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Prevalence and factors associated with tuberculosis mortality among clinically diagnosed tuberculosis patients in Rwanda: analysis of 2019 to 2022 national tuberculosis program data

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ABSTRACT

Background: Tuberculosis (TB) continues to be a public health challenge not only in Rwanda, but also worldwide. Existing literature indicates that TB is one of the most leading causes of death. However, the available evidence indicates a limited understanding of the association between TB and mortality, specifically in Rwanda. Therefore, the aim of this study was to investigate the prevalence, and factors associated with mortality among clinically diagnosed tuberculosis (TB) patients in Rwanda.

Method: This study employed a cross-sectional study design, using data from 4,028 TB patients who were clinically diagnosed and registered in the computerized TB case-based surveillance system used by health facilities nationwide from July 2019 to June 2022. Multivariate analysis was conducted to determine the adjusted association between TB and mortality, while controlling for confounding factors.

Results: Of the total sample, 506 (14.7%) died during treatment. The findings indicate that in the univariate analysis, most variables showed a significant association with TB mortality. For instance, individuals aged 50 and above (COR=2.5, 95% CI=2.10-3.03) and females (COR=1.30, 95% CI=1.09-1.56) were more likely to die. Additionally, having pulmonary tuberculosis (COR=1.21, 95% CI=1.01-1.44), being HIV-positive (COR=1.99, 95% CI=1.46-2.72), or being underweight (COR=1.39, 95% CI=1.14-1.69) showed a higher likelihood of mortality. After controlling for different variables, older age (AOR=2.54, 95% CI=2.10-3.06), underweight (AOR=1.39, 95% CI=1.14-1.69), and HIV-positive status (AOR=2.93, 95% CI=2.59-3.59) remained significantly associated with mortality.

Conclusion: This study highlights the high TB mortality rate among TB patients clinically diagnosed in Rwanda compare to the National target, which is 6.5% by the end of 2022. Additionally, the study illustrates the type of pulmonary TB need more attention as well as the patients aged above 50 years, the patients underweight as well as the patient's HIV positive. These findings could inform public health policies and interventions aimed at reducing mortality rates in TB patients in Rwanda and other similar settings.

Keywords: Tuberculosis (TB), Mortality, clinically diagnosed TB, Health facilities, Rwanda

BACKGROUND

Tuberculosis (TB) is a communicable disease that is a major cause of sickness, yet in 2022, TB was the second leading cause of death worldwide after coronavirus disease (COVID-19) and had caused as many deaths as HIV/AIDS. According to the world health organization estimates, more than 10 million people continue to fall ill with TB every year (WHO Report 2023). In 2021, the number of people felt ill of TB has increased from 10.1 million in 2020 to 10.6million (WHO, 2021), while around 1.6 million died from the illness, including 187,000 HIV-positive people. Furthermore, 54% of HIV-negative TB deaths were males, 32% were women, and 14% were children (WHO, 2022). Tuberculosis (TB) affects individuals of all sexes and ages; however, it most commonly affects adults. Men represent 56.5% of TB cases, while adult women account for 32.5%, and children for 11% (WHO, 2022). TB places a significant strain on the already overstretched health services in sub-Saharan Africa (SSA). Sub-Saharan Africa comprises 12% of the world's population, 23-29% of total TB cases in the world are found in SSA and 254,000 TB-related deaths occurred in SSA. According to WHO, the Sub-Saharan Africa has the highest global burden of TB/HIV co-infection, with over 50% of TB cases in the region being co-infected with HIV (WHO, 2023).

According to estimates from the World Health Organization, Africa is the second most affected region with a tuberculosis prevalence of 23%, following Southeast Asia with 45%. The Western Pacific region ranks third with an 18% prevalence. The Eastern Mediterranean, the Americas, and Europe exhibit lower percentages, standing at 8.1%, 2.9%, and 2.2%, respectively. In the same period, a significant portion of global tuberculosis infections, over two-thirds, were attributed to India (28%), Indonesia (9.2%), China (7.4%), the Philippines (7.0%), Pakistan (5.8%), Nigeria (4.4%), Bangladesh (3.6%), and the Democratic Republic of the Congo (2.9%). Although, Rwanda was not indicated in the countries with the highest prevalence of TB, the evidence shows that it also has higher numbers of TB patients (RBC, 2022).

According to Rwanda Biomedical Centre data, 5,538 TB patients were notified in 2022, with 26.9% clinically diagnosed, and men accounting for 72.6% while women made up 27.4% of the cases. Co-infection with TB and HIV was observed in 14.4% of all TB patients, with children under 15 years old constituting 5% of the diagnosed cases. In 2021, Rwanda predicted a TB incidence rate of 56 cases per 100,000 people, resulting in 7.3 deaths per 100,000 people.

Mortality showed a progressive increase from 4.9 in 2019 to 6.2 in 2020. Unfavorable TB treatment outcomes led to the death of 7.8% of all susceptible TB patients and 12.7% of those clinically diagnosed, while treatment coverage was reported at 71.6% (RBC, 2022). The case fatality ratio targets, set by both the Rwandan National Strategy and the End Tuberculosis Strategy, emphasize the need for a continuous reduction in CFR, underscoring the importance of timely TB diagnosis and treatment in primary healthcare settings (WHO, 2022b).

Research in different contexts has identified factors linked to mortality of Tuberculosis. A retrospective case-control investigation carried out in Cameroon revealed that TB-related deaths occurred within the initial two months of TB treatment. Contributing factors included HIV/TB coinfection, extra-pulmonary TB, sputum smear-negative pulmonary TB, and male gender (Djouma et al., 2015; Nanzaluka et al., 2021). Similarly, a study conducted in Taiwan found that the following factors were linked to an increased risk of all-cause death: male gender, end-stage renal disease, cancer, acid-fast bacilli-smear positivity, TB-culture positivity, pleural effusion on chest radiograph, and notification from an ordinary ward or intensive care unit. The study participants were 65–74 years old, (compared to the reference group of 65–74 years old). It's important to note that this study focused solely on TB mortality in elderly patients (Yen et al., 2017). A study conducted in Ethiopia, meantime, discovered that mortality from tuberculosis (TB) were highest during the first two months of treatment but gradually declined with antiretroviral therapy (ART), reaching 1 per 100 person-years after 24 months on ART. The study found a strong correlation between TB and death in HIV patients receiving antiretroviral therapy. Additionally, the same study identified an association between male gender and mortality among TB/HIV coinfecting patients (Nanzaluka et al., 2021).

TB mortality studies have been carried out in various countries and settings in the past. However, there has been no study conducted in Rwanda specifically addressing the predictors of TB mortality among clinically diagnosed patient. Understanding the prevalence and factors that contribute to tuberculosis mortality in order to develop strategies that will improve tuberculosis outcomes, stop the disease's spread, ultimately reducing mortality rates. Finding the factors that predict tuberculosis death in various practice contexts is crucial to understanding contextual obstacles and developing appropriate community- or population-based mitigation strategies. This

study was carried out to analyze the factors linked to death among TB patients clinically diagnosed in Rwanda with the aim gain deeper insights into these factors.

MATERIALS AND METHODS

Study design, setting and population

This retrospective cross-sectional study used quantitative methods to evaluate the prevalence of and factors associated with mortality among clinically diagnosed tuberculosis (TB) patients. Data were collected from the national computerized TB case-based surveillance system, covering a period from July 2019 to June 2022. The study included TB cases from 565 health facilities across the country, including 52 hospitals (8 referrals, 40 district, and 4 provincial hospitals) and 513 health centers.

The study population consisted of 4,028 clinically diagnosed TB patients who had their treatment outcomes documented in the electronic TB case-based surveillance system, following National TB Program guidelines. Patients with bacteriologically confirmed TB, treatment failures, those lost to follow-up, and individuals with outcomes reported as "not evaluated" were excluded from the analysis. The sample was nationally representative, and all TB patients meeting the inclusion criteria were retained.

Study variables.

Outcome variable:

The dependent variable in this study is ****mortality among clinically diagnosed TB patients****. Mortality was defined as death occurring during the treatment period and recorded in the national TB case-based surveillance system. This variable was treated as a binary outcome, where patients were classified as either deceased (mortality = 1) or alive (mortality = 0) during the study period.

Independent variables

Our independent variables include socio-demographic characteristics, gender (male/female), age, residence, etc., and clinical features. The clinical factors included the people who received nutrition support (Yes/No), BMI (underweight: 18.5 kg/m², normal: 18.5-24.9, overweight: 25-

29.9, obese: 30 and above), special high-risk groups (diabetes, inmates, miners), patients receiving follow up by community health workers (Yes/No), and previous TB (new/recurrent). Additionally, we also considered the HIV status (HIV negative, HIV positive, HIV unknown), Site of TB disease (pulmonary /extra-pulmonary), initiated on cotrimoxazole (Yes/No), and initiated antiretroviral (Yes/No).

Data analysis

After obtaining data from Rwanda Biomedical Centre, were cleaned, and cleaned data were exported to SPSS software version 25 package for further analysis. The study participants' clinical features and socioeconomic characteristics were described using frequency and proportions using table or figures. A bivariate logistic regression was performed to assess the association between each explanatory variable and the outcome of interest which is TB mortality. Furthermore, the multivariate logistic regression model was computed to control all significant variables retained in bivariate analysis. A p-value of less than 0.05, an adjusted odds ratio, and a 95% confidence interval were considered statistically significant.

Ethical considerations

Ethical clearance and approval were requested. A confidentiality agreement between the principal investigator and Rwanda Biomedical Center was agreed upon on data use and the privacy of patient information. To maintain anonymity both before and after the study, the primary investigator was the only individual with access to the entire dataset, with patient names and other identifiers being encrypted during the analytic process.

RESULTS

Demographic Characteristics of participants

The table 1 provides information on both sociodemographic and clinical characteristics of the study sample. The results indicate that the majority of participants were male (65.2%), with females comprising 34.8% of the sample. A significant portion of participants were below the age of 50 (74.8%), while only 24.2% were aged 50 and above. Geographically, the highest representation was from Kigali City (30.6%), followed by the Southern Province (23.7%), Eastern Province (19.5%), Western Province (18.4%), and Northern Province (7.9%). In terms of

occupation, 0.6% were mining workers, while 99.4% reported not being engaged in mining activities. Clinically, extrapulmonary TB was more prevalent (59.6%) than pulmonary TB (40.4%). Regarding HIV status, the majority were HIV-negative (82.8%), while 17.2% were HIV-positive. Treatment history revealed a majority of newly diagnosed TB cases (94.2%), with a significant proportion confirming they were on antiretroviral therapy (92.0%). About 0.8% of individuals reported being diabetic, while a quarter reported an unknown status (25%), and 74.2% reported not having diabetes. Concerning nutritional status, almost half were underweighted (48.1%), 6.7% were overweight, and 45.2% fell within the normal range. Furthermore, nearly all participants-initiated TB treatment (99.9%), with about a quarter receiving TB nutrition support (24.7%).

Table 1: Characteristics of participants

Study variables		Frequency	Percentage
Sociodemographic characteristics			
Province	West	740	18.4
	South	955	23.7
	North	317	7.9
	Kigali City	1232	30.6
	East	784	19.5
Age	<50	3011	74.8
	50 and above	1017	25.2
Sex	Male	2627	65.2
	Female	1401	34.8
Mining worker	No	4002	99.4
	Yes	26	0.6
Clinical characteristics			
Health facility worker	No	4010	99.6
	Yes	18	0.4
Site of disease	Pulmonary	1629	40.4
	Extrapulmonary	2399	59.6
HIV status	Positive	692	17.2
	Negative	3334	82.8
History of HIV	People Living with HIV	531	75.7

Previous treatment history	Newly Tested	170	24.3
	New	3794	94.2
	Previously treated	234	5.8
Currently on ART	Yes	642	92.0
	No	56	8.0
Diabetic	No	2988	74.2
	Yes	34	0.8
	unknown	1006	25.0
Start treatment	Yes	3992	99.9
	No	3	0.1
Nutrition	Underweight	1938	48.1
	Normal	1820	45.2
	Overweight	270	6.7
Received a TB Nutrition support	No	2454	75.3
	yes	805	24.7

Figure 1:Prevalence of TB mortality among clinically diagnosed Tuberculosis patients in Rwanda

The figure 1 the prevalence of TB mortality among clinically diagnosed Tuberculosis patients in Rwanda. The results show that 14.7 percent among clinically diagnosed Tuberculosis patients died.

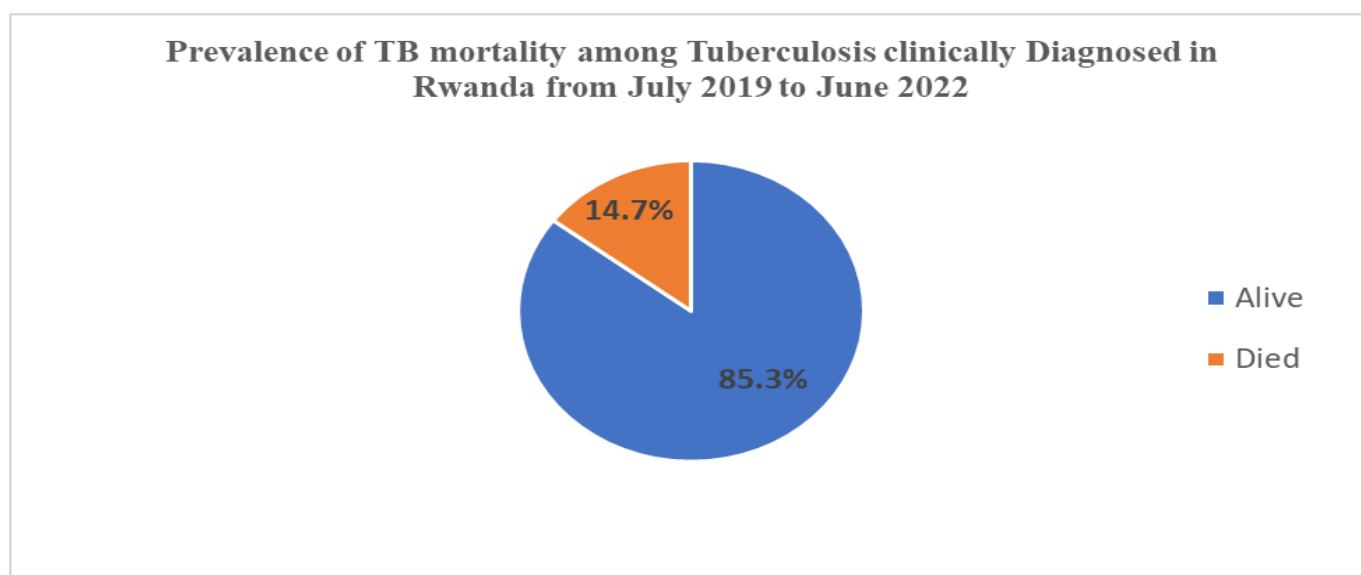


Figure 2:Prevalence of TB mortality among clinically diagnosed Tuberculosis patients in Rwanda.

During bivariate analysis, chi-square test was used to test if there is an association between sociodemographic and clinical characteristics, and TB mortality. The results show that age ($P<0.001$), sex ($P=0.004$), site of diseases, having HIV ($P<0.001$), currently being on ART ($P<0.001$), started treatment ($P<0.001$), as well as nutritional status ($P<0.001$) are significantly associated with TB mortality. No significant association was found province (0.115), being a mining worker ($p=0.312$), HIV history ($p=0.242$) or previous treatment history ($P=0.492$, being diabetic ($p=0.392$) and receiving nutritional support ($p=0.994$) (Table.2).

Table 2: Bivariate analysis of the association between sociodemographic and clinical characteristics, and mortality among TB mortality among clinically diagnosed tuberculosis patients in Rwanda.

Study variables		Died		X ²	P-value
		No Freq. (%)	Yes Freq. (%)		
Province	West	633 (85.5)	107 (14.5)	7.416	0.115
	South	814 (85.2)	141 (14.8)		
	North	278 (87.7)	39 (12.3)		
	Kigali City	1064 (86.4)	168 (13.6)		
	East	647 (82.5)	137 (17.5)		
Age	<50	2668 (88.6)	343 (11.4)	103.938	<0.001
	50 and above	768 (75.5)	249 (24.5)		
Sex	Male	2272 (86.5)	355 (13.5)	8.440	0.004
	Female	1164 (83.1)	237 (16.9)		
Mining worker	No	3412 (85.3)	590 (14.7)	1.024	0.312
	Yes	24 (92.3)	2 (7.7)		
Health facility worker	No	3420 (85.3)	590 (14.7)	0.185	0.667
	Yes	16 (88.9)	2 (11.1)		
Site of disease	Pulmonary	1366 (83.9)	263 (16.1)	4.573	0.032
	Extrapulmonary	2070 (86.3)	329 (13.7)		
HIV status	Positive	494 (71.4)	198 (28.6)	129.278	<0.001
	Negative	2940 (88.2)	394 (11.8)		
History of HIV	People Living with HIV	387 (72.9)	144 (27.1)	1.372	0.242
	Newly Tested	116 (68.2)	54 (31.8)		
Currently on ART	Yes	485 (75.5)	157 (24.5)	56.494	<0.001

	No	16 (28.6)	40 (71.4)		
Previous treatment history	New	3240 (85.4)	554 (14.6)		
	Previously treated	196 (83.8)	38 (16.2)	0.471	0.492
Diabetic	No	2541 (85.0)	447 (15.0)		
	Yes	27 (79.4)	7 (20.6)		
	Unknown	868 (86.3)	138 (13.7)	1.875	0.392
Started Treatment	Yes	3410 (85.4)	582 (14.6)		
	No	0 (0.0)	3 (100.0)	17.500	<0.001
Nutrition status	Underweight	1605 (82.8)	333 (17.2)		
	Normal	1597 (87.7)	223 (12.3)		
	Overweight	234 (86.7)	36 (13.3)	18.533	<0.001
Received nutrition support	No	2094 (85.3)	360 (14.7)		
	yes	687 (85.3)	118 (14.7)	0.000	0.994

The table 2 presents the results of univariate and multivariate analyses examining the association between study variables and TB mortality among clinically diagnosed tuberculosis patients in Rwanda. The findings indicate that in the univariate analysis, most variables showed a significant association with TB mortality. For instance, individuals aged 50 and above were 2.5 times more likely to die compared to those below 50 (COR=2.5, 95% CI=2.10-3.03). Females also exhibited a higher likelihood of mortality than males (COR=1.30, 95% CI=1.09-1.56). Patients with pulmonary tuberculosis were 1.2 times more likely to die than those with extrapulmonary TB (COR=1.21, 95% CI=1.01-1.44). Furthermore, HIV-positive patients (COR=1.99, 95% CI=2.46-3.64), showed a higher likelihood of mortality. Additionally, patients classified as underweight were 1.5 times more likely to die (COR=1.48, 95% CI=1.23-1.78).

During the multivariate analysis, several variables have also indicated a significant association with TB mortality, for example those aged 50 and above were 2.5 times more likely to die than those aged below 50 (AOR=2.54, 95%CI=2.1-3.06). On the other hand, HIV positive (AOR=2.93, 95%CI=2.59-3.59) and underweight (AOR=1.39, 95%CI=1.14-1.69) patients also showed a higher likelihood of mortality.

Table 3: Bivariate and multivariable analysis of the association between sociodemographic and clinical characteristics, and mortality among TB mortality among clinically diagnosed tuberculosis patients in Rwanda

Study variables	COR	95% C.I	Pvalue	AOR	95% C.I	Pvalue
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		Lower	Upper			Lower	Upper	
Age								
<50	1[Ref]				1[Ref]			
50 and above	2.52	2.1	3.03	<0.001	2.54	2.10	3.06	<0.001
Sex								
Male	1[Ref]				1[Ref]			
Female	1.30	1.09	1.56	<0.001	1.18	0.97	1.42	0.092
Site of disease								
Pulmonary	1.21	1.02	1.44	0.030	1.04	0.86	1.26	0.700
Extrapulmonary	1[Ref]				1[Ref]			
Nutritional status								
Underweight	1.48	1.23	1.78	<0.001	1.39	1.14	1.69	0.001
Normal	1[Ref]				1[Ref]			
Overweight	1.09	0.75	1.59	0.640	0.99	0.66	1.47	0.954
HIV status								
Negative	1[Ref]				1[Ref]			
Positive	2.99	2.46	3.64	<0.001	2.93	2.38	3.59	<0.001

COR: Crude Odd Ratio

AOR: Adjusted Odd Ratio

Ref: reference category

DISCUSSION

To the best of our knowledge, this is the first study to examine prevalence, and factors associated with tuberculosis mortality among clinically diagnosed tuberculosis patients in Rwanda. Overall, the study found that the prevalence of tuberculosis mortality among clinically diagnosed tuberculosis patients is 14.7 percent. Like other studies conducted in different countries, it was shown that the TB mortality range from 7% to 33.4% worldwide (Bukundi et al., 2021; Dizaji et al., 2018; Heunis et al., 2017; Kefale & Anagaw, 2017). The prevalence of TB mortality in Rwanda is still high when compared to the target of the End TB strategy. The strategy indicates that the case fatality rate (CFR) is required to fall to 6.5% by 2025 (Bukundi et al., 2021; Nicholson et al., 2023a). When comparing this with other African countries, the prevalence is still higher. For example, in Zambia, the proportion of deaths reported due to TB was 9% (Nanzaluka et al., 2021), in Addis Ababa, Ethiopia, it was 8.3%(Tola et al., 2019), in the WHO African Region, it was 9%, and in South Africa, it was 10.5% (Tola et al., 2019). The prevalence of mortality in our study was lower than the prevalence reported in Ethiopia and Cameroon,

which was 29.4% (Agbor et al., 2014). This observed variation might be due to differences in the quality of service in TB clinics, including proper diagnosis, health education, and appropriate follow-up by clinicians.

In univariate, our present study indicates several factors associated with TB mortality among clinically diagnosed tuberculosis patients, including age, gender, site of disease, nutritional status, and HIV positive. In multivariate analysis, after controlling for other variables, province, age, HIV positive, having underweight remained significantly associated with TB mortality. In line with our study findings, a number of studies have also indicated a significant association between and TB mortality, people with old age were more likely to die as compared to those with younger ages (Ananthakrishnan et al., 2013; Melese et al., 2016; Nanzaluka et al., 2021). This finding could be attributed to an increased risk of lower immunity, making them more susceptible to infections, as a person grows older which may lead to poor outcomes (Nanzaluka et al., 2021). Another factor that might explain this finding is that older patients are less likely to adhere to treatment compared to younger patients. This could be due to their fear of experiencing side effects (although some studies contradict this finding) and other factors related to the physical fitness and nutritional status of elderly individuals (Kim et al., 2012; Wondale et al., 2017).

Our study findings also indicate that males were more likely to die than females. These finding different from what other studies have found in many other studies (Burton et al., 2011; de Faria Gomes et al., 2015; Melese et al., 2016; Nanzaluka et al., 2021). In line with other findings from prior studies, our studies indicate that patients with the problem of underweight were also more likely to die (Seid & Ayele, 2020). Similar to other studies, (Ananthakrishnan et al., 2013; Burton et al., 2011; Nanzaluka et al., 2021; Nicholson et al., 2023b) this study also found HIV positive TB patients to be associated with TB mortality. HIV is known to affect the immune system of individuals making them more susceptible to opportunistic infections such as TB (Ukwaja et al., 2016).

LIMITATION OF THE STUDY

This study had certain limitations since I used the secondary data. As I extracted data from National routine TB surveillance, some variables such as socio-demographic (occupation,

education, marital status), social-economic characteristics (income, social category), clinical factors (adherence, level of drug absorption, viral load suppression for HIV-positive patients) and behavioral factors (knowledge and attitude, alcohol use, cigarette smoking), were not available for further investigation. Furthermore, using a cross-sectional study could not verify cause- effect relationship.

CONCLUSION

This study highlights the high case mortality rate among TB patients clinically diagnosed in Rwanda compared to the National target, which is 6.5% by the end of 2022. Additionally, it highlights the need of early tuberculosis diagnosis and treatment, as well as the necessity of complete medical care and follow-up, especially for patients who are underweight, the patients aged 50 years and above, the patient's HIV positive especially for those who present the pulmonary TB. These findings could inform public health policies and interventions aimed at decreasing mortality rates in TB patients in Rwanda and other similar settings.

Declaration

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed in this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no conflict of interest in this work.

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No funding was obtained for this study

Authors' contributions

FB conceptualized the study, had full access to the data, and conducted the data analysis and interpretation. PM Provided access to the data set. AKA supervised the study. VN provided the technical review and contributed in data analysis. FB also prepared the manuscript, incorporating essential feedback and comments from the supervisor. FB, VN, PM and AKA reviewed the manuscript. All authors reviewed and approved the final version of the manuscript for submission.

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