A Clinical Evaluation of COVID-19's Third Wave Symptoms Severity on Patients in Zomba City: A Case Study of University of Malawi Clinic

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Abstract

The impact of COVID-19 infections has been felt in Malawi since April 2020. Malawi readily benefited from the Coronavirus vaccine distribution program. While reagents were accessible for easy diagnosis, screening protocols kept changing. This paper assessed severity of symptoms among Coronavirus infected people as impacted by several factors in Zomba city. A cross-sectional study (n= 570) was conducted among patients accessing the University of Malawi COVID-19 clinic. Sex, age, disease outcome, vaccination status and underlying conditions data were collected. Log-linear multiple regression model was used for data analysis in R statistical analytical tool (Version 3.1). From July 2021 to October 2021, the clinic reported 179 (34.5%) third wave COVID-19 cases with a slightly higher males' representation (54.8%) than females (45.2%). Significant variation of infection prevalence was represented by 71.1% and 3.2% in age groups 18-29 and 1-17 respectively (χ^2 = 328.34, df = 4, p <.01). Majority of the infections were mild

(90%) with few severe (5.1%) and asymptomatic (4.6%) cases ($\chi^2 = 288.25$, df = 2, $p < .01$). Underlying conditions (5.6%, n=197) were present among few infected individuals. Infection significantly varied according to vaccination status categories ($\chi^2 = 284.63$, df = 2, $p < .01$) with most of the un-immunized patients (89.8%), vaccinated with one dose (8.6%) and two doses (1.5%). A negative association of disease severity with underlying conditions [0.1(R: -0.4, p=.02)] and vaccination status (R: -0.4, p=.01) were observed. Coronavirus symptoms severity was positively associated with a vaccination status and age interaction (R: 0.01, p=0.01). Underlying conditions in consideration of age negatively determined severity (R: -0.01, p=0.02). Further underlying conditions effect on severity assessment is needed to understand the relationship. Adherence to COVID-19 preventive and control measures i.e. vaccination, social distance and use of face masks reduce cases.

Keywords: *Coronavirus, COVID-19, Severity, Vaccination Status, Underlying Condition.*

1.0 INTRODUCTION

Coronavirus 2019 (COVID-19, SAR-COV 2) is a global pandemic that has affected approximately 385 million people leading to 6 million deaths. In Malawi, the infection recorded a total of 82,792 cases, 2,474 deaths and 1,859,497 vaccinations as of 18/01/2022 (MOH, 2021; WHO, 2022). The infection has been categorized into waves due to its fluctuating infections which have peaked at a particular time as well as the specific strain or variant of the virus causing the disease.

The first wave which affected at least 10 people per day in Malawi, occurred from March to November 2019, the second from December 2020 to May 2021, and the third from June to October 2021. Although the second wave is said to have generated ~500 cases per day, this statistics might have been under-estimate due to poor COVID-19 diagnostic tools, limited resources and poor data management health surveillance systems (Banda et al., 2021; Chimatiro & Majison, 2021). The country's health care sector managed the pandemic based on clinical interventions and preventative measures such as hand sanitization, social distancing and wearing of face masks (Chimatiro & Majison, 2021), which were compiled in the COVID-19 guidelines and clinical case management manuals by the Ministry of Health. These interventions notwithstanding, COVID-19 continued to be a national burden that was destabilizing lives.

Children are also susceptible to COVID-19 but in rare cases and are less likely to experience severe symptoms (Hyde, 2020). Literature has highlighted gender as an important factor on COVID-19 severity, often showing more infection affects in men than women(Gebhard et al., 2020). Women's immune response to vaccines is known to be faster than of men hence their ability to control infections (Takahashi et al., 2020). Consequently, the COVID-19 infection has a high morbidity and mortality in males than in females (Muula, 2020).

Vaccines are an important public health strategy in disease prevention and control (Machingaidze & Wiysonge, 2021). COVID-19 vaccine was made available in the country from March, 2021(Bono et al., 2021). Astra Zeneca (70.4% efficacy) was the first to be introduced, followed by Janssen (66.9% efficacy) and Pfizer (91.3% efficacy) (Prü, 2021). Poor vaccine acceptance has been recorded in most African countries including Malawi due to misinformation, disinformation, use of herbal medicine as an alternative and possibility of getting infected despite being vaccinated (Baker et al., 2021; Bono et al., 2021; Kanyanda et al., 2021; Malik et al., 2020; Mandala & Changadeya, 2021).

Pandemics have a natural history of eventually dying out which may have contributed to the end of the first two waves among other reasons (Kopel et al., 2020). In Malawi, the first two waves occurred prior to vaccine introduction. COVID-19 severity-linked factors studies have mostly been conducted among hospitalized patients with outcomes varying from country to country (Jordan et al., 2020). Assessing COVID-19 burden following vaccines is paramount in understanding prevention, control and management of possible upcoming waves. Based on out-patients, this study conducted at University of Malawi (UNIMA clinic), aimed at understanding the impact of vaccination status, underlying conditions and other factors on COVID-19 severity in the third wave experienced in Malawi.

2.0 METHODOLOGY

2.1 Study design and location

A quantitative cross-sectional study was conducted at the UNIMA Clinic in Zomba. The University clinic was an appropriate site for the study due to the huge population from the surrounding community it served during the third wave since only four clinics including UNIMA clinic, provided infection diagnosis services in Zomba city.

2.2 Study population

The study population included any person referred to the UNIMA clinic laboratory for a COVID-19 consultation. During the four-month duration of the study, individuals seeking medical help for all non COVID-19 related services were excluded from the study population.

2.3 Sample size

The study employed a purposive sampling technique hence data from everyone seeking COVID-19 services for the period July- October 2021 was recorded. Since this was not a typical experimental design, prior sample size calculations were not done and total of 570 individuals were incorporated in the study.

2.4 Data collection

Retrospective data on sex, age, vaccination status, presence of underlying conditions (Hypertension, Asthma, Diabetes, HIV/AIDS, Cardiovascular disease, cancer and chronic respiratory conditions), COVID-19 symptoms' severity and status were recorded on case-based surveillance forms and later entered in a Microsoft Excel 2010 sheet. The principal investigator (PI) of the study was actively involved in data entry in the surveillance forms. Disease severity was categorized as asymptomatic, mild, severe based on prescription provided by the Malawi Ministry of Health (MoH) and World Health Organization (WHO) (MOH, 2021; WHO, 2022). The dependent variable in this study was disease severity.

2.5 Informed consent, privacy and confidentiality

Permission to use COVID-19 data was not sought from the participants but the study used clinic-owned recorded data. Hence, UNIMA clinic management provided consent to use the data. However, the study assigned numbers and not names when recording data against variables in an excel sheet to ensure easy data management.

2.6 Data management and analysis

Data were recorded, sorted in Microsoft Excel 2010 and analyzed using R statistical package (Version 3.1). The data were subjected to descriptive analyses. Log-linear multiple regression model analysis was performed to determine relationship of dependent variable (Disease/infection severity) with explanatory variables (age, sex, underlying conditions and vaccination status). Strength of association between infection severity and each independent variable was determined using Chi-square test. A p-value of ≤ 0.05 was set as a cut-off point for statistical significance.

3.0 Results

A total of 570 participants aged between 6 and 63 years were included in the study (54.2% males and 45.8% females). Most participants were within the age range 18-29 (64.9%) while age range 54-65 (4.1%) had the least numbers. Overall, 34.6% of COVID-19 cases were observed (Table 1).

Table 1: *Demographic and variable Characteristics of participants*

Variable	Frequency	%
Age		
1-17	29	5.1
18-29	369	64.9
30-41	80	14
42-53	66	11.6
54-65	26	4.6
Sex		
Male	309	54.2
Female	261	45.8
Vaccine status		
None	521	91.4
1 DOSE	37	6.5
2 DOSES	13	2.3
COVID-19 Ag		
Positive	197	34.6
Negative	373	65.4

The number of infected people varied significantly across the three levels of severity (asymptomatic, mild, severe) ($\chi^2 = 288.25$, df = 2, p <.01), with the majority of the people (about 90%) exhibiting mild symptoms while an almost equal proportion were either asymptomatic (4.6%) or severely infected (5.1%). There was a significant association between age and infection rates ($\chi^2 = 328.34$, df = 4, p <.01); the infection was most prevalent (71%) among those in the age group 18 - 29 years and least prevalent in the age range 1-17 (3.6%). Few participants presented with underlying conditions (5.6%, n = 197). Infection prevalence did not significantly differ between males (35.0%, n = 309) and females (34.1%, n = 261) ($\chi^2 = 0.01$, df = 1, p = .91) (Table 2).

Table 2: *Demographic and variable characteristics for infected participants*

Variable	Frequency	%
Age [a]		
1-17	7	3.6
18-29	140	71.1
30-41	20	10.2
42-53	21	10.7
54-65	8	4.1
Sex[a]		
Male	108	54.8
Female	89	45.2
Severity[b]		
Asymptomatic	9	4.6
Mild	178	90.4
Severe	10	5.1
Underlying condition[a]		
None	186	94.4
Bp	11	5.6

[a] **Independent variables**
[b] **Dependent variable**

Both gender had an equal effect on disease severity [1(0.7-1.3)], p=.99. The odds of having severe infection was lower among those with underlying conditions [0.1(0.02-0.5)] with the effect being significantly associated (p=.02). Age (p=.8) alone was not significantly associated with infection severity however its interaction [1(0.9-1.0)] with vaccination status variable [1.1(0.7-1.5)] had a positive effect with a significant association (p<.01) (Table 3,4).

Table 3: *Severity characteristics against demographics and other variables for the infected participants*

Variable	**Asymptomatic**	**Mild**	**Severe**	**p-value**
Age[a]				0.2
1-17 18-29 30-41 42-53 54-65	0 4 1 3 1	17 123 18 15 5	0 6 1 2 1	197
Sex[a]				0.8
Male Female	5 4	98 80	5 5	197
Vaccination[a] **status**				0.2
None 1 Dose 2 Doses	8 1 0	162 13 3	7 3 0	197
Underlying Conditions[a]				0.001
Absence Presence	0 9	176 2	10 0	197

[a] **Independent variables**

Table 4: *Log-linear Multiple Regression for COVID-19 severity*

Variables	**MULTIVARIATE**	
	p-value	OR (95%CL)
Sex	0.9	1.0(0.7-1.3)
Age	0.2	1.0(0.9-1)
Underlying conditions*	0.02	0.1(0.02-0.5)
Cond & age*	0.02	
vaccination	<.01	1.1(0.7-1.5)
vaccination & age	<.01	

* High risk factors

4.0 DISCUSSION

Although the Malawi government implemented COVID-19 preventive and control measures, adherence, reduced compliance and relaxation of the measures among the University of Malawi surrounding community may be attributed to the increased cases (34.6%) (Table 1). Coronavirus third wave in Malawi occurred in cold season. Cold weather may have influenced the rapid spread of COVID-19 due to lowed immune response towards the virus. It is common knowledge that other corona virus infections are prevalent during cold seasons. Nevertheless, other studies have disputed the correlation between cold weather and COVID-19 incidence (Kamran & Ali, 2021; Mudenda, 2021).

While a sizeable number of people (34.6%) were infected, few patients presented with severe and asymptomatic infection symptoms (Table 1,2). Probably, the considerable recorded cases were due to poor adherence to preventive measures which was prevalent during the third wave. Improved diagnostic services i.e. adequate trained personnel and reagents availability, could also explain the diagnosed cases (Soriano et al., 2021). Similar findings which reported substantial number of cases, were observed with a highlight of significant association between severity of symptoms and infection (Jutzeler et al., 2020). Consistent with other findings, this study found a small proportion of individuals who had severe symptoms during the Covid-19 third wave (McAlister et al., 2021). This could possibly be due to overall development of immunity to otherwise virulent omicron variant in the third wave caused by general exposure to the earlier waves. In turn, the underlying immunity lead to less severe and milder symptoms. Generally, the third wave had less severe impact on the population in the country as noted in the MoH COVID-19 Dashboard data. Few cases were similarly recorded in studies done in other countries due to better adherence to infection preventive and control protocols (Arce et al., 2021; Iwasaki & Grubaugh, 2020).

This study's COVID-19 cases were not gender dependent (Table 3), although a slightly increased numbers of infected males than females was observed. This may be attributed to poor adherence towards preventive measures and higher exposure to viral infections in males than females. According to the MoH COVID-19 Dashboard, males also had a higher morbidity rate than females in the general population. COVID-19 infection seems to affect more men than women due to their immunological differences (Gebhard et al., 2020). A similar study in Pakistan had cases which were equally distributed among both genders (Ahmad et al., 2022). Several studies have revealed more cases among the male gender (Gebhard et al., 2020; Jutzeler et al., 2020; Ozgur et al., 2020; Takahashi et al., 2020) citing poor adherence by males towards COVID-19 control and preventive measures as the main probable factor (Fortunato et al., 2021). Other countries with increased numbers of COVID-19 cases among males than females included: USA, Italy, Germany, Norway, Iran and Australia among others. COVID-19 was however reportedly pre-dominant among females in other studies due to geographical location and social activities done by women which encourages contact hence rapid transmission (Kopel et al., 2020; Takahashi et al., 2020).

Children are less susceptible towards COVID-19 and if infected, they are less likely to experience severe symptoms as depicted in this study (Chen et al., 2021). Immune response is known to reduce with age hence most old people being prone to infections than children (Sanyaolu et al., 2020). The study registered few participants from the age bracket 1-17 which may have contributed towards low COVID-19 cases (Table 1, 2). Low susceptibility of children towards the infection was equally documented in China and Indonesia (Zhang et al., 2022). Like other studies, a rapid transmission was depicted in the age group 18-19 which was categorized as the most risk group with a reduction in below and above age groups (Ahmad et al., 2022). Active social interactions among this age group could be one of the reasons they were at most risk. Members from this age group are mostly in crowded places and prone to defying instructions hence the active spread (Monod et al., 2021; Tsankov et al., 2021). Although age played a role in determining cases, omicron variant which was detected in the third wave and characterized as highly infective may have also facilitated its rapid spread (Zawbaa et al., 2022). Similar studies found age range 20-49 to have been linked to severe Coronavirus transmission (Monod et al., 2021). A negative association of symptom severity with an interaction of age and underlying conditions (R= -0.01, p=0.02, Table 4) was observed. This finding implied that severe infections were likely to be found in young individuals without underlying conditions due to less number of young participants with underlying conditions registered. A global study reported that people in the age range 18-49 had underlying conditions than their younger and older counterparts (Sanyaolu et al., 2020) which was in line with this study.

Low vaccination reported in this study (Table 1) concurred with the nation data which had only <5% of the total population being fully immunized (Rasaq Kayode et al., 2022). Similarly, Kuwait, Jordan, Indian and Chinese studies had overall poorly immunized population for the third wave than the second wave (Sallam, 2021). Reluctance to get immunized may have led to low numbers of vaccinated individuals. Interaction of immunization and age had a significant response in infection severity among the participants. The significance was manifested in immunized older participants who were mildly affected, less vulnerable and susceptible to COVID-19 infection unlike their counterparts (Table 4). This outcome may have been influenced by the immunization status and observance of infection control measures among older participants. However, contrasting results were observed elsewhere with immunized older people being severely affected (Villela et al., 2021).

Several studies have recorded the positive impact of vaccines on disease severity (Afolabi & Ilesanmi, 2021; Theo et al., 2021; Young et al., 2020). However, fully immunized participants in this study were prone to getting infected unlike unimmunized individuals (Table 4). This may have been due to the overall in proportional immunized to unimmunized ratio which indirectly affected infection data interpretation among individuals. A similar finding with a significant association between infection severity and vaccination status was observed (Tenforde et al., 2021). Vaccines are known to be effective and several studies have demonstrated a link between not being fully immunized and vaccine short term effective profile (Haynes et al., 2020; Kaur & Gupta, 2020; Lytras et al., 2022; Q. Wu et al., 2021) hence more and few recorded cases of infection among those not immunized and partially immunized respectively (Table 3). A significant association between vaccine and infection severity was correspondingly observed (Table 4), i.e. a unit increase in vaccination status was directly proportion to an increase in infection severity status. Other studies however also linked influenza vaccine obtained immunity to have attributed to more asymptomatic cases among COVID-19 unvaccinated individuals (Amato et al., 2020). The third wave also coincided with COVID-19 Omicron variant which although highly transmissible, mostly caused mild infections (El-Shabasy et al., 2022; Rasaq Kayode et al., 2022), hence observance of more mild infections among participants.

Underlying conditions play a major role in general disease progression (Parveen et al., 2020). Individuals with underlying health conditions are mostly at risk of getting infections (Tsankov et al., 2021). Underlying conditions among Coronavirus patients determined presence of severe infections (Hashmi & Asif, 2020; Tsankov et al., 2021). However, this study observed a negative association between infection severity and presence of underlying conditions evidenced by the absence of severe cases among participants presenting with underlying conditions (Table 4). Since Omicron caused more mild than severe infections, presence of underlying conditions i.e. Diabetes, cardiovascular disease, Hepatic disorders etc, played a minor role in causing severe infections (Rasaq Kayode et al., 2022). Globally, 22% of the population has one or more underlying health conditions (Clark et al., 2020; Yang & Wang, 2021). A significant association between COVID-19 severity and underlying conditions has been observed in a number of studies in which >20% of participants presented with underlying conditions (Clark et al., 2020; Walker et al., 2021; J. Wu et al., 2020; Yang & Wang, 2021). Although other studies failed to explore the association mechanisms that are at play between the two factors (Clark et al., 2020; Kompaniyets et al., 2021), this study recorded a 1.9% of individuals with underlying conditions which may have attributed to the negative association of the two variables. Contrasting results were however recorded in several studies with a significant association of underlying conditions and infection severity (Jutzeler et al., 2020; Parveen et al., 2020; Tsankov et al., 2021; J. Wu et al., 2020), since the conditions weaken immune response towards COVID-19 infection. Presence of underlying conditions with a unit increase in age contributed towards few severe infections (Table 4), i.e. few severe infections were present among adults due to less number of adults with underlying health conditions.

5.0 CONCLUSIONS

This study provides an insight of the Coronavirus third wave pattern in relation to vaccination status, underlying conditions, demographics and severity. The results have highlighted that apart from age and gender, vaccination status is crucial in Coronavirus control. In this study, underlying conditions had no effect on infection severity, however further studies are needed to verify this outcome. The findings may assist institutions in informed decision making on COVID-19 screening exercises in the future.

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