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Prevalence and Indications for Antibiotic Prescription Among Patients Hospitalized with COVID-19 Disease at Kenyatta National Hospital, Kenya

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Abstract

Background: Overuse of antibiotics results in escalating the burden of antimicrobial resistance. Reports indicate high use of antibiotics (72%) among hospitalized COVID-19 patients despite low prevalence (8%) of bacterial infections. The 2021 Kenya Clinical Management for COVID-19 guidelines strongly discourage empirical use of antibiotics. Objectives: This study determined antibiotic prescription prevalence and indications among hospitalized COVID-19 patients Kenyatta National Hospital.

Materials and Methods: Using a data abstraction form, this cross-sectional study included data from 283 patient files obtained from COVID 19 patient archived files at Kenyatta National Hospital (KNH). Data was analyzed using frequency and percentages. A chi-square analysis was done to compare antibiotic prescriptions for patients with bacterial infection and patients without a diagnosis of bacterial infection.

Results: The prevalence of antibiotic prescription among the patients hospitalized with COVID-19 disease at KNH was 73.5% (95% CI: 68.0%-78.5%) and the most prescribed antibiotics was Azithromycin to 40.4% (95% CI: 33.7% - 47.4%) of the participants. Forty-six percent of the antibiotic prescriptions had no indication. About 33% of the participants had a clinical diagnosis of bacterial infection as an indication for antibiotic prescription, and 22 (7.8%) participants had a microbiology test result.

Conclusion: The findings of this study showed that the prevalence of antibiotic prescription among patients hospitalized with COVID-19 disease at KNH is high. Most antibiotic prescriptions had no indications, suggesting inappropriate antibiotic use. New policy and practice guidelines to support antibiotic stewardship programs are needed to reduce inappropriate antibiotic use.

Keywords: Antibiotic prescription, COVID-19, indications, Kenyatta National Hospital, prevalence

Introduction

Bacterial infections that occur during COVID-19 are associated with adverse outcomes, contributing to more than 50% of all COVID-19 mortalities [1] [2] [3]. Research on hospitalized COVID-19 patients shows that bacterial infections were low, with about eight percent prevalence, but 72% of all hospitalized patients were prescribed antibiotics [4]. In support, a multinational study indicated that 70% of COVID-19 patients got antibiotics for treatment or prevention of bacterial infections, and 54% had a clinical or microbiological diagnosis of bacterial infections [5]. Despite the minimum evidence of their efficacy, azithromycin and ceftriaxone are among the

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most frequently prescribed antibiotics [6] [7] [8] [9]. The widespread use of antibiotic therapy does not minimize adverse effects among COVID-19 patients. Researchers found that the death rate for COVID-19 in patients who received antibiotics was higher than that of those who did not [10]. For severe illnesses with high bacterial infection suspicion and where a clinical diagnosis has been made, the World Health Organization's (WHO) guideline for Clinical Management of COVID-19, recommends prescription of antibiotics [11]. The WHO advises against using antibiotics for mild to moderate COVID-19 illness unless a bacterial infection is diagnosed based on clinical presentation. Clinical judgment, host variables and the local epidemiological situation should all be considered when choosing antibiotic treatments [11]. Unfortunately, research shows that 72% of hospitalized COVID-19 patients are given antibiotics, regardless of the clinical suspicion of bacterial infections [10]. An increase in empirical antibiotic prescriptions may result from the overlap in clinical presentation and the absence of distinct biomarkers for patients with COVID-19 and secondary bacterial infections [3] [12].

Despite the high prevalence of resistant infections, uncontrolled antibiotic usage among COVID-19 patients remains high in most African nations, including Kenya. According to a study conducted at a private hospital in Nairobi, Kenya, only 6% of hospitalized COVID-19 patients had bacterial infections [14]. Nonetheless, antibiotics, with or without clinical indications, were administered to more than 70% of hospitalized COVID-19 patients [13] [14]. Excessive, inappropriate, or unnecessary antibiotic use threatens the efficacy of antibiotics-based treatment due to the escalating burden of antimicrobial resistance (AMR). This could lead to more extended hospital stays, higher rates of AMR-related morbidity and mortality, and higher healthcare costs for the healthcare system and patients. The Kenya Clinical Management for COVID-19 recommendations and the WHO clinical guidelines for managing COVID-19 discourage antibiotic use. The high rate of antibiotic use among hospitalized COVID-19 patients is not evidence-based, particularly at Kenyatta National Hospital (KNH), where majority of the COVID 19 patients were admitted in Nairobi. There is a lack of sufficient information in the local context to support antibiotic prescribing and guide future antimicrobial stewardship programs in pandemic-oriented diseases like COVID 19. Therefore, this study aimed to ascertain the prevalence and indications of antibiotic prescriptions among COVID-19 patients hospitalized at a National Public Referral Hospital in Kenya.

Materials and Methods

Study design and setting

The study was an analytical cross-sectional study which was selected for its suitability to collect data at a specific point in time. The study site was Kenyatta National Hospital (KNH), a major public national referral hospital in Nairobi that was suitable because over 80% of the national COVID-19 cases were situated there.

Participants, sampling, and sample size

The study participants were patients admitted at KNH between March 2020 and September 2023. Only patients' files with positive COVID-19 PCR test results regardless of the outcome of the admission were included. The study excluded hospitalized patients transferred within 24 hours of admission and those on continuous antibiotic therapy before admission. The sample was files of hospitalized COVID-19 patients admitted at KNH. A sample size of 283 was calculated using Cochran's formula [16] with a prevalence of antibiotic prescription of 72% [10] and adjusted using the finite population formula [17]. Multi-staged probability sampling was used to generate a representative sample, as described below. In stage 1, stratified sampling was used, with age admission age groups as the stratum from which a proportionate sample was calculated as described below:

Proportionate sample=Ni/N(n)

Where: Ni is the population in the stratum - COVID-19 admission per age group

N is the total population – total COVID-19 admissions at KNH = 3146

n is the calculated sample size = 283

Stage 2 used a systematic sampling technique to select the sampling units from the age-stratified sampling frame. This means files were picked at regular intervals based on calculations using the formula below:

k=N/n

where k is the systematic sampling interval

N is the population size, which is the specific age group population

n is the sample size, which is the specific age group sample size

The sample size per age group and interval is described in Table 1.

Data Collection and Management

Data collection occurred for two months, by three data enumerators due to the extensiveness of the process. A data abstraction form was developed to collect data on patient demographics, clinical presentation, the severity of COVID-19, comorbidities, coinfections, diagnosis at admission, and antibiotics prescribed, from files of eligible

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Table 1: Sample size as per age group

Age group	Number of admissions	Total sample
less than 20	235	21
21 - 34	570	52
35 -50	955	86
51 - 64	807	71
65 - 80	476	43
81 and above	103	10
Total	**3146**	**283**

patients. The enumerators (Doctors, Nurses and Laboratory personnel and The Health Information officers) reviewed the files and collected data as guided by the data abstraction form. For confidentiality, data did not have patient identifiers or hospital codes. All files were handled within the premises as found. A data or records officer was recruited to ensure accuracy of secondary data by crosschecking and verifying it for quality and providing feedback on data entry in real-time. All collected data were stored in Excel on one computer and in backup storage on iCloud.

Data Analysis

The Excel data was exported using statistical software for analysis. Descriptive statistics were used to report antibiotic prescriptions' frequency percentages and indications. A chi-square analysis was done to compare antibiotic prescriptions for patients with a bacterial infection diagnosis with patients without a diagnosis of bacterial infection. All analyses were done in Statistical Package for Social Sciences (SPSS) Version 25.

Ethical consideration

Ethical approval was obtained from the Jomo Kenyatta University of Agriculture and Technology Scientific and Ethics Review Committee and the Kenyatta National Hospital – University of Nairobi Ethics and Research Committee (KNH-UON ERC) (Ethical approval License Numbers: JKU/ISERC/02316/0822). The National Commission for Science, Technology, and Innovations (NACOSTI) permitted the study (NACOSTI/P/23/24703, KNH-UoN ERC: P426/05/2023). The collected data did not contain patient names and was coded to maximize privacy and confidentiality.

Results

Patient socio-demographic characteristics

Table 2 presents the socio-demographic characteristics of the patients hospitalized with COVID-19 at KNH, according to the medical records. The findings indicated that the majority of patients were male (55.48%, N = 157), aged between 40-49 years (18.73%, N = 53), and informally employed (48.41%, N = 137). Most of the patients were admitted into the Infectious Diseases Unit- Mbagathi COVID-19 ward (48.06%, N = 136) (Figure 1).

The prevalence of antibiotic prescription

The reported prevalence of antibiotic prescription among the patients hospitalized with COVID-19 disease at KNH was 73.5% [95% CI: 68.0%-78.5%] (Figure 2). The proportion of antibiotic prescriptions for patients admitted to ICU and HDU pediatric units was 100% (Table 3). The most prevalent antibiotic was azithromycin which was prescribed to 43.8% of the patients (N = 124). Antibiotic prescription was high among participants with moderate (78.8%, N = 119), severe (78.9%, N = 45), and critical (86.7%, N = 26) COVID-19 severity (Figure 3).

Table 2: Patient socio-demographic characteristics

Variable	Category	Frequency (%)
Gender	Female	126 (44.52)
	Male	157 (55.48)
Age (years)	0-9	12 (4.24)
	Oct-19	6 (2.12)
	20-29	35 (12.37)
	30-39	44 (15.55)
	40-49	53 (18.73)
	50-59	47 (16.61)
	60-69	52 (18.37)
	70-79	25 (8.83)
	80	9 (3.18)
Patient occupation	Formal employment	58 (20.49)
	Informal employment	137 (48.41)
	Retired	7 (2.47)
	Student	11 (3.89)
	Unemployed	63 (22.26)
	Unknown	7 (2.47)

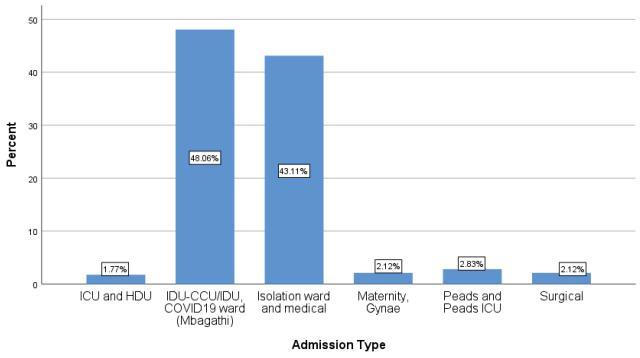

Figure 1: Patient distribution by ward allocation

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Table 3: Indication for antibiotic prescription for the study participants

Variable	Category	Frequency (%)
By clinical diagnosis (n = 93)	Meningitis	4 (4.30)
	Neonatal Sepsis	1 (1.08)
	Pneumonia	80 (86.02)
	Severe Pneumonia	5 (5.38)
	TB	1 (1.08)
	UTI	1 (1.08)
	UTI & Pneumonia	1 (1.08)
By microbiology test results (n = 22)	Candida Species	1 (4.55)
	Coagulase-negative Staphylococcus Aureus	2 (9.09)
	Gram-Positive Rods seen-Diphtheroid	1 (4.55)
	Klebsiella Pneumonia	2 (9.09)
	No growth	14 (63.64)
	Proteus Mirabilis & E. coli	1 (4.55)
	Staphylococcus Hominis	1 (4.55)

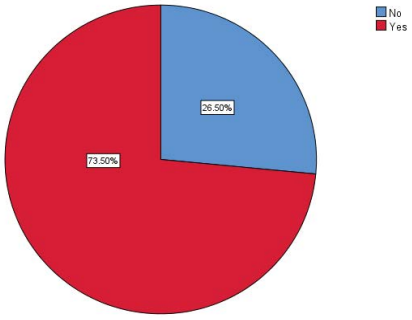

Figure 2: The prevalence of antibiotic prescription among study participants

Indications for antibiotic prescription

Of the 208 patients with antibiotic prescriptions, only 93 (33.21%) patients had a clinical diagnosis of bacterial infection as an indication for antibiotic prescription. Among the ninety-three, there were 22 files with a microbiology test result. By Clinical diagnosis, pneumonia was the most frequent indication of antibiotic prescription (86.02%, N = 80) (Table 4.3). According to the microbiology test results, Coagulase-Negative Staphylococcus Aureus (CoNS) and Klebsiella pneumonia were the most frequent indications of antibiotic prescription (9.09%, N = 2, each). However, most test results indicated no growth (63.64%, N = 14). Figure 4 shows that 82.8% (N = 77) of patient diagnosed with bacterial infection had antibiotics prescribed to them compared to 68.9% (N = 131) of those not diagnosed with bacterial infection, a difference that was statistically significant ($p = 0.013$).

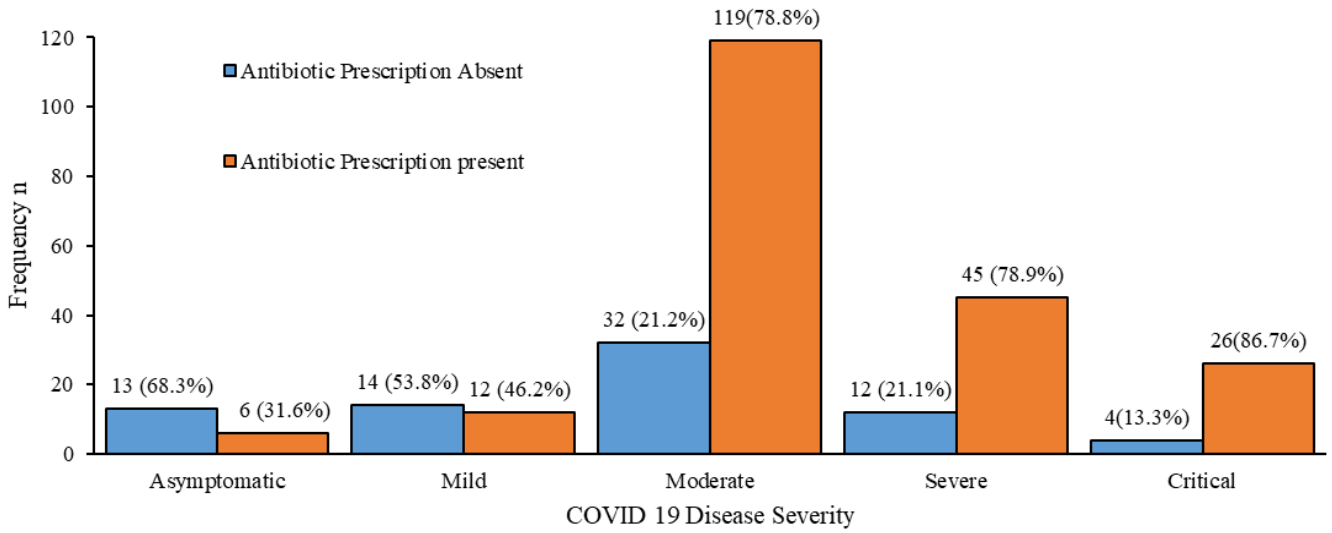

Figure 3: Distribution of Antibiotic Prescription by COVID-19 Disease Severity

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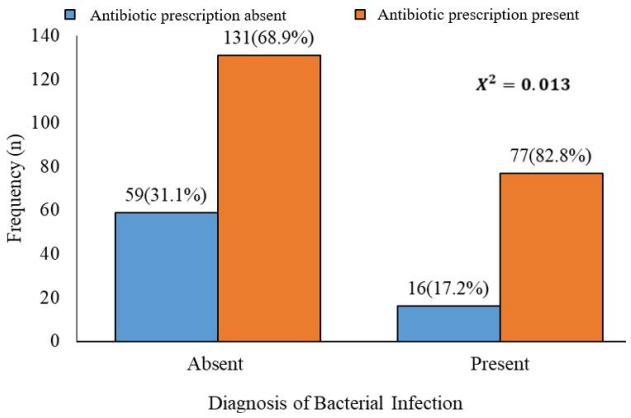

Figure 4: Distribution of Antibiotic Prescription by Clinical Diagnosis

Discussion

Prevalence of Antibiotic Prescription among Patients Hospitalized with COVID-19

The current study revealed that the prevalence of antibiotic prescriptions among hospitalized COVID-19 patients was approximately 75%. These findings are consistent with those reported in previous studies. Meta-analyses by Langford et al. [4] and Satria et al. [18] reported an antibiotic prescription prevalence ranging from 74.6% – 80%, despite a prevalence of 8.6% bacterial coinfections among COVID-19 patients. The findings from the current study supports literature by identifying the significant overuse of antibiotics. While the prevalence of antibiotic prescription occurred in almost 75% of the patients, only 33.21% of the patient had bacterial infections as an indication for the prescription. While the reason for the higher prevalence of antibiotic prescribing is unknown, the effects of injudicious antibiotic use are well known, including increased antimicrobial resistance, *Clostridium difficile* infection, and severe adverse events [4] [18]. Additionally, antibiotic prescription was significantly higher among patients with bacterial infection compared to those without the infection. These findings are inconsistent with previous studies [4] [18]. COVID-19 severity was not a deciding factor in antibiotic prescription, considering patients with moderate COVID-19 severity has the highest prescription. These overall findings indicate non-adherence to WHO recommendations and the Kenya Guidelines for Clinical Management of COVID-19, which both discourage administration of antibiotics for mild to moderate COVID-19 illness [11].

Indication for Antibiotic Prescription

The study findings revealed that 46% of the antibiotic prescriptions had no indication, which aligns with Satria et al. [18], who reported that majority of antibiotic prescriptions were inappropriate, particularly in low- and middle-income countries (LMICs). The findings do not support the implementation of the WHO & Kenya Clinical Management for COVID-19 treatment guidelines, which discourage antibiotic prescription for COVID-19 infections unless severe bacterial infections are laboratory confirmed or clinically suspected. In the current study, 32.85% had a clinical bacterial infection (BI) diagnosis, and seven percent of the total admissions had a confirmed microbiology-positive test for BI. These findings are inconsistent with previous studies reporting that the percentage of bacterial infection classified as coinfection is between 6.1% and 8.5% [4] [19]. Despite the differences, this study has shown a relatively high percentage of antibiotic prescription indications through a clinical diagnosis of BI, which may suggest limited access to microbiology diagnostics techniques at KNH. The findings further indicate that patients with pneumonia were primarily prescribed antibiotics, which is similar to findings from Nestler et al. [20], who established that most hospitalized COVID patients with symptoms similar to pneumonia symptoms were prescribed antibiotics.

Limitations of the Study

The study's limitations included its small sample size and the use of secondary data. The sample used in the study does not reflect the number of patients diagnosed with COVID-19 in the setting. For example, by the third COVID-19 wave in April 2021, 2979 cases were diagnosed at KNH [21]. The sample size is small to allow the generalizability of findings to other populations or settings. The use of secondary data which was not initially collected for the study introduces bias when extracting data, including data completeness or accuracy issues, depending on the recording quality. Missing or inaccurate records reduce the sample size, thus affecting internal reliability and external validity. Local researchers in this field should conduct further research using large sample sizes, such as national data from multiple sites and prospective data, to understand antibiotic prescription and associated factors. Such research would improve the external validity of findings, allowing for generalizability beyond a single setting and specific populations.

Conclusions

In conclusion, this study has revealed that the prevalence of antibiotic prescription among patients hospitalized with COVID-19 disease at KNH is high, despite the restrictions by the WHO COVID-19 treatment guidelines and the Kenya Clinical Management for COVID-19 guidelines. The aforementioned guidelines discourage empirical use of antibiotics among COVID-10 patients, except those with moderate to severe COVID-19 and highly suspected of having bacterial infections (BIs). Additionally, nearly half of the antibiotic prescriptions did not have an indication.

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Prescriptions that had an indication were mainly based on clinical diagnosis and not microbiology tests. This suggests limited resources of the facility to support necessary laboratory tests for the confirmation of the presence of BIs prior to antibiotic prescription. Based on the findings, clinical recommendations are that Kenyatta National Hospital (KNH) and other similar facilities must prioritize pandemic-tailored antimicrobial stewardship (AMS) activities aimed at optimizing antibiotic prescribing amongst healthcare professionals. These interventions should raise awareness of when to prescribe antibiotics for patients affected by diseases such as COVID-19, including the risks and adverse effects of unnecessary antibiotic prescription. Additionally, the Ministry of Health (MoH) must consider standardizing the diagnostic criteria to incline clinical presentation as there are uncertainties in influenza and pneumonia diagnosis. KNH and other local settings should have standardized guidelines on antibiotic prescription. Recognizing that antimicrobial susceptibility testing (AST) results are the key determinant of infection treatment in most clinical settings [22], it is essential that further research is conducted at KNH to establish the correlation between AST results and antibiotic therapy at KNH. Such research will speed the effort to promote effective and appropriate antimicrobial therapy in future practice.

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Conflicts of Interest

The authors declare no conflicts of interest. All authors have equally agreed to publish the final version of the manuscript.

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