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Assessing the impact of COVID-19 on prescription patterns and antibiotic use: Insights from three military health facilities

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A R T I C L E I N F O

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A B S T R A C T

Background: The COVID-19 pandemic disrupted health systems globally and there are suggestions it impacted antibiotics prescribing patterns in clinical practice.
Objectives: This study aimed to assess the effects of the COVID-19 pandemic on the prescribing patterns in three Nigerian military health facilities and investigate the factors associated with antibiotic prescriptions.
Methods: This was a two-year cross-sectional retrospective study. Three hospitals and a total of 11,590 prescriptions were purposively and conveniently sampled respectively. The World Health Organisation (WHO) and International Network of Rational Use of Drugs (INRUD) prescribing indicators were used to assess for polypharmacy, injection use, use of antibiotics, use of generic drugs and prescriptions from essential drug lists for the periods of the pandemic and before the pandemic. Indicators from both periods were compared for statistical significance using the independent *t*-test. Generalized linear modelling was applied to assess the factors associated with antibiotic prescriptions. The relationship between the receipt of antibiotics and independent variables was presented using incident risk ratios (IRR).
Results: Our findings showed that all five WHO/INRUD prescribing indicators were above the reference limit for the two-year study period. The study found there was a significant statistical difference between the COVID- and non-COVID-19 periods, with polypharmacy and antibiotic use indicators elevated during the pandemic compared to the latter. COVID-19 (IRR = 1.09), comorbidity (IRR = 1.74), pregnancy (IRR = 0.93), out-of-pocket payments (IRR = 1.10) and the inpatient department (IRR = 1.51) were associated with antibiotic prescriptions.
Conclusions: This provides insight on impact of the pandemic on prescription patterns and advocates for stewardship programs in clinical settings to ensure the rational use of drugs.

1. Introduction

Since its emergence, the COVID-19 pandemic has had a devastating impact on public health. By May 2023, over 765 million cumulative cases and 6 million deaths globally have been attributed to the pandemic, with 3000 of the deaths recorded in Nigeria.[1] There is also evidence that the pandemic disrupted health systems globally, with notable impacts on the delay of essential healthcare services such as routine immunizations, overburden of services and access to essential medicines.[2–4] In addition, varying consequences on antibiotics utilization in health facilities have also been observed.[5,6] Before the pandemic, it was established that more than half of medicines were inappropriately prescribed, dispensed, or sold especially in low- and middle-income countries (LMICs) where drug use monitoring is inadequate.[7]

There are indications that the patterns of use of medicines could have been impacted because of the pandemic and consequently, worsened the

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inappropriate use of medicines. For instance, the United States Centres for Disease Control (CDC) noted that as hospitalizations increased during the COVID-19 outbreak, antibiotic use – a key facilitator of antimicrobial resistance (AMR) – peaked.[8,9] In some cases, the use of these medicines were unnecessary.[10] Furthermore, the fact that antimicrobial-resistant infections kill about 700,000 people annually underscores the need to understand the effects of the pandemic on the use of medicines.[11] A possible change in prescription patterns in hospital facilities can be assessed using the Core Drug Use Indicators, a tool first published in 1993.[12]

The prescribing practice indicators are the metric of choice to measure the performance of health facilities.[12] The indicators measure the degree of polypharmacy, the tendency to prescribe in generic name, overall level use of injections, adherence to using of essential medicines list and use of antibiotics. It is imperative to add that the use of medicines, especially in hospital environments, is influenced by a complexity of factors. The Teixeira Antibiotic Prescribing Model (TAPBM) is a comprehensive framework, widely accepted by the research community, to understand the factors influencing antibiotic prescribing.[13,14] The Teixeira Antibiotic Prescribing Model (TAPBM) is a comprehensive framework, widely accepted by the research community, to understand the factors influencing antibiotic prescribing.[14] It contextualizes these factors into intrinsic and extrinsic factors, with intrinsic factors referring to factors directly influencing physicians' prescribing habits. These are mostly sociodemographic factors and physicians' attitudes. Extrinsic or external factors are centered on variables outside the control of physicians but nevertheless influence the prescribing of antibiotics. They include patient-related, healthcare system-related and cost saving factors. TAPBM have been used to understand predictors of antibiotics in several studies. In Nigeria, intrinsic factors associated with antibiotic prescriptions have been well described using a cohort of >1300 physicians across the six geopolitical regions of the country.[15] However, there is a dearth of studies on the extrinsic factors associated with antibiotic prescriptions. A few studies that have explored the issue from this dimension often exclude the ecosystem of military hospitals in the country. To the best of our knowledge, there is no existing drug utilization study that has investigated the factors associated with antibiotic prescriptions in Nigerian military health facilities.

The Nigerian military employs its workforce to supplement civil authorities during epidemics and most recently, the COVID pandemic. After the outbreak of the COVID-19 pandemic, military hospitals catered to both civil and uniformed patients. Specifically, the government designated 17 military medical facilities to isolate and treat confirmed cases, which enabled access to healthcare for patients at the climax of the crisis when public hospitals were overwhelmed.[16] This study aimed to understand the impact of the COVID-19 pandemic on prescription patterns in Nigerian military hospitals. Through this, we provided data on whether the pandemic worsened polypharmacy, injection, and antibiotic use. Additionally, our study assessed for extrinsic factors associated with antibiotic prescriptions in Nigerian military hospitals, which would be the first of such studies done in the country. Furthermore, our findings would help in developing interventions against AMR, as advocated by the Nigerian National Action Plan (NAP) on AMR of 2017–2022.

2. Methods

2.1. Study design and study setting

This was a two-year cross-sectional study conducted in inpatient and outpatient clinics of three military hospitals using retrospective data. Two hospitals are situated in the centre of Nigeria's capital Abuja while the third hospital is in the commercial city of Kano. All three hospitals are under the administration of the Nigeria Ministry of Defence. As with all military hospitals in the country, the three hospitals were set up to provide health services to service personnel, their families, and the civilian population.

2.2. Ethical clearance

Ethics approval was obtained from the National Defence College, with reference number, NDC/227/A. Subsequently, all three hospitals gave authorization for access to their data.

2.3. Inclusion criteria

All outpatient and inpatient prescriptions written between the period of January 1, 2019 to December 31, 2020 were eligible for this study. Patient data from the Accident and Emergency Department were excluded. This is because the modus operandi of some of these facilities requires attending to patients in need of emergency care before proceeding to document medicines administered, and hence, there is the possibility of recall bias.

2.4. Sampling technique and data collection

Purposive sampling was used in the sampling of the three hospitals for this study. The criterion for selection was hospitals willing to provide access to data. Patient and prescribing data were extracted from patient folders, domiciled in the records departments, using a Microsoft Excel spreadsheet developed by the investigators. Patient folders, used in these facilities, are paper documents for recording the details of patients and treatment plans. According to the usual practice in these facilities, all treatment plans are transcribed into prescription sheets for eventual transmission to the pharmacies. Hence, we assumed all treatment plans as prescriptions. WHO (1993) recommends a minimum of 600 prescriptions for drug utilization studies. However, we conveniently sampled 500 prescriptions per month for the two-year study period from the study sites, aggregating 12,000 prescriptions in total. Using our inclusion criteria, 407 prescriptions from the accident and emergency departments were excluded. The 407 prescriptions were excluded because they were prescribed for patients seen at the Accident and Emergency sections of the 3 hospitals. We excluded these prescriptions because they could introduce recall bias into our study since standard operating procedure in these military facilities was for physicians to attend to patients before documenting the administered medications. Of the 3 hospitals, 063 NAF Hospital had 198 excluded prescriptions, National Defence College had 66 excluded prescriptions and 465 Nigerian Air Force had 143. At the stage of data cleaning, three prescriptions with missing data were removed from the data set. Hence, the total sample size for the study was 11,590 prescriptions. All prescriptions within the study period were recorded in the Microsoft Excel spreadsheet. Variables collected from these folders were based on available literature reviews on external factors associated with antibiotic prescribing.[14] Additionally, we collected from the treatment plans the WHO/INRUD Prescribing Indicators provided in the 'How to investigate drug use in health facilities' document published by the WHO.[12] The Formulas for the calculations of each WHO/INRUD indicator adopted from the WHO/INRUD document is shown in Supplementary Table 1.

2.5. Data analysis

All statistical analyses were conducted in the statistical environment RStudio v.4.2.1 (packages: tidyr, MASS, ggplot2, dplyr, car). The csv format of the collected data was exported to R Studio. Data cleaning was done and all three data sets from the three hospitals were merged before data analysis was conducted. The assumptions of normality and linearity were tested before conducting the independent *t*-test and GLM analysis. Normality was assessed by examining for kurtosis and skewness of the distribution using frequency histograms and scatterplots. We also assumed that there was a straight-line relationship between the response and explanatory variables to infer linearity. This was assessed using bivariate scatterplots of each explanatory variable and the response variable. Multicollinearity was assessed on the continuous variables using the 'car' function. Tolerance of less than or equal to 0.5 was assumed as the absence of correlation between independent variables.

2.5.1. WHO/INRUD prescribing practice indicators

Descriptive statistics used to present data were averages, frequencies, percentages, and standard deviations. These values were compared to the WHO/INRUD reference limits to assess for five indicators namely: polypharmacy, injection use, use of generic names in prescriptions, adherence to the Nigerian Essential Medicines List (EML) and antibiotic use. The analysis was performed for two years. Subsequently, the same analysis was performed separately for the COVID period as well as the non-COVID period. All five indicators for both periods were compared for statistical difference using the independent *t*-test. The R Coding for the main tests conducted in this study is shown in Supplementary Table 2.

2.5.2. Factors associated with antibiotic prescribing

The response variable was the receipt of antibiotics. The number of antibiotics per prescription ranged from '0' to '5' and we assumed this as count data. Hence, we adopted a Poisson regression in the Generalized Linear Modelling (GLM). Explanatory variables were TAPBM-identified extrinsic/external factors extracted from the folders. Dates of hospital attendance were recorded to the period of care (COVID/Not COVID) as done in some studies that focused on other pandemics,[17,18] and included as an explanatory variable. Consequently, independent variables were the age of the patient, comorbidity, department of attendance, pregnancy, insurance status, and period of attendance. The age of the patient was grouped into adult and paediatric. We categorised patients from <18 years as paediatric. Comorbidity as presented in the patient folders was recorded as '0' and '1', where '0' implied there was no comorbidity and '1' represents patients with comorbidity as stated in the patient folders. The department of attendance was either outpatient or inpatient. Insurance status considered whether patients were insured or paid for their medicines (out-of-pocket) while the confirmation of pregnancy was recorded as either '0' for absent or '1' for present. COVID-19 and non-COVID-19 periods were 1 Jan19–1 Mar 20 and 2 Mar 20–31 Dec 20 respectively, considering when the virus was first reported in the country.

In conducting the GLM, we started by building the complex model which included all the explanatory variables. To identify the factors associated with the response variable, we worked towards the most parsimonious model, by dropping each explanatory variable in a stepwise manner and checking against the recent simpler model. At each stage of selection, likelihood ratios and p-values were used to assess the goodness of fit of the model. P-values less than 0.05 were considered statistically significant. Models were fitted using the 'glm' command in RStudio. P-values were reported alongside the correlates of antibiotic prescriptions. For the main effects with $p < 0.05$, Incident Rate Ratios (IRR) were calculated to estimate the relative risk of a predictor level over the reference category.

3. Results

3.1. Characteristics of the prescriptions for the period of 2019–2020

A total of 11,590 prescriptions were sampled for this study. Of the total prescriptions, 5729 prescriptions included one or more antibiotics while 5861 were non-antibiotic prescriptions. In terms of the age group of patients receiving prescriptions, 8760 (75.6%) of the sample size consisted of adults, while the remaining 2830 (24.4%) comprised the paediatric group. Concerning the gender of the prescription recipients, males accounted for 6284 (54.2%) of the sample size, while females constituted 5305 (45.8%). Regarding the departments where these patients received care, outpatient prescriptions constituted 7466 (64.4%) of the total number of prescriptions, whereas inpatient prescriptions accounted for 4124 (35.6%) of the prescriptions. Comorbid patients received 3485 (30.1%) of all the prescriptions while non-comorbid patients got 8105 (69.9%) of prescriptions. Additionally, 7379 (63.7%) of prescriptions were covered by insurance while 4211 (36.3%) of prescriptions were paid out of pocket. Table 1 shows the characteristics of the prescriptions collected and analysed for the study period. It also presents the percentages of antibiotic-containing prescriptions based on the variables assessed. Comparisons of the baseline characteristics and prescriptions before COVID-19 and during the COVID-19 period are shown in Supplementary Table 3.

3.2. WHO/INRUD prescribing practice indicators

From the 11,590 prescriptions, a total of 36,460 medicines were dispensed. The average number of medicines per prescription was 3.1 ± 1.5. This implies that of a total of 36460 medicines prescribed for the study period, 31690 (86.9%) were generics. 11326 (97.7%) prescriptions had one or more generic medicines out of the total of 11590 prescriptions. Additionally, the analysis also showed that 5725 (49.4%) and 4207 (36.3%) of the prescriptions contained antibiotics and injections respectively. These indicators were also assessed for the non-COVID- and COVID-19 periods (Table 2).

3.3. Factors associated with antibiotic prescribing

From our GLM analyses, the most parsimonious model (model 2), comorbidity ($p < 0.0001$), period of attendance ($p < 0.0001$, department visited ($p < 0.0001$), insurance status ($p < 0.0001$) and pregnancy ($p = 0.03$) were associated with antibiotic prescriptions. Table 3 summarises the model selection conducted to achieve parsimony.

3.4. Independent associates of antibiotic prescribing in three Nigerian military hospitals between the period of 2019–2020

Adjusted IRR and 95% confidence intervals were estimated for each predictor in the most parsimonious model (Table 4). Independent variables associated with antibiotic prescribing: inpatient (IRR = 1.51, 95% CI: 1.44–1.59), comorbidity (IRR = 1.74, 95% CI: 1.66–1.82), COVID

Table 1
Description of patients' prescriptions in three military hospitals in Nigeria.

Variable	N (Total) n (%)	Prescriptions with 1 or more antibiotics, %
Prescriptions	11590	5729
Antibiotic prescriptions	5729, (49.4)	
Non-antibiotic prescriptions	5861, (50.6)	
The age group of patients		
Adult	8760, (75.6)	4152, (35.8)
Paediatric	2830, (24.4)	1577, (13.6)
Gender of patients		
Female	5305, (45.8)	2703, (23.3)
Male	6284, (54.2)	3026, (26.1)
Department		
Inpatient	4124, (35.6)	2512, (21.7)
Outpatient	7466, (64.4)	3217, (27.8)
Comorbidity		
Comorbid	3485, (30.1)	2297, (19.8)
No Comorbidity	8105, (69.9)	3432, (29.6)
Period		
Non-covid	6435, (55.5)	2923, (25.2)
Covid	5155, (44.5)	2806, (24.2)
Insurance		
Insured	7379, (63.7)	3479, (30.0)
Out-of-pocket	4211, (36.3)	2250, (19.4)
Pregnancy		
Not pregnant	10178, (87.8)	5135, (44.3)
Pregnant	1412, (12.2)	594, (5.1)

Table 2
World Health Organisation (WHO) Prescribing Indicators from three health facilities in Nigeria during the study period of 2019–2021.

Indicators	Study Period	COVID period	Non-COVID period	Reference Limit	p-value
The average number of drugs per encounter	3.1 ± 1.5	3.4 ± 1.4	2.9 ± 1.4	1.6–1.8	<0.0001
Percentage of encounters with an antibiotic	49.4	54.4	45.4	13.4–24.1%	0.018
Percentage of drugs prescribed by generic name	86.9	87.1	86.7	100%	<0.0001
Percentage encounters with an injection	36.3	35.5	36.9	100%	0.001
Percentage drugs from the essential drugs list	84.2	70.3	97.4	20–26.8%	<0.0001

P significant at <0.05.

Table 3
Associations between the regression variables and antibiotic prescribing in three Nigerian military hospitals between the period of 2019–2020.

Variable	p-value	
	Model 1	Model 2
Age	0.9	–
Department	***	***
Comorbidity	***	***
Period	***	***
Insurance	***	***
Pregnancy	0.04	0.03

*** implies $p < 0.001$.

Table 4
Generalized Linear Modelling showing the Incidence rate ratios (IRR) for independent associates of antibiotic prescribing in three Nigerian military hospitals between the period of 2019–2020.

Variable	IRR (95%, CI)	
	Adjusted	Crude
Department		
Outpatient	1.00	
Inpatient	1.51 (1.44, 1.59)	1.62 (1.54, 1.69)
Comorbidity		
No Comorbidity	1.00	
Comorbid	1.74 (1.66, 1.82)	1.75 (1.68, 1.83)
Period		
Non-Covid	1.00	
Covid	1.09 (1.04, 1.14)	1.19 (1.14, 1.25)
Insurance		
Insured	1.00	
Out of Pocket	1.10 (1.04, 1.16)	1.32 (1.27, 1.38)
Pregnancy		
Not Pregnant	1.00	
Pregnant	0.93 (0.86, 1.00)	0.89 (0.83, 0.95)

period (IRR = 1.09, 95% CI: 1.04–1.14), pregnancy (IRR = 0.93, 95% CI: 0.86–1.00) and out of pocket payments (IRR = 1.10, 95% CI: 1.04–1.16). The Incidence rate ratios (IRR) for independent associates of antibiotic prescribing is shown in Table 4. Supplementary Table 4 shows the model selection for the Generalized Linear Modelling conducted to assess model parsimony.

4. Discussion

We evaluated the impact of the COVID-19 pandemic on antibiotics prescription patterns in Nigerian military hospitals. This study provided data on the impact of the pandemic on polypharmacy, injection, and antibiotic use. We also identified extrinsic factors associated with antibiotic prescriptions in Nigerian military hospitals. From all 3 hospitals, our data showed there was a cumulative of 223 patients who tested for COVID during the COVID period. Breakdown of the figures are 063 NAF Hospital: 53, National Defence Clinic: 74, 465 NAF Hospital: 96.

4.1. Drug utilization

The number of drugs per encounter (3 ± 1.5) across the study period was above the reference limit of 1.6–1.8. For both pre- and during COVID, the number of drugs per encounter was 3.3 ± 1.4 and 2.9 ± 1.4 respectively. Similar drug utilization studies in Africa also showed the indicator was above the reference limit.[19–22] This could be because of concerns about secondary bacterial infections and presence of comorbidities.[23] In addition, out-of-pocket payments for healthcare during the pandemic could have contributed to antibiotic overuse, as individuals sought quick relief and sometimes pressured healthcare providers for antibiotic prescriptions.[24] Our finding indicates that polypharmacy could be an issue pre-COVID and even heightened, during the pandemic. With its association with hospitalization and mortality, polypharmacy remains a major public health issue in and outside the African continent.[25] Hence, there is an emphasises on the importance of continuous education of physicians on the rational use of antibiotics.

In the present study, we observed the percentage of prescribed injections for the study period was higher compared to the reference limit of 13.4–24.1%. When categorised into pre- and during-COVID periods, it was found that there was a statistically significant difference between the COVID and non-COVID periods. Despite the high values in both periods and the study period generally, the difference in use pre- and during COVID might have been because of the impact of the lockdown during COVID. The Ministry of Defence's issuance of advisories to its hospitals on limiting injection use in outpatient departments during the COVID period could have contributed to the lower value in this period.[26,27] Nevertheless, the use of injection was above the limit. Above-limit injection use values had been noted as a problem in the African continent, before the pandemic.[28] Where moderate use of injection use has been shown, with a within-reference figure, the use of standard treatment guidelines was observed.[22] Hence, the implementation or use of standard treatment guidelines has been proffered as a strategy for rational drug use.[1]

The percentage of Encounters with an Antibiotic Prescribed, which measures the level of use of antibiotics in health facilities was higher when compared with similar studies.[28,29] The reported values in our study were consistent with antibiotic overprescription in other outpatient settings in Africa, Asia, and Europe.[19–21,30] A drug utilization study that focused on Nigerian army hospitals put the percentage of antibiotic encounters to be 28%, suggesting overuse of antibiotics is not limited to only public health institutions.[31]

4.2. Factors associated with antibiotic prescribing

In our study, we found that comorbidities, the COVID period, attendance in the inpatient department, pregnancy, and out-of-pocket payments were associated with antibiotic prescribing. The correlation between comorbidity and antibiotic receipt has been reported in China, Ethiopia, the UK, and the United States.[21,32,33] It has also been shown that patients with underlying comorbidities received antibiotic prescriptions during the COVID pandemic despite the paucity of evidence that the disease was linked with bacterial infections.[34]

In our study, patients who were attended to at the inpatient department were more likely to receive an antibiotic prescription compared to those who were attended to at the outpatient department. Studies in different LMIC settings have established the overuse of antibiotics in inpatient departments. In Ghana and Nigeria for instance, high rates of antibiotic use in inpatient departments have been reported.[35,36] A possible reason could be cultural tendencies in clinical settings, specifically, the hierarchical structure. Hierarchical structure here implies the nature of specialist training for physicians where prescriptions of resident doctors are influenced by specialists. Our study also showed the protective effect of insurance on antibiotic prescribing, with insured patients having lesser odds of receiving such prescriptions compared to patients who paid out-of-pocket. There is available literature indicating that out-of-pocket payments correlated with antimicrobial resistance, even when adjusting for poverty rates and sanitation.[37]

Our GLM analysis, after adjusting for other variables, showed that during the COVID period, the likelihood of receiving an antibiotic was higher than in the pre-COVID period. This contributes to the emerging knowledge of the impact of the pandemic on drug utilization, particularly on how antibiotics were used in clinical settings, especially in Nigeria. There is evidence to support that most of these antibiotic prescriptions for COVID-19 patients were unnecessary.[10] Distortions in antimicrobial stewardship programs have also been observed but where the integrity of such programs was maintained, antibiotic prescriptions stayed below expected levels.[38] Hence, we suggest the implementation of well-designed stewardship strategies to facilitate the rational use of antibiotics.

4.3. Strengths and limitations

Our study has some major strengths and is a first in different areas. It is the first study to show how prescribing patterns in clinical settings were influenced by the pandemic in Africa's most populous country, Nigeria. There is a particular paucity of data on how antibiotic use patterns changed due to the pandemic, especially in sub-Saharan Africa. Therefore, our study contributes data on the impact of the pandemic on antibiotics utilization in Africa. Additionally, to the best of our knowledge, with >11,000 prescriptions, our study is the largest drug utilization study in Nigeria. While our findings might not be generalizable because of our limitation to military facilities, our sample size provides a better understanding of how the pandemic impacted drug utilization in clinical settings in Nigeria. Also, this is the first study in sub-Saharan Africa where the TAPBM was adopted to understand the factors associated with antibiotic prescribing.

Nevertheless, we identified some limitations in our study. First, we used prescribing data from patient folders and hence, we could not include some variables, such as age of the patient, educational level, economic status, and time pressure, identified by the TAPBM. Most physicians did not specify the actual age of patients but instead used 'Ad' to denote adult patients and 'paed' to denote children, hence generalizations of the study findings should be treated with caution. Secondly, purposive sampling was used in selecting the health facilities in this study, which could raise issues of reliability. However, the homogeneity in the operations of Nigerian military hospitals should allow for the reproducibility of our findings even if conducted in other similar military facilities. Additionally, this is a cross-sectional study, and our findings would not necessarily translate to causality. Lastly, our study is quantitative and hence does not take to account the type or class of medicines prescribed in these facilities. In addition, we strictly followed the guideline of WHO/INRUD metrics hence we did not collect data on how many injections were for antibiotics. Further similar studies in this area perhaps could explore this limitation to show the patterns of the class or types of medicines prescribed pre and during the pandemic.

5. Conclusion

The COVID pandemic affected how medicines were used in clinical settings. Our study aimed to understand the impact of the pandemic on prescription patterns in Nigerian military hospitals. We found that there was a statistical difference across all WHO/INRUD core prescribing indicators in the pre and COVID periods. We also reported that comorbidities, inpatient departments, pregnancy, out-of-pocket payments and the COVID period were significantly associated with antibiotic prescribing. Our study aligns with a core objective of the National Action Plan on AMR which is to "promote antimicrobial stewardship through optimal prescribing and dispensing of antimicrobials to humans". Consequently, our findings contribute to the understanding of how antibiotics are used in Nigerian hospitals and underscore the need to pay attention to these antibiotic prescription correlates in the designing of antimicrobial stewardship strategies and future National Action Plan policies on AMR.

Ethical considerations

Ethics approval was obtained from the National Defence College, with reference number, NDC/227/A. Subsequently, all three hospitals gave authorization for access to their data. We confirm that all methods were performed in accordance with the guidelines of the Declaration of Helsinki.

Data availability statement

The datasets generated and/or analysed during this study are not publicly available to protect confidentiality, but aggregated data and Html files of all analyses is available from the corresponding author upon reasonable request.

Consent for publication

Not applicable.

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Authors' contributions

MMA, KL, AI, and BOU-K devised the study and developed/refined the main conceptual ideas. KL, MU, OF, IA, YI, and MDI led the study protocol development, ethical application, and gaining approvals, with input from the whole team. MMA, KL, MU, OF, IA, YI, and MDI undertook recruitment and data collection. AI and BOU-K provided support for study conduct and data collection. KL undertook the main analysis with critical input from MMA, AI, and BOU-K. MMA and KL drafted the manuscript. All authors helped refine the manuscript and approved the final version.

Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2023.10.013.

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