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Factors associated with death among hospitalized COVID-19 patients in Mulago Hospital, during Uganda's third wave.

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Summary

Background: *On 7 December 2021, the first case of Omicron variant was confirmed in Uganda. By 14 December 2021, COVID-19 cases rose sharply to form Uganda's third COVID-19 wave. This was followed by an increase in COVID-19 deaths by 24 December 2021. The wave was driven mainly by Omicron variant. We identified the factors associated with mortality among COVID19 hospitalized patients in Mulago Hospital during the third wave.*

Methods: *We retrieved treatment files for all COVID19 hospitalized patients at Mulago hospital, 14 December 2021-14 January 2022. We extracted data on age, sex, vaccination status, underlying conditions, and severity of COVID-19. We used modified Poisson regression to identify factors associated with mortality.*

Results: *We identified 206 patients, out of which 112(54%) were females, 127(62%) had comorbidities, 59 (29%) of the patients had received any vaccination with 38 (64%) being fully vaccinated and 40 (20%) died. Of the deaths, 19(47%) were females, 27(67%) had comorbidities, 10(25%) of the patients had received any vaccination with 7 (17%) being fully vaccinated. The median age of the deaths was 63 years ([IQR] 49 – 78 years). The log risk of death among patients aged 45-61 years was 7.4 times (CI 1.03 – 53) that of patients aged 0-25 years and the log risk of death among patients aged 66+ years was 7.9 times (CI 1.1 – 56) that of patients aged 0-25 years. There was no association between sex, having a comorbidity, hypertension, chronic heart disease, diabetes, and vaccination status with death among the patients.*

Conclusion: *There was increased log risk of death among older patients. There was no association of vaccination status, sex, and comorbidities with death. There is need to strengthen COVID-19 monitoring, and care among older persons.*

Background

COVID-19 continues to devastate health service and health care globally [1]. The first wave of COVID-19 occurred in November December although the numbers decreased quickly in early January 2021 with approximately 90 deaths [2]. The second wave of COVID-19 in Uganda which was mainly due to the Delta variant Delta variant [3-5] occurred from April-July 2021and spread faster overwhelming the health system [6]. It had about 2,379 deaths countrywide [2].

On 7 December 2021, the first case of Omicron variant was confirmed in Uganda [7] and by 14 December 2021, COVID-19 cases were noted to be rising sharply again, and by 24 December 2021, more than 1,000 cases a day were being recorded. By 10 January 2022 when the study was conducted, there were 168 deaths reported since the beginning of the wave [2]. This third wave was thought to be driven mainly by Omicron variant [8]. Studies done all over the world have showed that older age [9, 10], comorbidities (cardiovascular disease, diabetes) [10, 11], (chronic lung disease and chronic neurological disease), and men [9] were all associated with mortality among COVID -19 patients. A study done in Mulago National Referral Hospital COVID-19 Treatment Unit during the second wave showed that being female, aged 50+ years, and having oxygen saturation at admission of ≥92%, and admission pulse rate of ≥100bpm were associated with mortality [12].

In order to prevent the devastating effects of COVID-19, the Government of Uganda provided COVID-19 vaccines since March 2021 and by 9 December 2021 6,525,371 people had received at least one dose of vaccine and 1,287,799 were fully vaccinated [13]. There was mistrust and speculation about COVID-19 vaccines in the country[14, 15]. At the beginning of the third wave, there were anecdotal reports from public about deaths occurring among vaccinated cases. However, there was no data to support this. We investigated the factors associated with mortality among COVID19 hospitalized patients in Mulago Hospital during the third wave.

Methods

Study setting, design, population, and sample size consideration

We conducted a cross-sectional study at the Mulago National Referral Hospital (MNRH) COVID-19 Treatment Units (CTU) during 10th-17th January 2022. The MNRH CTU was the largest public facility in Uganda in terms of COVID-19 care and treatment with a total bed capacity of 315 beds comprising of 15 intensive care unit (ICU) beds and 300 HDU beds. We considered records of all COVID-19 patients admitted in the treatment Units, 14 December 2021-14 January 2022.

Study variables and data collection

We retrieved routine patient care files and collected data on demographic characteristics (age and sex), underlying comorbidities (hypertension, diabetes mellitus, previous or current chronic heart disease, HIV, kidney disease, liver disease, cancer, sickle cell disease, chronic lung disease, and obesity), and vaccination status. Our outcome of interest was the status of the patient as they left the hospital i.e., dead or alive. We additionally obtained data regarding the vaccination status of the patients through phone calls with either the patients or the next of kin.

We categorized patient's vaccination status as not vaccinated, partially vaccinated, and fully vaccinated. We defined not vaccinated as patients who tested positive but never received any vaccine, partially vaccinated as patients who tested positive but received one dose for two dose vaccines or tested positive in less than 2 weeks after second dose of two dose vaccines, and full vaccinated as patients who tested positive but received a full dose of the vaccine OR tested positive more than 2 weeks after the full vaccination that is 2 doses for 2 dose vaccines and 1 dose for single dose vaccines.

Data Analysis

Using Stata 14.0. for data analysis, we calculated proportions by sex, age, comorbidity, and vaccination status to describe the study population. We also calculated the p values for the tables of different categories of each predictor variable with the outcome to find out if they were significantly different. We assessed the risk factors for death among the patients with modified Poisson regression analysis because the prevalence of death was more than 10%.

This was done by running the association between death and each of the study variables. Any variable with a p-value < 0.2 was carried forward for multivariate analysis. We checked for confounding and interaction. We also checked to find the best model.

Ethical considerations

COVID-19 in Uganda had been declared a public health emergency. The Uganda Ministry of Health (MoH) gave the directive to conduct epidemiological investigations and response to COVID-19 disease in the country. Additionally, the Office of the Associate Director for Science, U.S. Centers for Disease Control and Prevention, determined that this activity was in response to a public health emergency with the primary intent to guide public health practice (epidemic disease control activity) and was not human subjects research.

We received permission from the Director of Mulago National Referral Hospital and the Head of COVID-19 Treatment Unit (CTU) to conduct the study. For confidentiality reasons, data from the files was extracted from the CTU. Verbal consent was sought from each the next of kin of the patients before asking about the patient's vaccination status. We stored data in password-protected computers and data was not shared with anyone outside the investigation team.

Results

Demographic and clinical characteristics of COVID-19 patients admitted in Mulago Hospital, Uganda, during Uganda's third COVID-19 wave

We identified 206 patients whose median age was 53 years (interquartile range [IQR] 20 – 74 years). Of these, 112(54%) were females, 59 (29%) of the patients had received any vaccination with 38 (64%) being fully vaccinated, and 127(62%) had comorbidities with 43% had 2 or more commodities. Hypertension was the commonest comorbidity affecting 44% of the patients and 40 (20%) of the patients died.

Of the deaths, 19(47%) were females, 10(25%) of the patients had received any vaccination with 7 (17%) being fully vaccinated, and 27(67%) had comorbidities with 21(52%) having hypertension. Among other commodities were liver disease, cancers, thyroid disease, obesity, and Parkinson disease. The median age of the deaths was 63 years ([IQR] 49 – 78 years).

The outcome was significantly different across the different age categories while sex, vaccination status, having a comorbidity were not significantly different across the different categories.

Table 1: Demographic and clinical characteristics of COVID-19 patients admitted in Mulago Hospital, Uganda, during Uganda's third wave

Variable	Total n (%)	Dead n (%)	Alive n (%)	P value
Total	206 (100)	40 (19)	166 (81)	
Sex				
Male	94(46)	21(53)	73(44)	
Female	112(54)	19(47)	93(56)	0.33
Age group				
0-25	30(15)	1(2)	29(18)	
26-40	35(17)	3(7)	32(19)	
41-65	69(33)	17(43)	52(31)	
66+	472(35)	19(48)	53(32)	0.012
Vaccinated				
No	145 (71)	30(75)	117(70)	
Partially	21(10)	3(8)	18(11)	
Fully	38 (19)	7(17)	31(19)	0.79
Comorbidity				
No	79(38)	13(33)	66 (40)	
Yes	127(62)	27(67)	100 (60)	0.40
Multiple comorbidities				
0	79(38)	13(32)	66(40)	
1	72(35)	15(38)	57(34)	
2+	55(27)	12(30)	43(26)	0.69
Hypertension				
No	116(56)	19(48)	97(58)	
Yes	90(44)	21(52)	69(42)	0.21
Diabetes				
No	169(82)	32(80)	137(83)	
Yes	37(18)	8(20)	29(17)	0.71
HIV				
No	187(91)	36(90)	151(91)	
Yes	19(9)	4(10)	15(9)	0.85
Lung disease				
No	194(94)	38(95)	156(94)	
Yes	12(6)	2(5)	10(6)	0.80
Kidney disease				
No	198(96)	39(98)	159(96)	
Yes	8(4)	1(2)	7(4)	0.61
Heart disease				

No	194(94)	37(93)	157(95)	
Yes	12(6)	3(7)	9(5)	0.61
Sickle Cell Disease				
No	200(97)	39(98)	161(97)	
Yes	6(3)	1(2)	5(3)	0.86
Others				
No	188(91)	37(93)	151(91)	
Yes	18(9)	3(7)	15(9)	0.76

Factors associated with death among COVID-19 patients admitted in Mulago Hospital, Uganda, during the third wave

At bivariate level, only age was significantly associated with death. Other factors including sex, comorbidities, and vaccination status had no significant association with death

At multivariate level, only age was associated with death and hypertension confounded age. The log risk of death among patients aged 45-65 years were 7.6 times that of patients aged 0-25 years while the risk of death among patients aged 66+ years were 8.1 times that of those aged 0-25 years (Table 2).

Table 2: Factors associated with death among COVID-19 patients admitted in Mulago Hospital, Uganda, during Uganda's the third wave

		Unadjusted		Adjusted	
Variable	**Death n (%)**	**lnRR**	**(95%CI)**	**lnRR**	**(95%CI)**
Sex					
Male	21(53)	1			
Female	19(47)	0.76	(0.44-1.3)		
Age					
0-25	1(2)	1		1	
26-40	3(7)	2.6	(0.28 – 23)	2.6	(0.28 – 23)
41-65	17(43)	7.4	(1.03 – 53)	7.6	(1.04 – 55)
66+	19(48)	7.9	(1.1-56)	8.1	(1.1-59)
Vaccinated					
No	145 (71)	1			
Partially	21(10)	0.70	(0.23-2.1)		
Fully	38 (19)	0.90	(0.43-1.9)		
Comorbidity					
No	79(38)	1			
Yes	127(62)	1.3	(0.71-2.4)		

Multiple comorbidities					
0	79(38)	1			
1	72(35)	1.3	(0.65-2.5)		
2+	55(27)	1.3	(0.65-2.7)		
Hypertension					
No	116(56)	1		1	
Yes	90(44)	1.4	(0.82-2.5)	0.95	(0.55-1.63)
Diabetes					
No	169(82)	1			
Yes	37(18)	0.94	(0.73 -1.2)		
HIV					
No	187(91)	1			
Yes	19(9)	1.1	(0.44-2.7)		
Lung disease					
No	194(94)	1			
Yes	12(6)	0.85	(0.23-3.1)		
Kidney disease					
No	198(96)	1			
Yes	8(4)	0.64	(0.99-4.1)		
Heart disease					
No	194(94)	1			
Yes	12(6)	1.3	(0.47-3.7)		
Sickle Cell Disease					
No	200(97)	1			
Yes	6(3)	0.86	(0.14-5.3)		
Others					
No	188(91)	1			
Yes	18(9)	0.85	(0.29-2.5)		

Discussion

We investigated the factors associated with death among COVID -19 hospitalized patients in Mulago Hospital. Our findings showed that increasing age, starting with 41 years was associated with death. However, not being vaccinated, and having comorbidities were not associated with dying.

Similar to this study, increasing age has been found to be associated with death and severe outcomes in many studies globally [9, 14, 16]. This could be due to the age-dependent defects

in B-cell and T-cell function and the excess production of type 2 cytokines which could lead to prolonged proinflammatory responses and deficiency in control of viral replication, predisposing the patients to poor outcomes including death [17]. Furthermore, there are many other risk factors in older patients like comorbidities and sarcopenia [18]. In addition, hypertension was found to confound age and this could be because mortality in patients with hypertension increases with advanced age [19].

In this study, there was no association between sex and death. This is contrary to other studies that have showed that males are more likely to have severe outcomes and death [9, 10, 14]. The male susceptibility has been associated to the differences in the levels and type of circulating sex hormones in males and females. This difference has been thought to influence the susceptibility of COVID-19 infection [20] and this has been supported by studies that show that adaptive and innate immunity responses are modulated by sex hormones [21]. Men have been showed to have an increased susceptibility to COVID-19 infection, susceptibility, higher viral spread, and more severe disease with worse outcome. This could be due to the increase in ACE2 expression in the lungs and the androgen stimulation of TMPRSS2 expression and/or the expression of TMPRSS2 variants among men [22] . Thus, it is important that male sex still be considered as a risk factor for death among COVID-19 patients.

Comorbidities were not associated with death in this study which is contrary to other studies that have showed that patients with comorbidities are more likely to die [9, 16]. This has been attributed to the high expression of angiotensin converting enzyme 2 (ACE2) receptor among patients with hypertension, diabetes, and cardio vascular disease especially in males [23, 24]. The reason for the lack of association of comorbidities and death in this study is unknown. However, comorbidities are still an important risk factor for severe disease and death among COVID-19 patients.

In this study, not being vaccinated was not associated with death. This is contrary to other studies which have showed that vaccination decreases hospitalization and severe outcomes due to COVID-19 [25, 26]. The lack of association between vaccination status and death could have been due to the low number of vaccinated patients in our study. Despite the lack of association between vaccination status and death among the patients, vaccination is known to have a big contribution to protection from severe COVID -19 disease. Thus, vaccination

should still be considered protective against severe disease and death among COVID-19 hospitalized patients.

Limitations

We could not assess effects of use of chronic medications and respiratory support among the patients yet they have been reported to increase someone's risk for death. Our conclusions are based on a relatively small sample size of 206, which may have led to either led to an underestimation or overestimation of the study outcomes. Despite the limitation, our study ruled out the speculation of people vaccinated against COVID19 dying at the time.

Conclusion and recommendation

There was increased risk of death among older patients. There was no association of vaccination status, sex, and comorbidities with death among the patients. There is need to strengthen COVID-19 monitoring, and care among older persons.

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References

1. World Health organization, *Coronavirus disease (COVID-19) Pandemic*. 2020.
2. World Health Organization, *https://covid19.who.int/region/afro/country/ug*. 2022.
3. file:///C:/Users/HP/Dropbox/My%20PC%20(DESKTOP-7JPG7SD)/Downloads/COVID-19-Resurgence-Plan-June2021-June-2022.pdf, 2021.
4. https://www., W.C.-c.p., *worldometers.info/coronavirus (accessed April 8, 2021). 2 Israel Ministry of Health. COVID-19 database (in Hebrew).* 2021.
5. https://observer.ug/news/headlines/70361-delta-variant-driving-up-covid-19-infections-in-uganda-drc, *Delta variant driving up Covid-19 infections in Uganda, DRC.* 2021.
6. https://healthpolicy-watch.news/the-time-bomb-in-ugandas-health-care-system-reflections-from-the-emergency-room/, *Can Uganda Contain Its COVID-19 Infection Spike? Reflections Of An Emergency Room Doctor.* 2021.
7. Kyeyune, H., *Uganda confirms 1st cases of omicron coronavirus variant: Detection of new virus strain, growing list of new restrictions expected to affect travel plans ahead of Christmas*, in *AAA News Broadcasting System*. 2021.
8. Kiconco, A., *Uganda is out of COVID-19 third wave, says health minister*, in *KIU news*. 2022.
9. Silva, P.V.D., et al., *Risk Factors for Death Among 120,804 Hospitalized Patients with Confirmed COVID-19 in São Paulo, Brazil.* Am J Trop Med Hyg, 2021. **105**(1): p. 88-92.
10. Wang, D., et al., *Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China.* Jama, 2020. **323**(11): p. 1061-1069.
11. Williamson, E.J., et al., *Factors associated with COVID-19-related death using OpenSAFELY.* Nature, 2020. **584**(7821): p. 430-436.
12. Bongomin, F., et al., *High Mortality During the Second Wave of the Coronavirus Disease 2019 (COVID-19) Pandemic in Uganda: Experience From a National Referral COVID-19 Treatment Unit.* Open Forum Infect Dis, 2021. **8**(11): p. ofab530.
13. *Coronavirus (COVID-19) Vaccinations*.

14. *Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) - United States, February 12-March 16, 2020.* MMWR Morb Mortal Wkly Rep, 2020. **69**(12): p. 343-346.
15. Samarasekera, U., *Feelings towards COVID-19 vaccination in Africa.* Lancet Infect Dis, 2021. **21**(3): p. 324.
16. *[The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]*. Zhonghua Liu Xing Bing Xue Za Zhi, 2020. **41**(2): p. 145-151.
17. Opal, S.M., T.D. Girard, and E.W. Ely, *The immunopathogenesis of sepsis in elderly patients.* Clin Infect Dis, 2005. **41 Suppl 7**: p. S504-12.
18. Wang, K., et al., *Clinical and Laboratory Predictors of In-hospital Mortality in Patients With Coronavirus Disease-2019: A Cohort Study in Wuhan, China.* Clin Infect Dis, 2020. **71**(16): p. 2079-2088.
19. Zhong, L., et al., *Effects of hypertension on the outcomes of COVID-19: a multicentre retrospective cohort study.* Ann Med, 2021. **53**(1): p. 770-776.
20. Parohan, M., et al., *Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies.* The Aging Male, 2020. **23**(5): p. 1416-1424.
21. Jaillon, S., K. Berthenet, and C. Garlanda, *Sexual Dimorphism in Innate Immunity.* Clin Rev Allergy Immunol, 2019. **56**(3): p. 308-321.
22. Pivonello, R., et al., *Sex Disparities in COVID-19 Severity and Outcome: Are Men Weaker or Women Stronger?* Neuroendocrinology, 2021. **111**(11): p. 1066-1085.
23. Patel, S.K., et al., *From gene to protein-experimental and clinical studies of ACE2 in blood pressure control and arterial hypertension.* Front Physiol, 2014. **5**: p. 227.
24. Patel, S.K., E. Velkoska, and L.M. Burrell, *Emerging markers in cardiovascular disease: where does angiotensin-converting enzyme 2 fit in?* Clin Exp Pharmacol Physiol, 2013. **40**(8): p. 551-9.
25. Tenforde, M.W., et al., *Association Between mRNA Vaccination and COVID-19 Hospitalization and Disease Severity.* Jama, 2021. **326**(20): p. 2043-2054.
26. Lauring, A.S., et al., *Clinical Severity and mRNA Vaccine Effectiveness for Omicron, Delta, and Alpha SARS-CoV-2 Variants in the United States: A Prospective Observational Study.* medRxiv, 2022.