted for 3-14 days. Only one health worker out of 15 that were studied by Tygi *et al.* (2021) had pneumonia and was hospitalised.

In the study by Gupta *et al.* (2021) symptoms were most reported among those with comorbidities. Symptoms reported included fever (the most consistent presentation), body ache, sore throat, cough, loss of smell and taste, ocular irritation, headache, nausea and diarrhea. 71% of the cases reported were symptomatic. Niyas, and Arjun, (2021) also reported that fever was reported by most of the participants followed by sore throat and myalgia.

In a study by Maroof *et al*. (2021) 94.4% of the health workers who were diagnosed with breakthrough infections were asymptomatic and mild. They also showed that those who were hospitalised did not need supplemental mechanical support. The study by Teran *et al*. (2021) showed that 64% of the nursing facility workers and residents were asymptomatic. Niyas and Arjun (2021) reported that only 6.4% of the participants were asymptomatic and most individuals (57.4%) presented with fever.

2.7 Demographic characteristics of COVID-19 breakthrough cases

In a study by Liu *et al*. (2021) on COVID-19 breakthrough infections, they reported a greater incidence of infection in males than females who were vaccinated. They however, there was no significant difference in incidence rate associated with other demographic variables. In the study by Maroof *et al*. (2021) the median age for health workers with breakthrough infections was 38.8 years. In the study more males (69%) developed breakthrough infections than females. The study by Angel et al.

(2021) however, showed more females (65.2%) with breakthrough infections than males. The mean age of their participants was 44.3 years. Teran *et al*. (2021) also showed more females (68.2%) than males with breakthrough infections. Butt, Khan et al (2021) reported that individuals who were black had less risk of infection than the whites however, the reason for this finding was unclear.

Bergwerk *et al*. (2021) showed that most of the breakthrough infections occurred in clinical workers with 46% being from the nursing department. In their study the majority of the health workers were female (64%) and the mean age of those with breakthrough infections was 42 years. Maroof *et al.* (2021) also showed that 36.3% of the breakthrough infections occurred in workers who were not directly involved with the patients. Health workers who work more directly with patients are more susceptible to the virus than those who don't.

Maroof *et al*. (2021) carried out a cohort study among the health workers who had tested positive to a PCR test after receiving 2 doses of Sinopharm vaccine in the military institutes of Pakistan. The median duration of occurrence of the infection reported was 36.5 days. Their results showed that 37.1% had a close contact with COVID-19 cases, 94.4% were asymptomatic or mild cases and there was statistically no significant association between ages, gender and job category with COVID-19 breakthrough infections

2.8 Clinical characteristics of COVID-19 breakthrough cases

Compromised immune systems affect the body's reaction to the COVID-19 virus. In the study by Liu *et al*. (2021) more COVID-19 breakthrough infections were

reported in those who had compromised immune systems, active tumors, history of organ transplant and use of immune suppressant drugs.

Several studies have highlighted the association between individuals with comorbidities and COVID-19 breakthrough infections. Butt, Nafady-Hego *et al*. (2021) in their study reported that at least one comorbid condition was reported in 61.2% of the people with breakthrough infections. The study by Lee *et al*. (2022) reported that hypertension, diabetes and cardiovascular disease were associated with breakthrough infections.

According to Wang *et al.* (2021) persons with substance use disorder had a higher possibility of breakthrough infections as they had high prevalence of comorbidities. Butt, Khan *et al*. (2021) reported that those who had multiple comorbidities were at risk of breakthrough infections.

Time between vaccination and infection is important as a loss in vaccine effectiveness after 6 months has been reported (Moreno-Perez *et al.,* 2022). 88.7% of the vaccinated health care professionals in the study by Maroof *et al.* (2021) developed infection within 3 months of receipt of the second dosage of the vaccine while 11.3% had the infection more than three months after receiving the vaccine. Liu *et al*. (2021) and Mizrahi *et al*. (2021) conducted analyses of effectiveness of vaccines over time and they found that the occurence and severity of breakthrough infections increased with time from the period of receiving the vaccine. Waning of immunity with time after 2 doses of the vaccines has been reported and the CDC recommends that people get a booster dose of the vaccines after 5 months of completing the primary doses (CDC, 2022).

2.9 Outcomes of breakthrough SARS-CoV-2 infections

Vaccines have a significant impact on reducing the incidence, severity and mortality among vulnerable people at risk of COVID-19 infection (Moghadas *et al.,* 2021). Evidence from several researches done shows that the vaccines prevent the recipients from getting severe sickness and death and recommends that people get vaccinated. According to Baltas *et al*. (2021), their study revealed that being vaccinated was associated with a relative risk reduction in mortality, hospital admission and the length of stay in hospital.

A study by Butt, Nafady *et al.* (2021) analysed the outcomes that presented with patients in Qatar with breakthrough infections after vaccination. In their study severe disease was defined as hospitalisation or death. They recorded severe disease in 10.5% of the vaccinated. The prevalence of severe disease was three times more in the unvaccinated individuals than in the vaccinated ones. In another study by Butt, Khan *et al.* (2021) having multiple comorbidities was significantly associated with severe illness.

The study by Maroof *et al*. (2021) showed that the health workers with break through infections did not experience any severe disease and there was no death reported. A similar study by Teran *et al*. (2021) found out that 64% of the patients had asymptomatic disease, while only 9% were hospitalised for COVID-19 related issues and only one person died. The study by Tyagi *et al* (2021) also showed that most of the health workers studied had mild disease**.** AlQantani *et al.* (2020) in their study also showed a notably higher percentage of individuals who were hospitalised, had intensive care admission and deaths in the unvaccinated people compared to the vaccinated. Findings from Glatman-Freedman *et al.* (2021) study also showed that

vaccination was effective in lowering hospitalisation, severe illness and death in SARS-CoV-2 breakthrough cases.

Tenforde *et al.* (2021) assessed the association between vaccination and COVID-19 disease severity and they found out that there was a lower likelihood of vaccination in those hospitalised with COVID-19. They also found out that among those hospitalised, breakthrough cases less commonly required intensive care admission and mechanical ventilation. In the study unvaccinated patients contributed to 91% of deaths and deaths occurred in 6.3% of those with breakthrough infections.

Contrary to the studies which reported low rates of severe illness was the study by Brosh-Nissimov *et al*. (2021) who found out that 61% of the cases had severe COVID-19 illness. They also recorded a high mortality rate of 22% in those with recorded breakthrough infections. Such high results were due to 96% of the patients having multiple comorbidities. According to Brosh-Nissimov *et al*. (2021) the severe illness recorded and including the deaths might have been due to the comorbidities reducing vaccine effectiveness or the risk of aggravation of comorbidities after breakthrough infections or both. Also contrary to the other results were the results from Butt, Yan, *et al.* (2021) where they found out that there was no association between vaccination and reduced risk of severe illness or death in one of their matched groups.

2.10 Factors associated with severe COVID-19 illness

COVID-19 has a clinical spectrum of mild to critical illness or death with an overall CFR of 0.5–2.8% (Balkhair, 2020). The risk of one contracting the virus (increased in health workers) and the risk of deteriorating after infection (increased in

advancing age) largely constitute the possibility of severe illness (Leshem, Nelson, & Lopman, 2021). In a study by Li, Huang, *et al*. (2021) they found that factors associated with increased severity of disease included older age, male sex, hypertension, diabetes, immunosuppression and malignancy. They also found that cases who had severe gastrointestinal symptoms and respiratory symptoms had increased risk of severe disease and those who presented with end-organ damage and pneumonia were associated with death (Li, Huang, *et al*., 2021).

In a research by Butt, Yan, *et al.* (2021) they found that among those who were vaccinated, age and anaemia were statistically associated with severe COVID-19 disease or death. Butt, Nafady-Hego *et al*. (2021) also found that increasing age together with being symptomatic at baseline were associated with severe COVID-19 illness and death. Scobie *et al.* (2021) also showed increased hospitalisation for individuals 65 years and older than did those who were in the younger age groups. Contrary to this, the study by Brosh-Nissimov *et al*. (2021) showed no statistically significant risk factors between the compared groups however, a higher viral load was associated with poor outcome.

Leshem, Nelson, & Lopman, (2021) in their study found out that severe outcomes were associated with being male, older age, having higher risk occupation like health workers, comorbidities and being an ex-smoker. Another study by Juthani *et al.* (2021) showed that 26% of the breakthrough cases had critical illness and the pre-existing comorbidities in these patients included cardiovascular disease, overweight, diabetes, lung disease, cancer and use of immunosuppressive treatment. Havers *et al*. (2001) reported that breakthrough cases admitted with COVID-19 had more

likelihood of having multiple underlying medical comorbidities and were long term care facility residents.

Parameswaran *et al*. (2022) in their study of severity of breakthrough infections among Indian doctors reported that factors associated with severe sickness were male sex, increasing age, presence of comorbidities and increased exposure to COVID-19 patients. They reported a significant association between day to day exposure to patients with COVID-19 and hospitalisation.

2.11 Chapter summary

In spite of COVID-19 vaccines being important in the control of the disease none is 100% effective in prevention of COVID-19 illness. Breakthrough infections occur in persons who are fully vaccinated against COVID-19. The clinical features of COVID-19 disease in vaccinated individuals are similar to those in unvaccinated individuals however, they might differ in severity Most of the studies showed that vaccines were effective in reducing severe disease. Factors which were associated with severe illness included increasing age, male sex, comorbidities and being a health worker. The literature review however, showed a gap in literature on COVID - 19 breakthrough infections in Zimbabwe**.**

CHAPTER 3 METHODOLOGY

3.1 Introduction

This chapter gives the methodology that was used for this study. It describes the study design, the study population, data collection procedure and data analysis used. Furthermore, the chapter contains the ethical considerations for the study.

3.2 The Research Design

A retrospective cohort design was used for the study using a secondary data set analysis. It was ideal for the study as a well-defined group of health workers (cohort) was used. The research design method was also ideal as the outcomes had already occurred (Setia, 2016). The exposed group comprised of the records of health care workers in Marondera District who had COVID-19 breakthrough infections and the unexposed group included records of unvaccinated health workers who had tested positive to SARS-CoV-2 in 2021.

3.3 Study Setting

The study was carried out in Marondera District. Marondera District is among the 9 districts in Mashonaland East Province and it is the provincial capital. It is found in region 2 of Zimbabwe and is surrounded by commercial farms making it a center of agricultural activities. It has 22 public health facilities which include two public hospitals, Marondera Provincial Hospital and Mahusekwa District Hospital. Three of the facilities are under the Zimbabwe Republic Police (ZRP) and the Zimbabwe Prisons and Correctional Services (ZPCS). The total number of health care workers

working in the public institutions of the district are 1219. The mother language used in the district is Shona. A map of Marondera District is shown below (Figure 3.1).

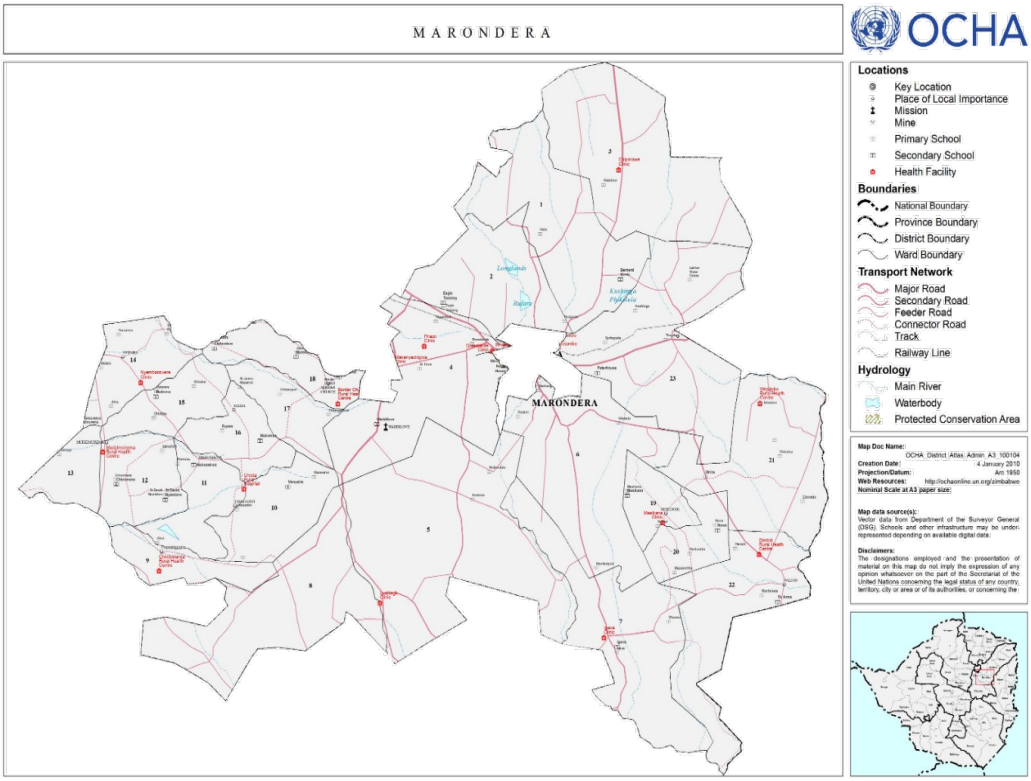


Figure 3.1: Marondera District map

3.4 Study Population

The study population comprised of the records of all the health care workers in Marondera District who tested positive to SARS-CoV-2 between 1 April and 31 December 2021.

Inclusion Criteria

- Records of Marondera District health workers who were tested positive to SARS-CoV-2 between 1 April and 31 December 2021.

Exclusion criteria

- Records of Marondera District health workers who tested negative to SARS-CoV-2
- Records of Marondera District health workers who had tested positive to SARS-CoV-2 after receiving 1 dose of the COVID-19 vaccine or after testing positive to SARS-CoV-2 less than 14 days from the date of the second dose.
- Records of Marondera District health workers who had a reinfection of SARS-CoV-2.

3.5 Sampling

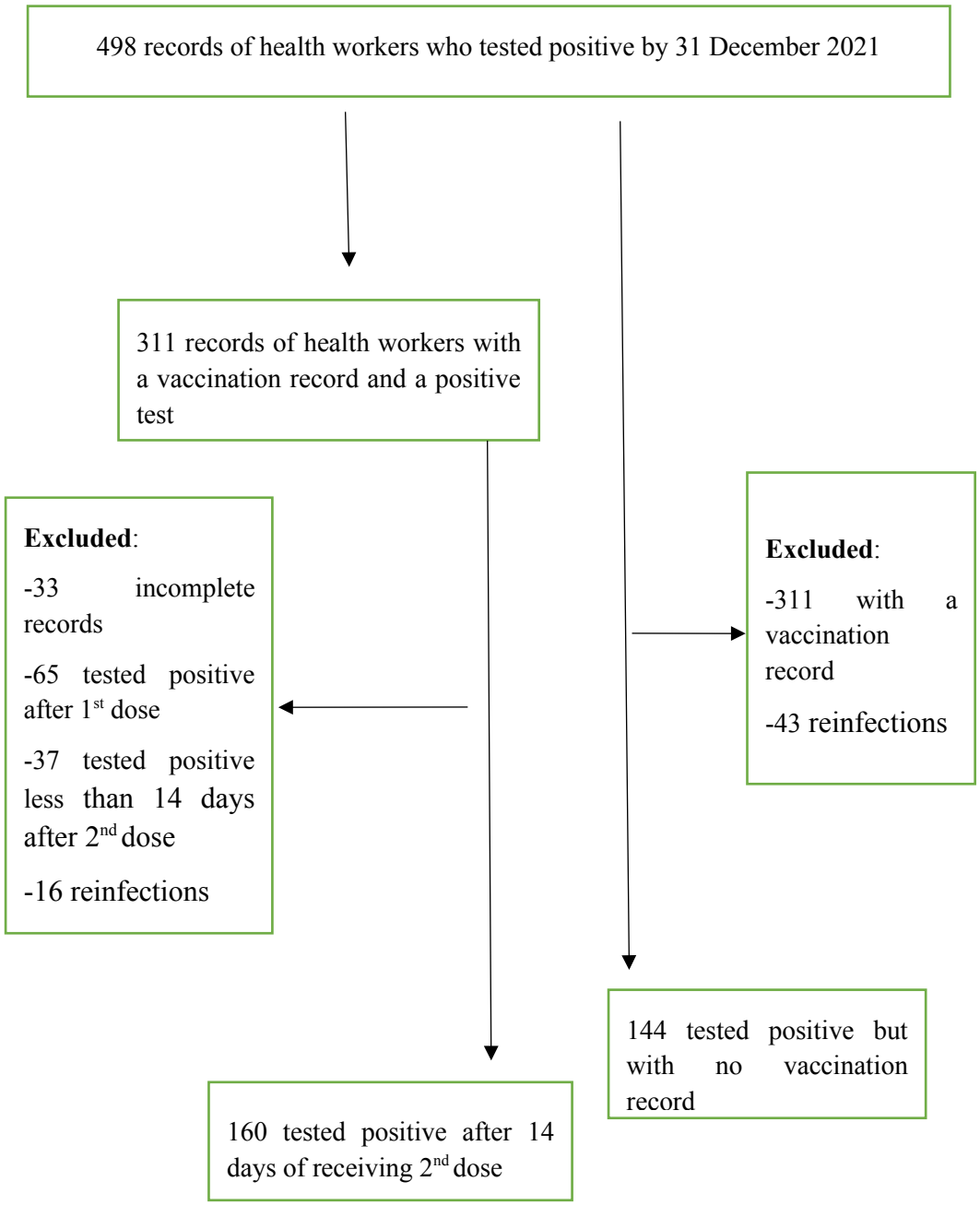
Total population sampling was used for the records of all the health workers (cohort) who tested positive to SARS-CoV-2 in Marondera District, 2021. A total sample of 304 records met the eligibility criteria for the study. Figure 3.2 below shows the consort diagram of the sample.

3.6 Data Collection Procedure

The researcher requested the line list for COVID-19 cases from the district health information officer (DHIO). The researcher then selected records of health workers who tested positive for SARS-COV-2 (which included those who were unvaccinated and breakthrough infections). The line lists were then used by the researcher to collect data on variables of concern in the study excluding the records which were ineligible for the study. The format of the line list is shown in appendix 1. The researcher also requested vaccination record books and admission records from the isolation wards to complement the missing data on the line list. The data was collected within a duration of a month. This allowed the researcher and the DHIO to

collect the necessary information from all the health facilities in the district using other records for the missing information on the line list. The researcher was responsible for the storage of data and ensured security of the data. Collected data was secured and locked up in a lockable steel cabinet to ensure security of the data.

Figure 3.2 Consort diagram of the sample



3.7 Variables

The socio-demographic variables collected included the age, sex, occupation and residence of the health workers. The researcher also collected data on the clinical factors which included comorbidities, type of vaccine and period between vaccination and positive test. Clinical course variables included symptoms experienced and hospitalisation. Outcome variables indicated whether the patient recovered or died. The primary outcome was severe disease which was defined as either hospitalisation or death from COVID-19 illness.

3.8 Analysis and Organization of Data

The data was exported from Microsoft excel to Epi Info version 7.2.2 where it was recoded and sorted to facilitate the analysis. The data was cleaned prior to analysis. Univariate, and bivariate and multivariate analysis of the data was done. Data was analysed for frequencies, means, risk ratios and confidence intervals at 95%. Data was presented in form of tables, charts and graphs. Baseline characteristics of health workers with breakthrough infections and without breakthrough infections was compared using chi-squared tests.

3.9 Ethical Consideration

Permission to carry out the study was sought from the Provincial Medical Director (PMD) for Mashonaland East (Appendix 4). Ethical approval was sought from the Africa University Research Ethics Committee (AUREC). Patients' names and surnames were not used during the study, unique identifiers (numbers) were used instead.

3.10 Chapter summary

The researcher used a retrospective cohort study design for the study. The exposed group was defined as records of health workers with breakthrough infections whilst the unexposed group consisted of records of unvaccinated health workers with confirmed infection. Total population sampling was used for all the records of health workers who tested positive to COVID-19 and 304 records were used in the study. The research used the data set of those who tested positive to SARS-CoV-2 (vaccinated and unvaccinated) in Marondera District. Epi info version 7.2.2 was used for data analysis. Permission was sought from the PMD Mashonaland East and ethical approval was be sought from AUREC.

CHAPTER 4 DATA PRESENTATION, ANALYSIS AND INTERPRETATION

4.1 Introduction

This chapter focuses on the results of the study. Descriptive statistics and analytical statistics are shown as tables, graphs and charts. Chi-square tests were used to measure the association between dependent and independent variables and negative binomial regression was used to analyse independent risk factors for severe illness.

4.2 Demographic characteristics of the health workers in Marondera District who tested positive to SAR-CoV-2

A total of 304 records of health workers who tested positive to SARS-CoV-2 were used for the study. The unvaccinated were 144 (47.4%) whilst those with SARS-CoV-2 breakthrough infections were 160 (52.6%). Most of the breakthrough infections (86.9%) and unvaccinated (88.9%) health workers were aged below 50years. The median age for the vaccinated health workers with breakthrough infections was older than the median age for the unvaccinated (38 years and 36 years respectively). There were more female in the breakthrough infections and unvaccinated groups (75.6% and 69.4% respectively). The unvaccinated group consisted of more health workers who were married (88.9%) and who resided in urban areas (81.9%) than the rural areas similar to those vaccinated who had more who were married and living in urban areas. Health workers with breakthrough infections who were involved in clinical work were more (68.1%) than the unvaccinated who were involved in clinical work (54.2%). The results are summarised in table 4.1 below.

Table 4.1: Demographic characteristics of health workers in Marondera District who tested positive to SARS-CoV-2 among the vaccinated and unvaccinated individuals

Variable	Unvaccinated (%) N=144	Vaccinated (%) N=160
Age (years)		
50 years and above	16 (11.1)	21 (13.1)
Below 50 years	128 (88.9)	139 (86.9)
Median age (Q_1, Q_3) years	36 (29.0,43.0)	38 (33.0, 44.0)
Sex		
Female	100 (69.4)	121 (75.6)
Male	44 (30.6)	39 (24.7)
Marital status		
Married	128 (88.9)	126 (78.7)
Not married	16 (11.1)	34 (21.3)
Residence		
Rural	26 (18.1)	41 (25.6)
Urban	118 (81.9)	119(74.4)
Occupation		
Non-clinical work	66 (45.8)	51 (31.9)
Clinical work	78 (54.2)	109 (68.1)

4.3 Clinical characteristics of the health workers in Marondera District who tested positive to SAR-CoV-2

Among those with breakthrough infections 30.6% had comorbidities while 32.6% of those unvaccinated had comorbidities. Of those with breakthrough infections, 26.3% had hypertension and 7.5% had diabetes and among the unvaccinated 23.6% had

hypertension and 4.2% had diabetes. Most of those who were symptomatic at baseline were from the unvaccinated group. 91.7% of the unvaccinated were symptomatic while 65% of the breakthrough infections group were symptomatic at baseline. 50.6% of the vaccinated health workers had a period of less than 5 months between vaccine receipt and infection while 49.4% of them had received the vaccine more than 5 months before infection. The results are displayed in table 4.2 below.

Table 4.2: Clinical characteristics of health workers in Marondera District who tested positive to SARS-CoV-2 among the vaccinated and unvaccinated individuals

Clinical Characteristics	**Unvaccinated (%) N=144**	**Vaccinated (%) N=160**
Comorbidities		
No	97 (67.4)	111 (69.4)
Yes	47 (32.6)	49 (30.6)
Hypertension		
No	110 (76.4)	118 (73.7)
Yes	34 (23.6)	42 (26.3)
Diabetes		
No	138 (95.8)	148 (92.5)
Yes	6 (4.2)	12 (7.5)
Comorbidity count		
None	97 (67.4)	111 (69.4)
1	39 (27.1)	35 (21.9)
>1	8 (5.5)	14 (8.7)
Symptomatic at baseline		
Yes	132 (91.7)	104 (65.0)
No	12 (8.3)	56 (35.0)

4.3 Vaccine type among health workers with SARS-CoV-2 breakthrough infections in Marondera District

Most (62.5%) of those who had breakthrough infections had been vaccinated with the Sinopharm vaccine while the rest had received the Sinovac vaccine. Figure 4.1 below shows the distribution of vaccine type among health workers with SARS-CoV-2 breakthrough infections in Marondera District.

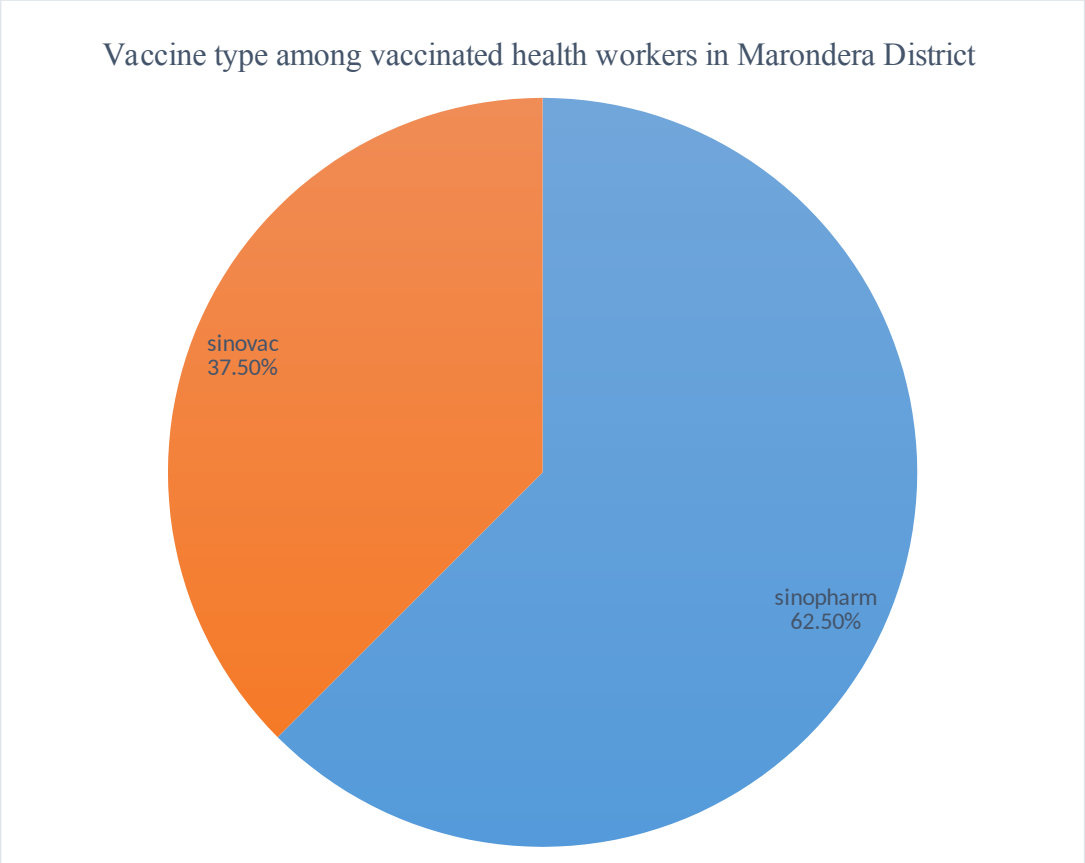


Figure 4.1: Vaccine type among health workers with SARS-CoV-2 breakthrough infections in Marondera District

4.5 Experienced symptoms by vaccinated and unvaccinated health workers

Asymptomatic cases accounted for 22.4% of all the records used in the study. Those who were asymptomatic among the breakthrough infections and unvaccinated groups

were 35.0% and 8.3% respectively. Altogether, asymptomatic cases with breakthrough infections were 82.4% compared with 17.6% who were not vaccinated. Figure 4.2 below shows vaccinated and unvaccinated health workers who were asymptomatic.

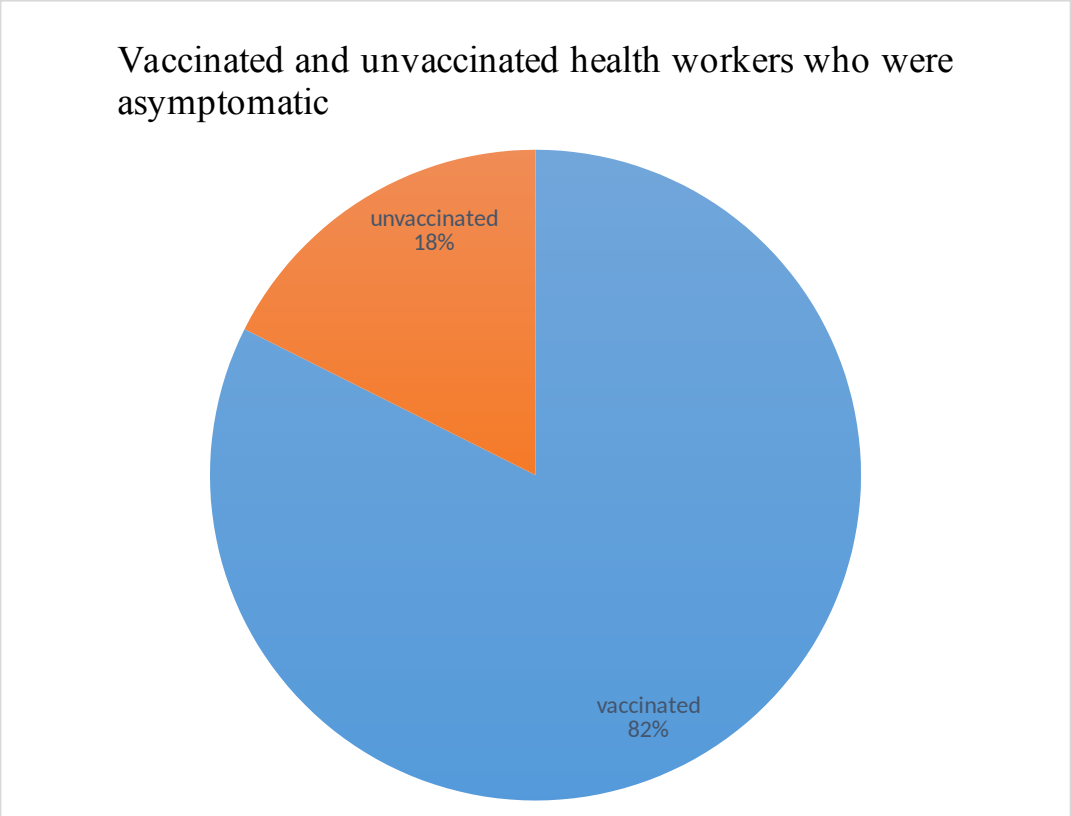


Figure 4.2: Vaccinated and unvaccinated health workers who were asymptomatic

The most presented symptoms among the unvaccinated were fever (83.3%), sore throat (82.6%), cough (76.4%), headache (68.8%), runny nose (63.9%), shortness of breath (43.1%), chest pain (37.5%)and loss of taste and smell (37.5%) in that order. The most presented symptoms in those with breakthrough infections were sore throat (46.25%), headache (45.6%), fever (36.9%), cough (35.6%), loss of smell and taste (20%), runny nose (17.5%), shortness of breath (14.4%) and chest pain (13.1%) in that order. 71.3% of those unvaccinated presented with at least 5 symptoms while 20

% of the health workers with breakthrough infections presented with at least 5 symptoms. Figure 4.3 below shows symptoms experienced by SARS-CoV-2 positive health workers in Marondera District.

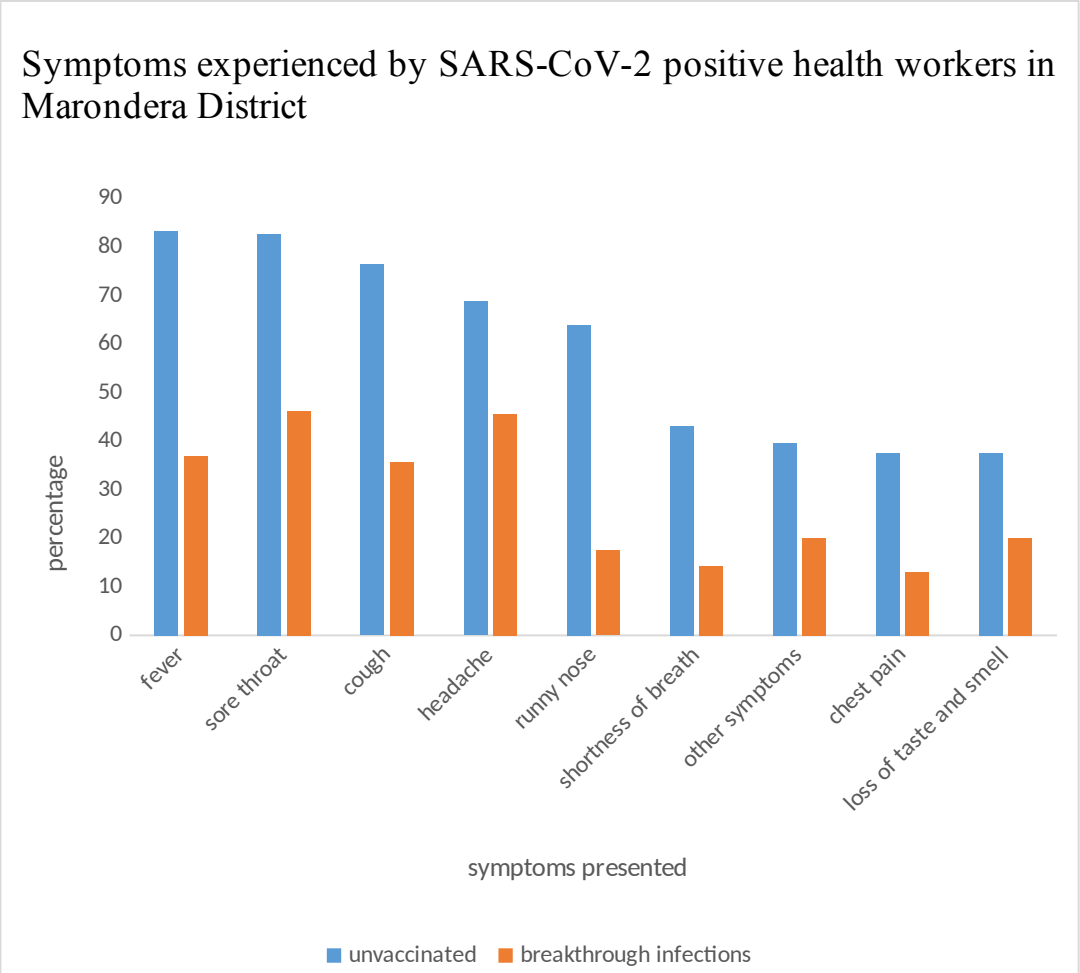


Figure 4.3: Symptoms experienced by SARS-CoV-2 positive health workers in Marondera District

4.6 Outcomes of health workers in Marondera District who tested positive to SARS-CoV-2

A total of 44 (14.5%) of the SARS-CoV-2 positive health workers were hospitalised. Among health workers with breakthrough infections, 6.2% were hospitalised and 1.9% were admitted in the ICU. All (100%) of the COVID-19 breakthrough infected

health workers recovered and only one death was recorded among those who were not vaccinated. Most of those vaccinated (65.6%) recovered in less than a week while most of those who were unvaccinated (80.4%) took more than a week to recover. Thus most of those with breakthrough infections took a shorter time to recover than the unvaccinated health workers. Table 4.3 shows the outcomes among those who were vaccinated and unvaccinated.

Table 4.3: Outcomes among health workers in Marondera District who were vaccinated and unvaccinated

Outcome	Unvaccinated (%) N=144	Vaccinated (%) N=160
Hospitalised		
No	110 (76.4)	150 (93.8)
Yes	34 (23.6)	10 (6.2)
ICU admission		
No	131 (91.0)	157 (98.1)
Yes	13 (9.0)	3 (1.9)
Recovered		
No	143 (99.3)	160 (100.0)
Yes	1 (0.7)	0 (0.0)
Recovery period		
<week	28 (19.6)	105 (65.6)
>week	115 (80.4)	55 (34.4)

4.7 Factors associated with severe disease

Factors significantly associated with severe illness were; having comorbidities (RR=4.2; 95% CI: 2.3-7.6; p<0.001), hypertension (RR=2.6; 95% CI: 1.5- 4.5; p<0.001), diabetes (RR=5.1; 95% CI: 3.0- 8.7; p<0.001) and having five more or symptoms at baseline (RR= 50.4; 95% CI: 7.0- 362.2; p<0.001).

Health workers in Marondera District who had comorbidities were 4.2 times as likely to develop severe disease as those who had no comorbidities. Health workers in Marondera District with hypertension were 2.6 times as likely to develop severe disease as those who had no hypertension. Health workers in Marondera District who had diabetes were 5.1 times as likely to develop severe disease as those who had no diabetes and those who presented with five or more symptoms at baseline were 50.4 times as likely to develop severe disease as those who had less symptoms.

Being vaccinated was protective against severe disease (RR=0.2; 95% CI: 0.1- 0.5; p<0.001) including being aged below 50 years (RR= 0.3; 95% CI: 0.2- 0.5; p<0.001). Thus health workers in Marondera District who were vaccinated had 0.2 times the risk of severe disease compared to those who were not vaccinated and those who were below the age of 50 years had 0.3 times the risk of severe disease compared to those aged above 50 years. Table 4.4 below shows these results.

Table 4.4: Factors associated with severe disease among health workers with breakthrough infections and unvaccinated health workers with infection

Variable	Severe (%) n=41	Severe (%) n=263	Risk ratio (95% CI)	p-value
Below 50 years of age				
Yes	26 (63.4)	241 (91.6)	0.3	<0.001*
No	15 (36.6)	22 (8.4)	(0.2-0.5)	
Sex				
Male	13 (31.7)	70 (26.6)	1.2	0.496
Female	28 (63.3)	193 (73.4)	(0.7-2.3)	
Residence				
Urban	36 (87.8)	201 (76.4)	2.0	0.102
Rural	5 (12.2)	62 (23.6)	(0.8-5.0)	
Occupation				

Clinical work	26 (63.4)	161 (61.2)	1.1	0.788
Non-clinical work	15 (36.6)	102 (38.8)	(0.6-2.0)	
Presence of comorbidities				
Yes	27 (65.8)	69 (61.2)	4.2	<0.001*
No	14 (34.2)	194 (73.8)	(2.3-7.6)	
Hypertension				
Yes	19 (46.3)	57 (21.7)	2.6	<0.001*
No	22 (53.7)	206 (78.3)	(1.5-4.5)	
Diabetes				
Yes	10 (24.4)	8 (3.0)	5.1	<0.001*
No	31 (75.6)	255 (97.0)	(3.0-8.7)	
Vaccinated				
Yes	8 (19.5)	152 (57.8)	0.22	<0.001*
No	33 (80.5)	111 (42.2)	(0.1-0.5)	
5 or more symptoms at baseline.				
Yes	40 (97.6)	94 (35.9)	50.4	<0.001*
No	1 (2.4)	168 (64.1)	(7.0-362.2)	

*statistically significant; 95% CI- 95% Confidence Interval

4.8 Vaccine type, period between vaccine and infection and severity of illness

There was no statistically significant association between vaccine type and severity of illness. The results also showed no statistically significant association between period between vaccine and infection and severity of illness. These results are shown in table 4.5 below.

Table 4.5: Association between vaccine type, period between vaccine and infection and severity of illness

	None Severe N=152	Severe N=8	Risk ratio (95% CI)	p-value
Vaccine type				
Sinopharm	92 (62.5)	5 (62.5)	1.0	1.000
Sinovac	57 (37.5)	3 (37.5)	(0.9-1.1)	
Period from vaccination				
<5 months	78 (51.3)	3 (37.5)	1.03	0.492
≥5 months	74 (48.4)	5 (62.5)	(0.9-1.1)	

4.9 Independent risk factors associated with severe illness

After controlling for other variables, having five or more symptoms at baseline was independently associated with having severe illness (ARR=25.0; 95% CI: 3.1-199.6; p=0.002). Thus after adjusting for other variables, the risk of developing severe disease among health workers in Marondera District in those who had 5 symptoms and more was 24.9 times compared to those who had less than five symptoms. The results are given in table 4.6 below.

Tables 4.6: Independent risk factors associated with severe disease

	B	S.E	p-value	ARR	95% CI
Having 5 symptoms or more at baseline	3.2	1.1	0.002	24.9	3.1-199.6

B- Beta; S.E- Standard error; ARR-adjusted risk ratio; *statistically significant

4.10 Chapter summary

A total of 304 records of health workers who had positive results from the SARS-CoV-2 test were included in the study and 47.37% were unvaccinated whilst 52.63% were vaccinated. There were more females in the study. 68.1 % of vaccinated health

workers were involved in clinical work and those who were involved in clinical work among those not vaccinated were 54.2%. Among those vaccinated 30.6% had comorbidities while 32.6% of those unvaccinated had comorbidities. Most (62.5%) of those who had breakthrough infections had received the Sinopharm vaccine. All of the health workers in the district with breakthrough infections recovered and only one death was recorded among the unvaccinated. Factors associated significant with severe disease were; having comorbidities hypertension diabetes and having five more or symptoms at baseline. Being vaccinated was protective against severe disease including being aged below 50 years. Having five or more symptoms was an independent factor associated with severe illness.

CHAPTER 5 SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

In this chapter, the researcher gives a summary of the study findings in accordance with the study objectives. It also gives conclusions which were based on the findings of the study. The researcher will also give recommendations to the policy makers and suggest areas for further study.

5.2 Discussion

5.2.1 Demographic characteristics of health workers in Marondera District who tested positive to SARS-CoV-2

A total of 304 records of health workers in Marondera District who tested positive to SARS-CoV-2 were used for the study. The total cohort consisted more of health workers who were vaccinated (52.6%) than those who were unvaccinated (47.4%). This was because vaccination was encouraged for all health workers and more of them were being vaccinated as they were at more risk of being infected with the virus due to their occupation than the general population. Most of the vaccinated health workers had breakthrough infections during the third and fourth waves of COVID-19 which occurred in July 2021 and December 2021 thus health workers were susceptible to the virus during these periods as they were seeing more cases of COVID-19 than before.

Most of the health workers were aged below 50 years and the median age recorded was 36.0 years for the unvaccinated and 38.0 years for the vaccinated. This was because the older and more experienced health care workers leave the country in

search for greener pastures considering the low salaries in the country compared to other countries leaving newly trained staff manning the public health institutions. The results were similar to the results of the study by Maroof *et al.* (2021) where the median age for health workers who had breakthrough infections was 38.8 years. The median age of recorded was however, younger than for the participants with breakthrough infections in a study by Parameswaran *et al*. (2022) where their mean age was 44.39 years. Similar to the findings by Angel *et al.* (2021) the health care workers with breakthrough infections were older than the unvaccinated health care workers.

In the study there were more females on both the vaccinated and unvaccinated groups contrary to the research by Angel *et al*. (2021) where vaccinated health workers were more frequently males and the unvaccinated were more frequently females. The studies by Teran *et al.* (2021) and Bergwerk *et al.* (2021) however, also showed more females (68.2% and 64% respectively) than males with breakthrough infections. Females were more than males in this study as there were generally more female health workers compared to male health workers in the district. In the district 73% of the health care workers are female and that could explain why the majority of both the vaccinated and unvaccinated were females.

Most of the recorded health workers were involved in clinical work (68.1% of those with breakthrough infections and 54.2% of those unvaccinated). These results were similar to the studies by Maroof *et al.* (2021) and Bergwerk *et al*. (2021) who reported most of the COVID-19 breakthrough infections among clinical workers. More clinical workers had breakthrough infections as they were more involved directly with patients and were at the frontline in regards to fighting the disease

hence were more exposed to the virus. Most of the health workers who had breakthrough infections, similar to the study by Bergwerk *et al*. (2021) were from the nursing department. This is because most of the health facilities were manned by the nursing staff, they were also at the point of first contact with the patients at points of entry where they tested patients and they also spent more time with the patients than any other staff.

The majority of health workers resided in Marondera town urban areas. This was because most of them worked at Marondera Provincial Hospital which is the largest health facility in the district and most of the health facilities are close to the town hence most of them preferred staying in urban areas than the rural areas.

5.2.2 Clinical characteristics of health workers in Marondera District who tested positive to SARS-CoV-2

The records showed that the majority of health workers in the district who tested positive to SARS-CoV-2 did not have comorbidities. This might have been linked to the younger median age reported as older age is associated with more comorbidities. Only 30.6% of those with COVID-19 breakthrough infections had comorbidities. Contrary to this was the study by Butt, Nafady-Hego *et al*. (2021) where 61.2% of the participants with breakthrough infections had one or more comorbid conditions. This might have resulted from the older ages in the study by Butt, Nafady-Hego *et al*. (2021) where the mean age recorded was older (45) than the mean age in our study. The study by Niyas and Arjun (2021) however, showed a lower prevalence in comorbidities recorded among the health workers with breakthrough infections (8.3%) than our study because the mean age of their participants (31.9 years) was younger than in our study.

Among those with breakthrough infections the most recorded comorbidities were hypertension and diabetes, 26.3% had hypertension while 7.5% had diabetes. This was because the most prevalent comorbidities among people infected with COVID-19 are diabetes and hypertension. Different studies done also show diabetes and hypertension as the most prevalent comorbidities among those with COVID-19 breakthrough infections (Niyas and Arjun, 2021; Butt, Nafady-Hego *et al*., 2021; Butt, Yan *et al.,* 2021).

Only two vaccines, Sinopharm and Sinovac were being given in the district. In the study most of those with SARS-CoV-2 breakthrough infections (62.5%) had received the Sinopharm vaccine. This was because the Sinopharm vaccine was the mostly available vaccine in the district health facilities.

5.2.3 Clinical symptoms presented by health workers in Marondera District who tested positive to SARS-CoV-2

In our study, 35.0% of the vaccinated were asymptomatic and these findings were similar to the findings by Angel *et al.* (2021) where asymptomatic cases were 38.7% of the cohort. Vaccines induce production of different antibodies in the body which fight off the virus thus providing protection against symptomatic disease. The results of the study were also similar to the findings by Oran and Topol (2020) who reported that asymptomatic cases ranged approximately from 40% to 45%. A higher value of asymptomatic breakthrough infections of 94.4% was reported by Maroof *et al.* (2021). Contrary to these findings were the findings from Lee *et al.* (2022) where 92% of the participants with breakthrough infections were symptomatic. In their study Martínez-Baz *et al*. (2021) highlighted the effectiveness of the COVID-19 vaccines towards preventing symptomatic illness. Thus the vaccines were associated

with a lower incidence of symptomatic cases. Asymptomatic individuals are however dangerous as they can harbour the virus making them a potential source of virus transmission to other health personnel, patients and in the community.

In our study the most recorded symptoms amongst those with breakthrough infections were sore throat (46.3%), headache (45.6%) and fever (36.8%). The most common recorded symptoms by Bergwerk *et al*. (2021) were respiratory congestion (36%), loss of taste or smell (28%) and myalgia (28%). In the study by Niyas and Arjun (2021) the most reported symptoms were fever (57.4%), myalgia (51.8%) and sore throat (50.9%).

5.2.4 Outcomes among health workers in Marondera District who had SARS-CoV-2 breakthrough infections

In the study only 6.2% of those who had breakthrough infections had severe illness (hospitalised) as compared to 23.6% who were unvaccinated. This is because of the antibodies produced by the virus that boost immune response to the virus thus fighting the virus and preventing severe illness. Contrary to the results of this study were the results of Maroof *et al.* (2021) where all of the participants did not experience severe illness. This might have been due to most of the health workers (88.7%) in the study by Maroof *et al.* (2021) being diagnosed within three months after the receiving the second vaccine. In this study only 18.3% were diagnosed within three months of receiving a vaccine.

Studies have indicated time-dependent decline in antibody levels after receiving COVID-19 vaccines contributing to breakthrough infections and severe illness (Leshem, Nelson, & Lopman, 2021). The CDC is recommending people with more

than five months after completing their two doses of the vaccines to get a booster dose due to waning of immunity after this time period (CDC, 2022). Antibodies from the COVID-19 vaccines wane over time reducing the effectiveness of the virus. In the current study 49.4% of the vaccinated health workers had breakthrough infections more than five months after receiving the second vaccine and according to CDC they were all eligible for a booster dose.

No mortality was reported among the breakthrough infections in this study. These results show the importance of vaccines in preventing death. This was also contributed by the younger ages and the low prevalence of comorbidities in the health workers studied. Similar results were also recorded in a study by Angel, Spitzer and Henig (2021) where no mortality was recorded among participants with breakthrough infections. Brosh-Nissimov *et al.* (2021) however, recorded a higher mortality of 22% among hospitalised cases with breakthrough infections which was contributed by the increased age (mean=71.1 years) and the high comorbidity prevalence recorded among the patients as compared to the younger age of health workers in our study.

In the study 65.6% of those with breakthrough infections recovered in less than a week as compared to only 19.6% of the unvaccinated who recovered within a week. This was because most of the vaccinated had mild illness and showed fewer symptoms than the unvaccinated. This also shows effectiveness of the vaccines against disease severity. In the study by Tyagi *et al.* (2021) symptoms in those with breakthrough infections lasted for 3 to 14 days that is up to two weeks.

5.2.5 Factors associated with severe illness

In our study the presence of comorbidities, hypertension, diabetes, and having 5 symptoms or more at base line were risk factors that were associated with severe COVID-19 disease. However, being vaccinated and having an age below 50 years were protective factors against severe illness.

Similar results were recorded by studies by Leshem, Nelson and Lopman, (2021); Li, Huang, *et al*. (2021); Parameswaran *et al*. (2022); Butt, Nafady-Hego *et al*. (2021) and Butt, *Yan et al.* (2021) who recorded that severe illness in COVID-19 breakthrough persons was associated with advanced age. This association has been also been described in people with SARS-CoV-2 primary infection (Gao, 2021) and it holds true in populations with recorded breakthrough infections. Advanced age is linked with an increased burden of comorbidities which suppress the immune system and overall frailty caused by aging are possible explanations for this association. Advanced age is also linked to multimorbidity which might have an impact on illness severity.

Having comorbidities was also associated with severe illness. Similar results were recorded by Li, Huang, *et al*. (2021); Juthani *et al.* (2021) and Parameswaran *et al*. (2022) in those with breakthrough infections and in those with primary infection (Gao *et al*., 2021). The existence of comorbidities affects the immunity system and the body's ability to fight infection thus leading to severe infection. Comorbidities also inhibit the development of sufficient levels of immunity thus after infection with the virus people with comorbidities have a greater possibility of having severe infection than whose without comorbidities. Exacerbation of the comorbidity after infection might also contribute to severe illness. Similar to our study, Li, Huang, *et*

al. (2021) also found hypertension and diabetes associated with increased severity of illness.

In our study having five symptoms or more at baseline was independently associated with a higher severity of illness. Having more symptoms in itself is an indication that the infection was not mild. Butt, Nafady-Hego, *et al*. (2021) reported that persons who had symptomatic infection were associated with increased risk of severe illness.

In the study having been vaccinated was a protective factor against severe illness. The results were similar to those reported by Butt, Nafady-Hego, *et al*. (2021) where those without vaccination were three times at more risk of hospital admission and death than those who were vaccinated. Butt, Yan, *et al.* (2021) also found that being unvaccinated was statistically associated with severe sickness or death. The study by Maroof *et al.* (2021) showed no severe disease among the breakthrough infections indicating the effectiveness of vaccines against severe illness. The production of antibodies from the vaccines has an impact on decreasing new infections, symptoms experienced, time of recovery and ultimately severe illness thus vaccines are important in protection against severe illness.

5.3 Conclusion

From the findings of this study, it can be concluded COVID-19 vaccines were protective against severe illness. Factors associated with severe illness among the health workers in Marondera District were age above 50 years, the presence of comorbidities, hypertension, diabetes, and having five symptoms or more at baseline presentation. Health workers presenting with such factors should be monitored for severe illness. The findings of the study underscore the significance of health

workers getting vaccinated and the adherence to precautionary measures of preventing SARS-CoV-2 infection among the health workers despite getting vaccinated.

5.4 Implications

Vaccination provides a protective effect towards COVID-19 hospital admission and or death among health workers with breakthrough infections.

5.5 Recommendations

Based on the study findings, the researcher recommends that all health workers should be vaccinated against COVID-19 so as to prevent severe illness after infection. The researcher also recommends all health workers who have more than five months after receiving the second vaccine to receive vaccine booster doses. The researcher also suggests that health facility administrators enforce adherence of infection, prevention and control measures in order to prevent transmission of the virus from the asymptomatic cases and to prevent breakthrough infections in those vaccinated. In addition, the researcher suggests that those with comorbidities and older age are not put in high risk COVID-19 working areas. The researcher also recommends that complete data on breakthrough infections should be captured by the responsible people (nurses, doctors and health information officers) so that future analyses of the data includes all the cases. All the recommendations need to be implemented immediately.

5.5 Suggestions for Further Research

The researcher suggests the further investigation of COVID-19 variants among people with breakthrough infections. The researcher also suggests studies on waning

of immunity among health workers vaccinated as lower antibodies against SARS-CoV-2 are linked to breakthrough infections and severe disease.

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APPENDIX 1: Line list form

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA
1																											
2																											
3																											
4																											
5																											
6																											
7																											
8																											
9																											
10																											

Key: A- age; B- sex; C- marital status; D- residence; E- profession; F- Vaccinated?; G- vaccine type; H- date of second dose; I- date tested positive; J- symptomatic?; K- fever; L- sore throat; M- cough; N- runny nose; O- shortness of breath; P- headache; Q- chest pain; R-loss of taste and smell; S- other symptoms; T- hypertension; U- diabetes; V- other comorbidities; W- hospitalised?; X- ICU admission?; Y- length of admission; Z- outcome; AA- date of outcome

APPENDIX 2: Approval letter from the PMD Mashonaland East

Telephone: 24207/8, 24571

Telegraphic Address:
"PROVMED, MARONDERA"
Fax: 23967

ZIMBABWE

Reference:

MINISTRY OF HEALTH AND CHILD CARE
PROVINCIAL MEDICAL DIRECTOR
(MASHONALAND EAST)
P.O.BOX 10
MARONDERA

26 November 2021

Africa University
Fairview Road
Old Mutare
MUTARE

RE: PERMISSION TO UNDERTAKE A RESEARCH IN MARONDERA DISTRICT

Permission has been granted for Memory Mwadziwana from Africa University, Student Reg (192008) to conduct a research on COVID-19 Breakthrough outcomes in Marondera District, Mashonaland East Province.

Thank you.

MIN. OF HEALTH & CHILD CARE
P.M.D. MASHONALAND EAST
26 NOV 2021
P.O. BOX 10, MARONDERA
ZIMBABWE

Dr. P.F. Matsvimbo
ACTING PROVINCIAL MEDICAL DIRECTOR- MASHONALAND EAST

/sj