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Antibiotic usage patterns in COVID-19 patients in five tertiary hospitals from Bangladesh: A countrywide picture

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ABSTRACT

Objectives: Irrational and injudicious use of antibiotics in COVID-19 patients could be detrimental in a tropical country with a weak antibiotic stewardship policy such as Bangladesh. This study aimed to focus on the antibiotic usage patterns in COVID-19 patients in Bangladesh.

Methods: This prospective observational study was performed from July 2020 to June 2021 in five tertiary hospitals in Bangladesh. Data on demographic profile, disease severity, and antibiotic usage were collected directly from the patients' hospital documents.

Results: A total of 3486 (94.4%) patients were treated with at least one antibiotic; 3261 (93.6%) patients received a single antibiotic, and 225 (6.5%) received multiple antibiotics. The most used antibiotics were ceftriaxone (37.3%), co-amoxiclav (26.3%), azithromycin (10.6%), and meropenem (10.3%). According to the World Health Organization AWaRe categorization, most (2260; 69.6%) of the antibiotics prescribed in this study belonged to the "Watch" group. Culture and sensitivity reports were available in 111 cases from one center. Only 18.9% of the patients were found to be co-infected with multi-drug-resistant bacteria (52.4% yield from sputum, 28.6% from urine, and 14.3% from blood).

Conclusions: Strict antibiotic prescribing policy and antibiotic stewardship should be implemented immediately to limit the future threat of antimicrobial resistance in countries such as Bangladesh.

Introduction

Bacterial antimicrobial resistance (AMR) has raised concerns over the years due to the escalating use of antibiotics, particularly in the COVID-19 era. A systematic analysis concluded that, in 2019, an estimated 4.95 million deaths were associated with AMR, including 1.27 million deaths attributable to bacterial AMR. Although AMR affects all countries globally, the burden is disproportionately higher in low-to-middle-income countries (LMICs) [1]. The rise in AMR during the COVID-19 pandemic can be amplified in LMICs because of weak monitoring systems and lack of awareness and preparedness [2]. A meta-analysis conducted in 2016 analyzed 145 studies and demonstrated a 35% relative risk reduction in mortality with guideline-directed anti-

microbial prescription [3]. Thus, this concern could be greatly reduced by the appropriate implementation of an antibiotic stewardship program.

High prevalence of resistant microorganisms in Bangladesh has been identified in a systematic analysis in the pre-COVID-19 era [4]. Although antibiotics have no proven role against viral infections, irrational and injudicious use of antibiotics has been observed due to the easy availability of antibiotics in Bangladesh [5]. This is particularly very alarming for countries such as Bangladesh because of the tropism and higher incidence of infectious diseases. The erratic use of antimicrobials in the COVID-19 era may escalate this situation, making Bangladesh one of the major contributors to the future global AMR crisis. A single-center study conducted in Dhaka, Bangladesh also reported heavy antibiotic usage in COVID-19 patients [6]. However, only one multicenter study

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on antibiotic usage patterns in COVID-19 patients during the first wave has been reported [7]. This study was conducted in five tertiary hospitals across the country to focus on antibiotic usage in COVID-19 patients in Bangladesh. Through this study, we want to highlight the importance of strict prescribing policy, monitoring of antibiotic access, and antibiotic stewardship in LMICs such as Bangladesh, to reduce the burden of global AMR.

Materials and methods

Study design

This prospective, observational study was conducted on SARS-CoV-2-positive patients from July 2020 to June 2021. Data were collected directly from the patients and their folders through a case record form from the dedicated COVID units (both outpatient and inpatient departments) of five tertiary hospitals in Bangladesh. The study sites were (i) Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, (ii) Mymensingh Medical College Hospital (MMCH), Mymensingh, (iii) Sylhet Shahid Shamsuddin Ahmed Hospital (SSSAH), Sylhet, (iv) Rangpur Medical College and Hospital (RpMCH), Rangpur, and (v) Khulna Medical College and Hospital (KMCH), Khulna.

Study variables

Data for the following variables were recorded from each enrolled patient throughout the study period:

- (a) Demographic characteristics of the patients, including age, sex, presence of comorbidities including hypertension, diabetes mellitus, malignancy, respiratory disease (chronic obstructive pulmonary disease, asthma), ischemic heart disease, obesity, chronic kidney disease, smoking.
- (b) Severity of COVID-19 illness; the following case definitions of COVID-19 were followed as per the National Guidelines on Clinical Management of COVID-19 Bangladesh [8]:
 - Mild case: Patients with mild clinical symptoms (fever, cough, sore throat, headache, muscle pain) without shortness of breath or abnormal imaging.
 - Moderate case: Fever and respiratory symptoms with radiological evidence of pneumonia, and/or respiratory distress with a respiratory rate <30 breaths/min, and/or pulse oximetry showing oxygen saturation $>93\%$ at ambient air.
 - Severe case: Patients with respiratory distress with a respiratory rate ≥ 30 breaths/min, and/or oxygen saturation $\leq 93\%$ at room air, and/or arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ≤ 300 mmHg.
 - Critical case: respiratory failure requiring mechanical ventilation, and/or shock, and/or other organ failure(s) requiring ventilatory support.

All patients were categorized into two groups: non-severe and severe. Mild to moderate diseases were categorized as “non-severe” and severe to critical cases were categorized as “severe.”
- (c) Details of the prescribed antibiotics, including the generic name of the antibiotics, route of administration, number of prescribed antibiotics in each patient, average number of antibiotics per patient, and duration of antibiotics. The antibiotics were further classified into “Access,” “Watch,” and “Reserve” categories according to the World Health Organization (WHO) AWARe classification. As the study was exclusively focused on antibiotic usage in COVID-19 patients, usage of other antimicrobials including antifungals, antivirals, and antimalarial drugs was not recorded.
- (d) Bacteriological evidence in COVID-19 patients with their sensitivity pattern. The culture sensitivity reports from sputum, urine, and blood were collected from the patient's folders, if available. The culture reports were only from BSMMU to maintain the uniformity of bacterial isolation and identification. The isolation

and identification of bacteria were done in the Department of Microbiology, BSMMU. The method of isolation and identification of bacteria is based on the standard microbiology procedure of Mackie and McCartney's Practical Medical Microbiology. Antimicrobial susceptibility testing was performed using the Kirby-Bauer disc diffusion method in accordance with the 2019 guidelines from the Clinical and Laboratory Standards Institute in the USA.

Data collection procedures

All SARS-CoV-2-positive patients who visited the outpatient department (OPD) or were admitted in inpatient departments (IPDs) of the study sites were approached for data collection. An informed written consent form was provided to all patients with appropriate information. One regional site investigator was responsible for enrolling patients and data collection from each study site. Data were collected directly from the patients and their folders during their hospital stay or OPD visit by the investigator. Sputum, urine, and blood culture and sensitivity reports were extracted from the patients' available investigation reports. All data were collected on a structured questionnaire and were later updated on a Microsoft Excel sheet.

Inclusion and exclusion criteria

All patients with reverse transcriptase-polymerase chain reaction (RT-PCR)-positive SARS-CoV-2 infection who visited the OPD or were hospitalized in IPDs of dedicated COVID units of study sites during the study period were included in this study. Patients who were suspected to have COVID-19 but tested negative via RT-PCR were excluded from this study.

Statistical analysis

All data were uploaded in Microsoft Excel after ensuring coding and then analyzed using GraphPad Prism Version 10.0. Continuous data were presented as mean with standard deviation. All categorical data were expressed as frequency, percentage, and proportion. All descriptive data were illustrated as tables or figures. The association of disease severity with age, sex, and comorbidities was analyzed by chi-square test and Fisher's exact test.

Ethical consideration

This study was approved by the Institutional Review Board (IRB) of BSMMU (IRB approval number: *BSMMU/2020/6104*). A written informed consent form was provided to each patient and/or their guardian with necessary and accurate information regarding the purpose and process of this study. All patient-identifying data were kept confidential and encoded before being entered into the online database.

Result

A total of 3693 patients from five regions of Bangladesh were enrolled in this study. During the study period, 111 cases from BSMMU, 2591 cases from MMCH, 153 cases from SSSAH, 811 cases from RpMCH, and 27 patients from KMCH were enrolled.

Demographic characteristics of COVID-19 patients

Demographic characteristics of the patients according to disease severity are described in [Table 1](#).

In this study, 2370 (64.5%) patients were male, with a male-to-female ratio of 1.8:1. Patients' age ranged from 11 to 110 years, with the mean age being 52.1 ± 16.7 years. More than half of the patients (58.6%) were aged between 30 and 60 years. However, a severe form

Table 1

Demographic characteristics of the patients enrolled in the study according to disease severity (n = 3693).

	Non-severe cases (n, %)	Severe cases (n, %)	P-value	Total (n, %)
Age (in years)				
0-30	490 (13.3)	0	<0.0001 ^a	490 (13.3)
30-60	1240 (33.6)	848 (23)		2088 (56.5)
>60	0	1115 (30.2)		1115 (30.2)
Sex				
Male	1129 (30.6)	1253 (33.9)	0.7867 ^a	2382 (64.5)
Female	613 (16.6)	698 (18.9)		1311 (35.5)
Comorbidities (n = 2528)				
No comorbidities	775 (62.2)	730 (56.9)		1505 (59.5)
Diabetes mellitus	143 (11.5)	178 (13.9)	0.0238 ^a	321 (12.7)
Hypertension	185 (14.9)	228 (17.8)	0.0158 ^a	413 (16.3)
Renal disease (chronic kidney disease)	15 (1.2)	17 (1.3)	0.6049 ^a	32 (1.3)
Cardiac disease	24 (1.9)	29 (2.3)	0.3739 ^a	53 (2.1)
Respiratory disease (chronic obstructive pulmonary disease, asthma)	77 (6.2)	96 (7.5)	0.0817 ^a	173 (6.8)
Others ^c	27 (2.2)	4 (0.3)	<0.0001 ^b	31 (1.2)

^a Chi-square test was applied to calculate P-value^b Fisher's exact test was applied to calculate P-value^c Stroke, parkinsonism, nephrotic syndrome, tuberculosis, malignancy, recent surgery, obesity, intestinal obstruction.**Table 2**

Details of the prescribed antibiotics in enrolled patients according to different regions (n = 3486).

	BSMMU	MMCH	SSSAH	RpMCH	KMCH	Total
Patients prescribed antibiotics (n, %)	101 (91%)	2496 (96.3%)	151 (98.7%)	711 (87.7%)	27 (100%)	3486 (94.4%)
Number of patients receiving >1 antibiotic (n, %)	33 (32.7%)	46 (1.8%)	32 (21.2%)	99 (13.9%)	15 (55.6%)	225 (6.5%)
Average number of antibiotics used per patient (mean ± SD)	1.3 ± 0.8	0.98 ± 0.2	1.25 ± 0.6	1.02 ± 0.6	1.56 ± 0.5	1.01 ± 0.4
Antibiotics prescribed according to disease severity (n, %)						
Non-severe	28 (80%)	970 (94.8%)	64 (97%)	501 (83.4%)	4 (100%)	1567 (90.6%)
Severe	73 (96.1%)	1517 (97.5%)	86 (100%)	208 (100%)	22 (100%)	1906 (97.8%)
Duration of prescribed antibiotic (in days)						
Mean	9 ± 3.8	7.9 ± 2.9	9.9 ± 4.3	8.8 ± 4.5	8.9 ± 2.1	8 ± 3.4
Maximum duration of antibiotic	22	26	27	32	14	32
1-5 days (n, %)	16 (15.8%)	437 (17.5%)	18 (11.9%)	9 (1.3%)	0	501 (13.6%)
6-10 days (n, %)	53 (52.5%)	1661 (66.6%)	80 (53%)	562 (81.3%)	20 (76.9%)	2376 (64.3%)
>10 days (n, %)	32 (31.7%)	397 (15.9%)	53 (35.1%)	120 (17.4%)	6 (23.1%)	608 (16.5%)

BSMMU, Bangabandhu Sheikh Mujib Medical University; KMCH, Khulna Medical College and Hospital; MMCH, Mymensingh Medical College Hospital; RpMCH, Rangpur Medical College and Hospital; SSSAH, Sylhet Shahid Shamsuddin Ahmed Hospital.

of the disease (P -value <0.0001) was observed in the age group of >60 years (28.4%). Data about comorbidities were available for 2528 participants. Of these, 1023 (40.46%) had comorbidities, among which the most prevalent comorbidities were hypertension (413; 16.3%), diabetes mellitus (321; 12.7%), respiratory disease (173; 6.8%), and cardiac disease (53; 2.1%). A severe form of disease was significantly associated with diabetes mellitus ($P = 0.0238$) and hypertension ($P = 0.0158$).

Antibiotic prescribing pattern in COVID-19 patients

A total of 3486 (94.4%) COVID-19 patients were treated with antibiotics, with a mean duration of 7.99 ± 3.4 days and a maximum duration of 32 days (Table 2). Among them, 3261 (88.3%) patients received a single antibiotic and 225 (6.5%) patients were prescribed multiple antibiotics. Among the patients who were prescribed multiple antibiotics, 195 (5.3%) patients received two antibiotics, and 30 (0.8%) patients received more than two antibiotics (Figure 1a). The commonly used antibiotics observed in this study were ceftriaxone (1378; 37.3%), co-amoxiclav (971; 26.3%), azithromycin (393; 10.6%), and meropenem (380; 10.3%) (Figure 1b).

The antibiotic use in COVID-19 patients was highest in KMCH (27; 100%) and lowest in RpMCH (711; 87.7%) among the study sites. The use of multiple antibiotics was also highest among patients in KMCH (15; 55.6%) and lowest in MMCH (46; 1.8%). The average number of antibiotics used per patient was 1.01 ± 0.4 (Table 2). No difference in antibiotic usage among patients with comorbidities was observed in this study (Table S1).

Antibiotic usage pattern according to disease severity

Figure 2 depicts the antibiotic usage pattern according to COVID-19 disease severity.

Among the non-severe cases, 574 (36.6%) patients received ceftriaxone, followed by co-amoxiclav (388; 24.8%), azithromycin (305; 19.5%), and meropenem (120; 7.6%). The most used antibiotics in severe cases were ceftriaxone (799; 41.9%), followed by co-amoxiclav (580; 30.4%) and meropenem (257; 13.5%) (Figure 2). The use of broad-spectrum intravenous antibiotics such as ceftriaxone, co-amoxiclav, and meropenem was significantly higher in severe cases ($P = 0.0015$, 0.0002 , and <0.0001 , respectively). Conversely, oral antibiotics, such as azithromycin ($P \leq 0.0001$) and cefixime ($P \leq 0.0001$), were used significantly more often in non-severe cases (Figure 2).

Antibiotic usage in COVID-19 patients observed in different regions

Table 2 and Figure S1 depict antibiotic usage patterns in different regions of Bangladesh. Among the study sites, KMCH had the highest percentage of antibiotic use; all patients from this hospital received antibiotics irrespective of disease severity. The lowest percentage of antibiotic use was observed in RpMCH (87.7%). Alarmingly, a large proportion of patients were treated with meropenem in KMCH (18; 66.7%) and RpMCH (182; 25.6%). In RpMCH, 0.2% of patients were treated with linezolid. Co-amoxiclav (25; 24.8%) and ceftriaxone (25; 24.8%) were the most prevalent antibiotics used in BSMMU. Other antibiotics used in this site were meropenem (8; 7.92%) and moxifloxacin (5; 5%).

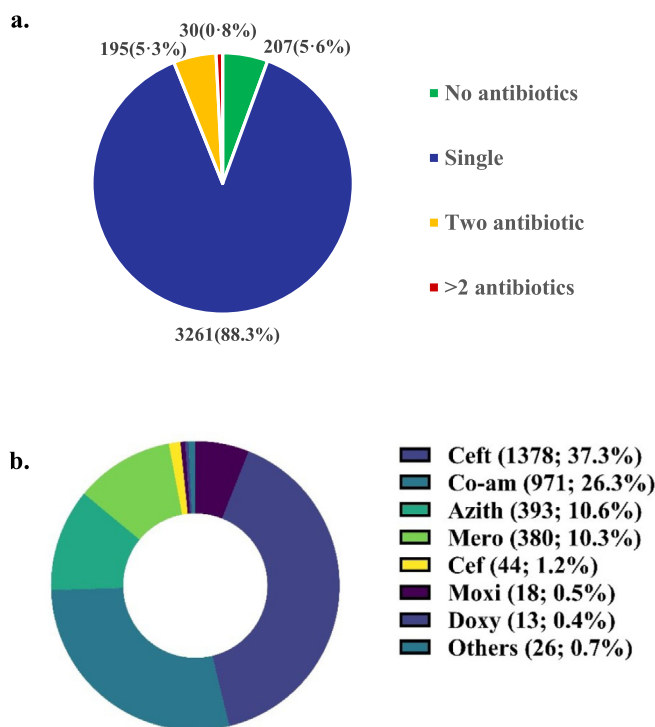


Figure 1. (a) Amounts of antibiotics used in COVID-19 patients (n, %). (b) Names of antibiotics used in COVID-19 patients (n = 3693). Azith, azithromycin; Cef, cefixime; Ceft, ceftriaxone; Co-am, co-amoxiclav; Doxy, doxycycline; Mero, meropenem; Moxi, moxifloxacin.

MMCH most commonly used ceftriaxone (1110; 44.5%), followed by co-amoxiclav (905; 36.3%), azithromycin (218; 8.7%), and meropenem (174; 6.9%). In SSSAH, the most used antibiotics were ceftriaxone (89; 58.9%), followed by azithromycin (9; 6%), meropenem (8; 5.3%), and co-amoxiclav (5; 3.3%).

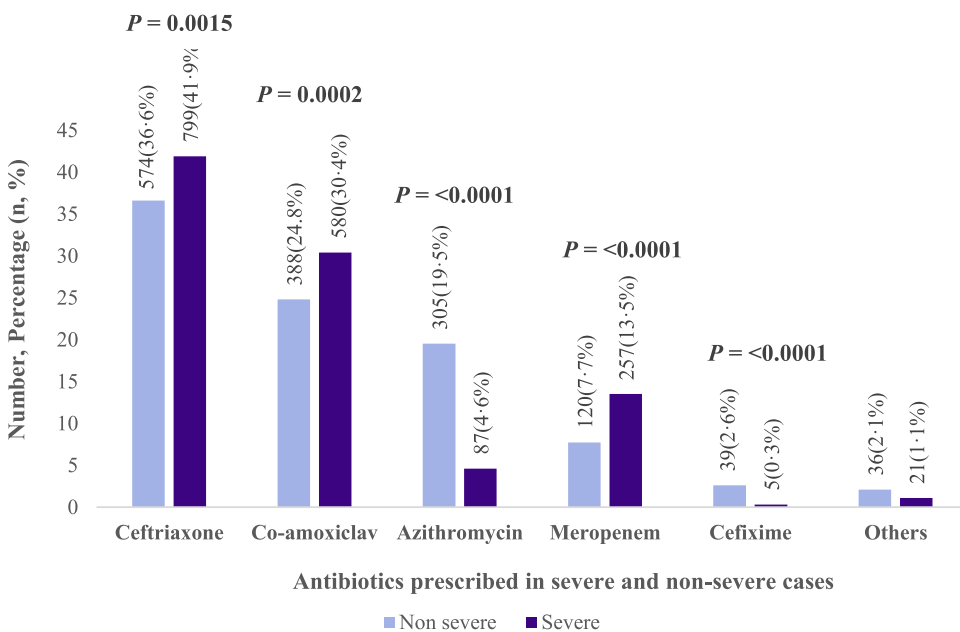


Figure 2. Antibiotics prescribed in COVID-19 patients according to disease severity (n, %).

Table 3
Culture and sensitivity pattern of COVID-19 patients in BSMMU (n = 111).

	Number, percentage (n, %)
Culture unconfirmed	90 (81.1%)
Culture confirmed	21 (18.9%)
Blood	3 (14.3%)
	Prevalent organism: <i>Staphylococcus epidermidis</i>, <i>Pseudomonas aeruginosa</i>
Sputum	11 (52.4%)
	Prevalent organism: <i>Acinetobacter</i> spp, <i>Klebsiella pneumoniae</i> (ESBL)
Urine	7 (28.6%)
	Prevalent organism: <i>Klebsiella pneumoniae</i> (ESBL), <i>Escherichia coli</i> (ESBL)

ESBL, extended-spectrum beta lactamase.

Categorization of antibiotics used according to the WHO AWaRe classification

Most antibiotics (2260; 69.6%) prescribed in this study to COVID-19 patients belonged to the WHO “Watch” group, 985 (30.4%) to the “Access” group, and only 1 (0.03%) antibiotic belonged to the “Reserve” group. In KMCH, all the prescribed antibiotics were from the “Watch” group, followed by 95.8% in SSSAH and 93.6% in RpMCH (Figure 3a). Among the “Watch” group antibiotics, the most prescribed were ceftriaxone (61%), azithromycin (17.4%), and meropenem (16.8%) (Figure 3b).

Bacteriological evidence in COVID-19 patients

Culture and sensitivity reports from sputum, blood, and urine samples were available in 111 cases enrolled in BSMMU. The culture and sensitivity patterns of the grown organisms are shown in Table 3.

A total of 21 (18.9%) patients were culture-positive. The most common bacteria identified were *Acinetobacter* and extended-spectrum beta lactamase (ESBL)-producing *Klebsiella* in sputum samples (11; 52.4%), followed by ESBL-producing *Escherichia coli* and *Klebsiella* in urine samples (7; 28.6%) (Table 3). Blood culture of the patients revealed growth of *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* (3; 14.3%); the growth of *S. epidermidis* could be attributable to contamination during sample collection and handling.

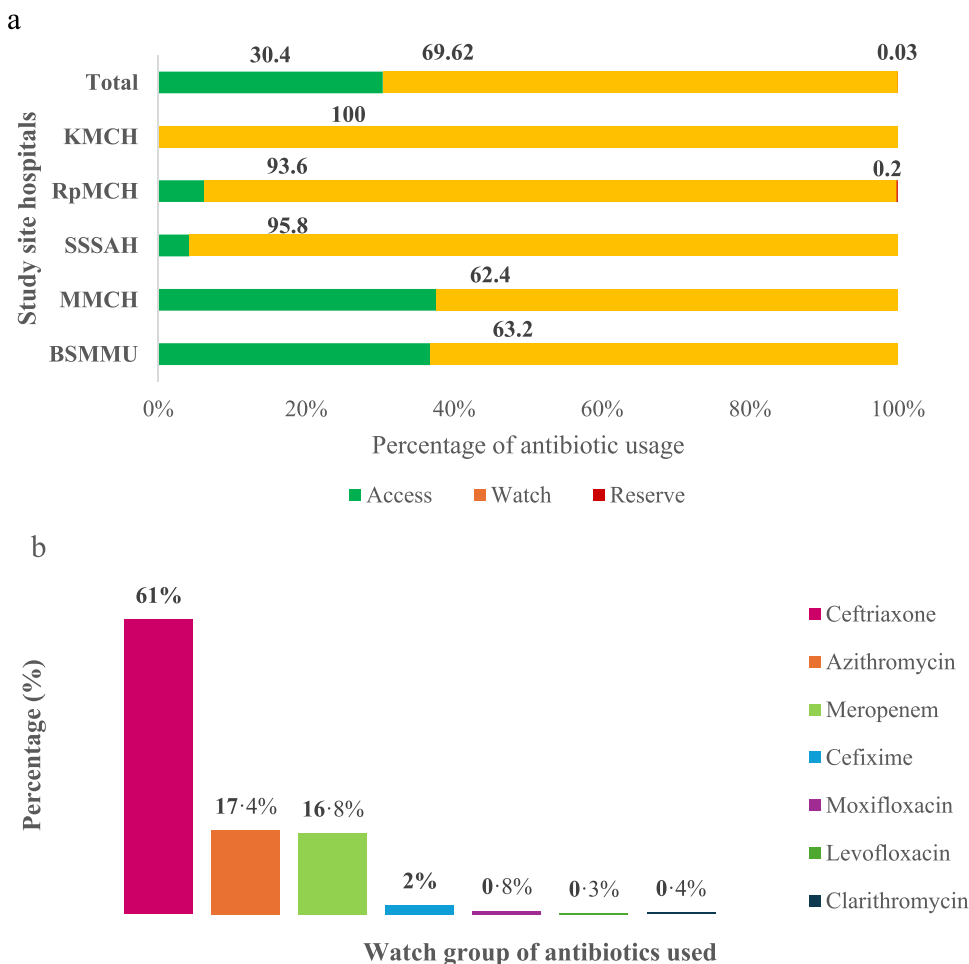


Figure 3. (a) Antibiotic usage in COVID-19 patients, categorized according to the World Health Organization AWaRe classification ($n = 3486$). (b) Pattern of “Watch” group antibiotic usage in COVID-19 patients ($n = 2260$).

BSMMU, Bangabandhu Sheikh Mujib Medical University; KMCH, Khulna Medical College and Hospital; MMCH, Mymensingh Medical College Hospital; RpMCH, Rangpur Medical College and Hospital; SSSAH, Sylhet Shahid Shamsuddin Ahmed Hospital.

Discussion

According to the findings of our study, a total of 94.4% patients received antibiotics irrespective of disease severity, whereas 90.7% of patients with non-severe disease and 97.9% of patients with severe disease received at least one antibiotic. Although antibiotics are not indicated for COVID-19 except in cases with bacteriological evidence, these findings suggest irrational antibiotic use in COVID-19 patients in Bangladesh. Broad-spectrum intravenous antibiotics were used in severe cases, whereas oral antibiotics were more commonly prescribed in non-severe cases. Among the five study sites, KMCH had the highest percentage of antibiotic use, where all patients received at least one antibiotic irrespective of disease severity. Among the 111 cases in BSMMU, 91% of the patients were treated with at least one antibiotic, although bacteriological evidence was limited. The WHO recommends 60% use of the “Access” antibiotics at the country level [9]. However, 69.5% of antibiotics prescribed to COVID-19 patients belonged to the “Watch” group in this study, and only 30.4% of patients received the “Access” group of antibiotics.

COVID-19 can present as an asymptomatic, mild, moderate, severe, or critical disease. According to the national guideline for COVID-19 disease management in Bangladesh, antibiotics are not routinely recommended in mild or moderate cases [8]. Although COVID-19 is a viral disease with no role of antibiotics in management, it causes an acute respiratory syndrome indistinguishable from bacterial infections [10]. The use of azithromycin, a macrolide antibiotic, has been advocated in treating COVID-19 since the beginning of the pandemic because of its antiviral and immunomodulatory effects, demonstrated in preclinical studies against the Zika virus, rhinovirus, and Ebola virus [11,12].

However, it was later on discouraged by the WHO because of weak evidence and potential cardiotoxic side effects [13].

The previously experienced influenza pandemic was associated with higher mortality due to secondary bacterial infections and co-infections, which might have accelerated the tendency to prescribe antibiotics to COVID-19 patients [14]. Overuse of antibiotics in COVID-19 can be attributable to (i) difficulties in distinguishing COVID-19 pneumonia from other bacterial pneumonia, as both have similar presentations (fever, cough, respiratory distress), (ii) unavailability of specific treatment options, (iii) anxiety and uncertainty of disease outcome, (iv) lack of available evidence, (v) lack of confidence among physicians, (vi) possible industry pressure, and (vii) presumption of secondary co-infections with bacteria or fungus [15].

It has been previously reported that 71.9% of COVID-19 patients have received antibiotics, whereas only 7-8% have been diagnosed with bacterial or fungal co-infection [16]. During the first wave of COVID-19, a survey among suspected COVID-19 patients in Bangladesh found that the use of antibiotics was 92%; 89% of them received antibiotics on hospital admission, and 47% of the suspected patients were prescribed with antibiotics before hospital admission [7,17]. According to our study findings, 94.4% of patients received antibiotics irrespective of disease severity, and 90.6% of patients received at least one antibiotic despite presenting with non-severe disease manifestations, which is a higher percentage than that previously reported (78%) in non-COVID patients [18]. However, the rate of antibiotic use in our study was lower than that observed in a study conducted in another center in Dhaka (100%) [6], but higher than those reported in other Asian countries such as Pakistan (89.7%) and Japan (13.21%) [19,20]. Global surveys conducted worldwide have concluded that increased use of anti-

otics has been reported in more than half of the countries, with higher prevalence in LMICs [21,22]. Higher incidence of prescribing third-generation cephalosporins, co-amoxiclav, macrolides, and carbapenem was observed in this study, which is almost consistent with previous report [23].

The WHO Expert Committee developed the AWaRe classification of antibiotics, categorizing the antibiotics into “Access,” “Watch,” and “Reserve” groups to emphasize the importance of their appropriate use in clinical settings. According to this, the “Access” group antibiotics should be widely available and can be used as first-line agents, as they have a relatively lower chance of resistance [24]. A previous study conducted by Budd *et al.* showed that following AWaRe recommendations has led to increased use of the “Access” antibiotics in England [25]. Bangladesh developed its National Action Plan (NAP) for AMR containment in 2017, which focused on eight major objectives including proper planning, monitoring of rational use of antimicrobials, strengthening infection prevention control, measures to minimize the emergence of AMR, strengthening the surveillance system of antimicrobial usage, etc. [26]. However, implementation of AWaRe categorization and NAP has not been possible in Bangladesh because of weak monitoring systems, poor health care facilities, and lack of awareness. Previous studies concluded that in LMICs, including Bangladesh, the vast majority of antibiotics used in COVID-19 patients belonged to the “Watch” group [18], and similar findings were also observed in this study.

In our study, 30.4% of antibiotics from the “Access” group, 69.5% of antibiotics from the “Watch” group, and only 0.03% of antibiotics from the “Reserve” group were observed to be prescribed in COVID-19 patients. These findings are almost similar to those of another study conducted in Bangladesh [18]. The most commonly used antibiotics among the “Watch” group were ceftriaxone, azithromycin, and meropenem.

This increasing use of the “Watch” group antibiotics can prove to be alarming in a country such as Bangladesh, where infectious diseases are very common and injudicious use of antibiotics may contribute to the development of difficult-to-treat multi-drug-resistant (MDR) organisms. Among the 111 available culture and sensitivity reports in this study, bacteriological co-infection was found in only 18.9% of the patients. Most of these co-infections were with MDR gram-negative organisms. Similar results have been reported previously, showing a higher incidence of bacterial co-infections with MDR organisms in COVID-19 patients, predominantly caused by gram-negative bacteria [27,28]. Globally, *Staphylococcus aureus*, *E. coli*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *P. aeruginosa*, and *Acinetobacter baumannii* are the six leading bacterial causes of death [29]. Our study also observed significant growth of *E. coli*, *Acinetobacter*, *Klebsiella*, and *Pseudomonas* in blood, sputum, and urine. The rise in MDR organisms due to inappropriate use of antibiotics may contribute significantly to the development of a future pandemic caused by global bacterial AMR [29].

Antibiotic stewardship programs are developed to promote rational antibiotic usage and improve clinical outcomes, with the aim of preventing the development of AMR. Following the global surge in COVID-19 cases and inappropriate use of antibiotics, AMR has been one of the major concerns of national and international institutions all over the world. Developed countries have benefitted from strong policymaking and monitoring of antibiotic usage. However, this could not be implemented properly in LMICs including Bangladesh because of a lack of diagnostic tools, social drives influencing the prescription of antibiotics, lack of awareness, and availability of antibiotics without prescriptions.

We are aware that our study has some limitations. First, data collection was dependent on the data collector’s knowledge and competence. Although regional data collectors were trained with detailed information and procedures, variability among data collectors could not be excluded. Second, bacteriological evidence could not be collected from all patients among the five sites. Third, this was a prospective, observational study. We only collected data on antibiotic usage in COVID-19 patients and available bacteriological evidence. Our data collection did not influence any treatment modifications in the enrolled patients. Hence,

most of the patients might have been treated with empirical antibiotic therapy. Fourth, the depth of knowledge of treating physicians and hospital staff could not be assessed properly because of the high burden of COVID-19 patients in dedicated hospitals. Fifth, the treatment outcome of the patients was not assessed, as this study was primarily focused on the usage of antibiotics in COVID-19 patients.

Conclusion

Excessive use of antibiotics in COVID-19 treatment has been observed in Bangladesh, despite limited bacteriological evidence. Pertinent knowledge gaps among prescribers should be addressed with proper education on updated guidelines and emphasis on minimal use of antibiotics to prevent the threat of AMR. Strict policymaking on antibiotic prescribing and strong antibiotic stewardship programs should be introduced at the earliest, with the highest priority in Bangladesh, to prevent it from being a vital contributor to the global AMR threat.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical statement

This study was approved by the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU) (IRB approval number: *BSMMU/2020/6104*).

Author contributions

FRC was directly involved in conceptualization, methodology, and project administration. MMK, BB, MZA, PT, SP, TMAA, MAAA, and TBH were involved in data collection. FRC, MSR, MMK, BB, and MZA were involved in resources. FRC, MSR, and SP were involved in formal analysis and interpretation. TBH wrote the first draft. FRC, MSR, and SP were involved in editing the manuscript. All authors revised the draft manuscript and agreed upon the final version.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ijregi.2024.100381](https://doi.org/10.1016/j.ijregi.2024.100381).

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