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COVID-19 Vaccination: Impact on Disease Severity and Mortality in an African Setting

Vacunación COVID-19: Impacto en la gravedad y mortalidad de la enfermedad en un entorno africano

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Abstract

Objectives: Ending the current COVID-19 pandemic entails attaining herd immunity, requiring high vaccination rates. However, vaccination rates remain very low in our setting, vaccine hesitancy due to lack of sufficient data on actual benefits of being vaccinated being a major cause. This study aimed at assessing the benefits of COVID-19 vaccination on disease severity and mortality.
Methods: Retrospective cohort study for COVID-19 patients managed by the Bamenda Regional Hospital from August 2021 to February 2022, using regression to asses relationship between vaccination status and disease severity, as well as mortality.
Results: The 1389 participants included in our study had a mean age of 49.5 (±19.5) years and a female predominance 60.2% (836). A total of 81(5.8%) patients were fully vaccinated and 77(5.5%) were partially vaccinated. Overall, 485(34.9%) had comorbidities, 419(30.2%) were admitted with moderate to severe disease, among which 137(32.7%) died. Among patients admitted with moderate to severe disease, only 2 (0.5%) were fully vaccinated and 6 (1.4%) partially vaccinated, where those fully vaccinated had lower odds of having severe disease (OR =0.05; $CI_{95\ (0.01\text{-}0.18)}$; *p=0.000*), as well as partially vaccinated (OR =0.15; $CI_{95\ (0.06\text{-}0.35)}$; *p=0.000*). Among patients who died, only 2 (1.5%) were partially vaccinated and none fully vaccinated, where being vaccinated (partially) did not affect odds of mortality (OR =1.02; $CI_{95\ (0.19\text{-}5.65)}$; *p=0.980*).
Conclusion: Being fully vaccinated and to a lesser extent partially vaccinated was associated with lower odds for severe disease. As for mortality, complete vaccination was suggestive for being protective while partial vaccination had no effect.

Key words: COVID-19, mortality, severe disease, vaccination.

Resumen

Objetivos: Poner fin a la actual pandemia de COVID-19 implica lograr la inmunidad colectiva, lo que requiere altas tasas de vacunación. Sin embargo, las tasas de vacunación siguen siendo muy bajas en nuestro medio, siendo la reticencia a la vacunación por falta de datos suficientes sobre los beneficios reales de vacunarse una de las principales causas. Este estudio tuvo como objetivo evaluar los beneficios de la vacunación COVID-19 sobre la gravedad y la mortalidad de la enfermedad.
Métodos: estudio de cohorte retrospectivo para pacientes con COVID-19 atendidos por el Hospital Regional de Bamenda desde agosto de 2021 hasta febrero de 2022, utilizando regresión para evaluar la relación entre el estado de vacunación y la gravedad de la enfermedad, así como la mortalidad.
Resultados: Los 1389 participantes incluidos en nuestro estudio tenían una edad media de 49,5 (±19,5) años y un predominio femenino del 60,2% (836). Un total de 81 (5,8%) pacientes estaban completamente vacunados y 77 (5,5%) estaban parcialmente vacunados. 485 (34,9%) tenían comorbilidades, 419 (30,2%) ingresaron con enfermedad moderada a grave, de los cuales 137 (32,7%) fallecieron. Entre los pacientes ingresados con enfermedad de moderada a grave, solo 2 (0,5%) estaban completamente vacunados y 6 (1,4%) parcialmente vacunados. Los que estaban completamente vacunados tenían menos probabilidades de tener una enfermedad grave (OR = 0,05; IC95 (0,01-0,18); p=0,000), así como parcialmente vacunados (OR =0,15; IC95 (0,06-0,35); p=0,000). Entre los pacientes que fallecieron, solo 2 (1,5 %) estaban parcialmente vacunados y ninguno completamente vacunado, por ello estar vacunado (parcialmente) no afectó las probabilidades de mortalidad (OR = 1,02; IC95 (0,19-5,65); p = 0,980).
Conclusión: estar completamente vacunado y, en menor medida, parcialmente vacunado se asoció con menores probabilidades de enfermedad grave. En cuanto a la mortalidad, la vacunación completa fue sugerente por ser protectora mientras que la vacunación parcial no tuvo efecto.

Palabras clave: COVID-19, mortalidad, enfermedad grave, vacunación.

Introduction

Coronavirus disease (COVID-19) is an acute respiratory disease caused by the highly contagious novel coronavirus (SARS-CoV-2) which emerged from Wuhan, China in December 2019[1] which was declared a global pandemic in March 2020 by the World Health Organization (WHO)[2,3]. As of the 11th November 2021, WHO weekly epidemiologic reports indicated a global rise of new COVID-19 confirmed cases and deaths with a cumulative 251 million cases for 5 million deaths since the start of the pandemic[4]. In Africa there were overall 6.2 million cases and 151 thousand deaths while Cameroon cumulatively had 105,719 cases for 1,758 deaths[4]. The several drugs currently in clinical trials for treatment, and recommended preventive measures such as social distancing and wearing of face masks have so far not been sufficient to stop the spread of the disease[5-7].

This led to emergency development of several vaccines in order to decrease transmission and prevent progression to severe and fatal disease, and as of the 5th November 2021, WHO had approved 8 vaccines for use[7,8]. The first mass vaccination program started in the early December 2020 and in Cameroon vaccination began in April 2021[9,10].

Vaccination rates as high as 67% are crucial to achieving herd immunity[11-13]. However, vaccine trackers as of the 11th November 2021, indicated that vaccination rates were at 40.3% globally, 9.5% in Africa and only 0.6% in Cameroon[14].

Despite availability of several approved vaccines, vaccine hesitancy remains a major barrier for achieving herd immunity with the major reasons being concerns related to vaccine efficacy, safety, side effects and the historic speed with which the vaccines were developed[12].

From our literature review, very little studies have been done in our context to assess the relationship between vaccination and COVID-19 related morbidity and mortality. This study will help increase our knowledge of benefits of vaccination. Hence, reduce vaccine hesitancy, thereby driving vaccination rates towards achievement of herd immunity.

Methods

This was a 7 months hospital based retrospective cohort study from the 18th August 2021 to 28th February 2022, carried out in the COVID-19 treatment centre of the Bamenda Regional Hospital. This is a second level referral hospital in the North West Region of Cameroon.

We included files of all patients aged ≥ 18 years managed by the COVID-19 treatment centre of the Bamenda Regional Hospital within the study period with RT-PCR (polymerase chain reaction) and/or a rapid antigenic test (RDT) confirmed COVID-19, with exclusion criteria being files with incomplete data on essential elements (age, vaccination status, SpO_2, outcome).All files meeting our selection criteria were included following a consecutive non-probability sampling method. However, with expected prevalence of vaccination in Cameroon to be 15.1% from a WHO survey done in 2021[15], a minimum sample size of 200 was required, with a 5% precision and 95% confidence interval. Among the recruited cases, we proceeded with extraction of data using pre-designed data collection sheets(questionnaires) which did not disclose the patient's identities. In a bit to attain our objectives and answer our research question, data on the following variables was extracted: Socio-demographic parameters (age, gender), COVID-19 vaccination status (unvaccinated, vaccinated, partially vaccinated, fully vaccinated), co-morbidities, clinical presentation, Clinical staging (asymptomatic, mild, moderate, severe/critical disease), outcome (survived, death).

We considered fully vaccinated as haven received the second dose in a 2-dose series (Sinopharm, AstraZeneca, Spoutnik, Moderna and Pfizer-BioNTech COVID-19 vaccines) or after 1 dose of the single dose Janssen (Johnson & Johnson); partially vaccinated after receipt of the first dose or <14 days after the second dose in a 2-dose series (Sinopharm, AstraZeneca, Spoutnik, Moderna and Pfizer-BioNTech COVID-19 vaccines), and unvaccinated as one who did not receive any COVID-19 vaccine dose. Regarding clinical staging, it was: asymptomatic for individuals with positive COVID-19 RDT and/or PCR in the absence of symptoms of the disease; mild for individuals who have any of the various signs and symptoms of COVID-19 (e.g. fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting diarrhoea, loss of taste and smell) but who do not have shortness of breath, dyspnoea, or abnormal chest imaging; moderate for patients presenting with fever and signs of acute respiratory infection such as cough, difficulty in breathing, respiratory rate 20-29 bpm, heart rate > 90 but < 120 bpm, SPO_2> 92% with or without manifestations of pneumonia can be seen on imaging; and severe illness considered for presentation with fever (temperature > 38.5ºC), signs of acute infection and at least one of the following criteria: Respiratory rate > 30 bpm, severe respiratory distress, SpO_2<92% in ambient air, progression of pulmonary lesions in imaging> 50% in 24-48h, cyanosis, impaired consciousness[16]. Admission criteria being patients with moderate to severe disease[16].

Ethical considerations

Ethical clearance was obtained from the Institutional Review Board (IRB) of the Faculty of Health Sciences of the University of Bamenda (No: 2022/0395H/UBa/IRB) and administrative authorization to carry out the research in the North West Region was obtained from the North West Regional Delegation of Public Health.

An administrative authorization to carry out the research in the COVID-19 treatment center of the BRH was also obtained from the Director of the hospital.

Data management and analysis

Data was collected using a password protected REDCap (Research Electronic Data Capture) account designed to capture data for clinical research and create a data base which was exported to Microsoft office excel 2016. Analysis was done using the statistical software SPSS (Statistical Package for the Social sciences) version 26, with statistical significance defined by a p-value <0.05 using logistic regression analysis to assess cause to effect between predictor and outcome variables. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as proportions or percentages.

Results

From 18th August 2021 to 28th February 2022, 1917 records of patients managed by the COVID-19 treatment centre during our study period were retrieved. Two hundred and eighteen (218) were aged < 18 years and three hundred and ten (310) had incomplete data on our important variables. The remaining one thousand three hundred and eighty-nine (1389) were included in our study.

Out of 1389 patients, majority 836 (60.2%) were females, giving a male to female sex ratio of 0.7.The age ranged from 18 to 100 years, with a mean of 49.52 (± 19.48) years; 34.9% (485) had comorbidities; majority 40.4% (561) had the mild form of the disease (**Table I**).Of the 485 patients with comorbidities, the most common were Hypertension 351 (72.4%), Diabetes mellitus 145 (29.9%) and HIV 46 (9.5%) (**Figure 1**).

A total of 157 were vaccinated giving a vaccination rate of 11.3%. Four hundred and twenty-three (30.5%) where admitted while 966 (69.5%) where managed on home confinement. Of the 423 admissions, 8 where vaccinated giving a vaccination rate of 1.9% among hospitalised. Also, 81 (5.8%) were fully vaccinated and 76 (5.5%) partially vaccinated (**Figure 2**). Among those fully vaccinated, majority were females 47 (58.0%), aged ≤ 60 years 68 (84.0%), had no comorbidities 60 (74.1%), and had mild disease 52 (64.2%) (**Table II**). Regarding the vaccines, 139 vaccine doses were received by our participants, majority of which were the Johnson and Johnson vaccine 62 (44.6%).

Table I: Characteristics of the study population (N =1389).

Variables	Number	Percentage (%)
Sex		
Male	553	39.8
Female	836	60.2
Age (years)		
≤ 60	931	67.0
> 60	458	33.0
Comorbidities		
Present	485	34.9
Absent	904	65.1
Classification		
Asymptomatic	62	4.4
Mild	561	40.4
Moderate	451	32.5
Severe	315	22.7

Among the 419 patients with moderate to severe form of the disease, majority, 411 (98.1%) were not vaccinated, 221 (57.7%) were females, 303 (72.3%) were aged > 60 years, and 255 (60.9%) had comorbidities. Being fully vaccinated (aOR=0.015; $CI_{95(0.00-0.09)}$; *p=0.000*) and partially vaccinated (aOR=0.129; $CI95_{(0.04-0.419)}$; *p=0.001*) were protective factors whereas, being a male (aOR=2.15; $CI_{95(1.46-3.18)}$;*p=0.000*); being aged > 60 (aOR=24.74; $CI_{95(16.38-37.35)}$;*p=0.000*) and having comorbidities (aOR=12.43; $CI_{95(8.14-18.99)}$;*p=0.000*) increased the risk (**Table III**).

Among the 137 patients who died, majority, 135 (98.5%) were not vaccinated, 78 (56.9%) were males; 121 (88.3%) aged > 60 years and 87 (63.5%) had comorbidities. After adjusting for confounders, the odds of dying were increased by being of male gender (aOR=1.83; $CI_{95(1.19-2.81)}$; *p=0.006*) and being aged > 60 years (aOR=4.30; $CI_{95(2.41-7.68)}$; *p=0.000*). Vaccination status had no significant effect on mortality (**Table IV**).

Discussion

This study was aimed at determining the vaccination rate, assess the relationship between vaccination status and disease severity as well as mortality in patient managed by the COVID-19 treatment centre of BRH. The results were analysed in accordance with our objectives making it possible to meet the said objectives.

However, there are limitations to this study. It was a retrospective study and some missing data was noted in some files. Some of the severe cases and/or deaths might have been directly related to comorbidities rather than COVID-19. Vaccination was done only in adults above 18 years, so we could not assess severity and mortality in all age groups. That notwithstanding, despite these limitations, we attained our prior set objectives.

The vaccination rate of 11.3% we found was similar to a WHO survey done in 2021 in the south west region of Cameroon which had 15.1% vaccination rate15, but was far lower from the 43% findings of Muthukrishnan et al in India, 2021. That was half that of Naleway et al, 2021 US who found a vaccination rate of 22.3%17. This difference could be due to the fact that Cameroon has higher vaccination hesitancy rates compared to high-income countries and unavailability of all vaccines all the time[18].

Table II: Characteristics of the study population according to vaccination status (N =1389).

Variables	Fully Vaccinated* N = (81)		Not Vaccinated** N = (1308)		TOTAL N = (1389)	
	Number	%	Number	%	Number	%
Sex						
Male	34	42.0	519	39.7	553	39.8
Female	47	58.0	789	60.3	836	60.2
Age (years)						
≤ 60	68	84.0	863	66.0	931	67.0
> 60	13	16.0	445	34.0	458	33.0
Comorbidities						
Present	21	25.9	464	35.5	485	34.9
Absent	60	74.1	844	64.5	904	65.1
Classification						
Asymptomatic	4	4.9	58	4.4	62	4.4
Mild	52	64.2	509	38.9	561	40.4
Moderate	23	28.4	428	32.7	451	32.5
Severe	2	2.5	313	23.9	315	22.7

* Any patient who has received one dose of Johnson and Johnson or 2 doses of Sinopharm or Astrazeneca
**Any patient who hasn't received any dose of vaccine or just one dose of Sinopharm or Astrazeneca.

Table III: Vaccination status and other factors related to disease severity (N =1038).

Variables	Group 1*	Group 2**			Multivariate logistic regression	
	Number (%)	Number (%)	OR [95% CI]	P-value	aOR [95% CI]	P-value
Vaccination status						
Not vaccinated	411 (98.1)	513 (82.9)	Reference		Reference	
Fully vaccinated	2 (0.5)	56 (9.0)	0.05 [0.01-0.18]	**0.000**	0.015 [0.002-0.087]	**0.000**
Partially vaccinated	6 (1.4)	50 (8.1)	0.15 [0.06-0.35]	**0.000**	0.129 [0.040-0.419]	**0.001**
Gender						
Female	221 (57.7)	386 (62.4)	Reference		Reference	
Male	198 (42.3)	233 (37.6)	1.48 [1.15-1.91]	**0.002**	2.15 [1.46-3.18]	**0.000**
Age (years)						
≤ 60	116 (27.7)	560 (90.5)	Reference		Reference	
> 60	303 (72.3)	59 (9.5)	24.79 [17.59-34.94]	**0.000**	24.74 [16.38-37.35]	**0.000**
Comorbidities						
Absent	164 (39.1)	545 (88.0)	Reference		Reference	
Present	255 (60.9)	74 (12.0)	11.45 [8.38-15.65]	**0.000**	12.43 [8.14-18.99]	**0.000**

Group 1*: patients with asymptomatic to mild form (not hospitalised)
Group 2**: patients with moderate to severe form (hospitalised)

Table IV: Vaccination status and other factors related to mortality in admitted patients (N= 419).

Variables	Died	Survived			Multivariate logistic regression	
	Number (%)	Number (%)	OR [95% CI]	P-value	aOR [95% CI]	P-value
Vaccination status						
Not vaccinated	135 (98.5)	276 (97.9)	Reference		Reference	
Fully vaccinated	0 (0.0)	2 (0.7)	**Undefined**		**Undefined**	
Partially vaccinated	2 (1.5)	4 (1.4)	1.02 [0.19-5.65]	0.980	1.31 [0.21-8.12]	0.765
Gender						
Female	57 (43.1)	162 (54.4)	Reference		Reference	
Male	78 (56.9)	120 (42.6)	1.79 [1.18-2.70]	**0.006**	1.83 [1.19-2.81]	**0.006**
Age (years)						
≤ 60	16 (11.7)	100 (35.5)	Reference		Reference	
> 60	121 (88.3)	182 (64.5)	4.16 [2.34-7.39]	**0.000**	4.30 [2.41-7.68]	**0.000**
Comorbidities						
Absent	50 (36.5)	114 (40.4)	Reference		Reference	
Present	87 (63.5)	168 (59.6)	1.18 [0.78-1.80]	0.440	1.27 [0.82-1.97]	0.287

Being fully and partially vaccinated were found to be protective factors against severe forms of the disease, with fully being more protective than partially. This was similar to results of a study by Mohammed et al, in 2022 which showed that vaccination effectively reduces the chances of getting severe disease[19], as well as with findings of Macchia et al in Argentina, 2021 which found that being fully as well as partially vaccinated was associated with lesser risk of getting severe disease[20].

On the other hand, other factors were found to increase the risk of severity. These included Being of male gender; which could be explained by the fact that androgen play an important role in COVID-19 infectivity. Following

binding to ACE 2 receptors, SARS-CoV-2 requires Type II transmembrane Serine Protease (TMPRSS2) to enable fusion and entry into the host cell. This receptor has been found to be up regulated by androgens, so with males having higher levels of androgens compared to females; this could explain more severe disease in males[21]. Being aged > 60 years; which could be explained by the increased expression of ACE2 receptors in older patients. This receptor has been established as the functional host receptor for SARS-CoV-2. As a recall, vaccines against COVID-19 all lead to the production and exposure of the immune system to viral-like antigens which stimulate both cellular (through T cells) and Humoral (through B cells which produce antibodies) to keep a memory of the offending agent thereby mounting a strong and fast response when confronted to the infection. This response diminishes with aging (immunoscence), which can explain increased severity in older patients as a result of inadequate vaccine-induced protection[22].

And having comorbidities; which could be explained by the fact that majority of patients with comorbidities had hypertension and diabetes mellitus among others which are associated with increased expression of ACE2 receptors[23]. Moreover, it could equally be explained by the fact that comorbidities are associated to the process of immunoscence mentioned earlier making such patients more susceptible to severe disease.

The effect of being fully vaccinated on mortality couldn't be assessed as no fully vaccinated died, whereas, being partially vaccinated had no significant effect on mortality. This was consistent with to the findings of Muthukrishnan et al in India, 2021 where being partially vaccinated equally had no significant effect on mortality[24], but was different from findings of Macchia et al in Argentina 2021 who found that being fully as well as partially vaccinated was associated with lesser chances of mortality[20]. These differences can be explained by the effects of various variants in certain populations conferring certain degrees of resistance to vaccine-induced protection[5]. Moreover, there is the implementation of vaccine boosters in some countries which could influence the degree of protection conferred by vaccination. Furthermore, administration of different vaccine types could be related to different degrees of vaccine-induced immunisations.

That notwithstanding, certain factors were found to increase the odds of mortality. They include: Being of male gender which was consistent with findings of Hippisley-cox et al in 2021 in the United Kingdom which showed increased mortality among males[25], but contrary to the findings of Muthukrishnan et al in India, 2021 where it was rather being a female which was associated with mortality[24].This difference could be due to different gender and racial characteristics of different populations.

In addition, being aged > 60 years equally increased the odds of dying. which was similar to the findings of Muthukrishnan et al in India, 2021 where increasing age was associated with an increased odds of mortality[24]. This is consistent with the fact that older patients are prone to poorer outcomes in infectious diseases due to higher expressions of ACE2 receptors and also dysfunction of immune response (immunoscence) after vaccine administration or prior infection[22,26].

The vaccination rate in the COVID-19 treatment centre of the BRH was 11.3%, with 5.8% actually being fully vaccinated for 5.5% partially, with Johnson & Johnson being the most frequently received vaccine (44.6%). Vaccination against COVID-19 was associated with decreased odds of having severe disease, which was more in fully vaccinated compared to partially vaccinated. Being of female gender, aged ≤ 60 years and absence of comorbidities decreased the odds of severe disease. The effect of complete vaccination on mortality could not be assessed due absence of any deaths among admitted patients who were fully vaccinated, whereas partial vaccination had no significant effect on mortality. However, the absence of any fully vaccinated among deaths is suggestive of protective effect of complete vaccination. Moreover, being a female and aged ≤ 60 years decreased odds of dying.

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Authors' Contributions

1.Conception – A.C, P.K.U; 2. Design – A.C; 3. Supervision A.C, A.M.T, S.A; 4. Resources- D.N.N, S.A; 5. Materials -D.N.N; 6. Data Collection and/or Processing - P.K.U, A.M.T. A.M.J.P, 7. Analysis and/or Interpretation – P.K.U, A.M.T, 8. Literature Review - P.K.U, A.C, A.M.T; 9. Writing – P.K.U, A.C; 10. Critical Review –A.C., A.M.T, L.L.N, A.M.J.P.

Ethical statement

Ethical clearance was obtained from the Institutional Review Board (IRB) of the Faculty of Health Sciences of the University of Bamenda (No: 2022/0395H/UBa/IRB) an administrative authorization to carry out the research in the North West Region was obtained from the North West Regional Delegation of Public Health. An administrative authorization to carry out the research in the COVID-19 treatment center of the BRH was also obtained from the Director of the hospital.

Conflict of Interest Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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