Antimicrobial prescribing behaviors in Covid 19 patients: A multicenter survey at Tertiary Care Hospitals of Chittagong division in Bangladesh

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Abstract

Inappropriate use of antimicrobials in the treatment of Covid-19 can result in patient harm and worldwide antimicrobial resistance. The study's objective was to explore the physician choices of empirical antimicrobial treatment in Covid-19Patients. A multicenter web-based survey was performed to explore the trend of empirical antimicrobial prescribing reported by physicians involved in Covid-19 care from June to December 2021. A questionnaire linked to a Google form was distributed via several online platforms to physicians working in the Covid specialist unit of tertiary care hospitals in Chittagong, Bangladesh. The questionnaire was distributed to 120 physicians, and 74 (89%) responded to the survey. According to 69% (n=51) of participants, there was no local antimicrobial guideline in the hospital. Almost half of the physicians (87%, n=64) mentioned that the severity of the condition was the most crucial component in starting antimicrobials. The majority of participants considered empirical antimicrobial coverage for Pseudomonas aeruginosa (68%, n=51), Klebsiella pneumonia (65%, n=48), and Streptococcus pneumoniae (57%, n=49). Meropenem and ceftriaxone were the most common antimicrobials prescribed in Patients in the Covid ward, reported by 54% (n=40) and 41% (n=30) participants, respectively. ICU patients' most commonly prescribed antimicrobials were Meropenem (84%, n=62) and Piperacillin/tazobactam (42%, n=31). According to 67% (n=49) of participants, the average length of antimicrobial treatment was seven days. The survey suggests that physicians' selections of empirical antimicrobials in Covid patients were predominantly broad-spectrum. An initial lack of national Covid management guidelines and overall inadequacy of regional or hospitalized-based antimicrobial guidelines are the confounding factors behind antimicrobial overprescribing. The study findings can be utilized to design interventions for effective antimicrobial stewardship, allowing physicians to prescribe appropriately.

Keywords: Antimicrobial, prescription, Covid-19, ICU, physician, antimicrobial stewardship, antimicrobial registance.

Introduction

In 2019, the world experienced a terrifying foreshadowing of a global pandemic caused by a novel corona virus known as SAR-CoV-2[1]. Controlling the spread of infection and developing treatments and vaccines were the main emphasis of the global action plan[2]. The Covid-19 virus can produce an acute respiratory illness that is difficult to distinguish from bacterial infections and can result in secondary infections[3]. As a result, antimicrobials were routinely recommended for various reasons, all of which could contribute to AMR. Moreover, Antimicrobial overuse may aggravate the global problem of antimicrobial resistance while rendering presently accessible antimicrobials ineffective[4].

Presumably, various factors contribute to resistance, including unnecessary antimicrobial prescribing for common viral illnesses in health clinics, over-the-counter antimicrobial access, inadequate knowledge of prescriber[5], antimicrobial dispensation by medicine sellers[6], and preventive use due to fear of sickness[7-9]. The severity of the condition among hospitalized patients may worsen the problem, resulting in antimicrobial over-prescription, which can result in more significant selective pressure for antimicrobial resistance[10,11]. As a result, the current pandemic's consequences may extend into the "Post Covid-19 era"[3].

In Bangladesh, Covid-19 patients quarantined at home with minor symptomatic infections were given single or more antimicrobials with or without a prescription, complicating the current fight against Antimicrobial resistance[12]. Furthermore, all patients admitted to the hospital were routinely given broad-spectrum antimicrobials. Studies conducted in England have shown a progressive decline in antimicrobial prescribing all through 2020 compared with pre-pandemic[13] with similar patterns observed in Northern Ireland[14], Scotland[15] and other states[16,17].

Physicians are the frontline warriors in the battle to save Covid-19patients during this outbreak, providing their services to hospitalized patients. Initially, physicians were under enormous pressure to expose to a high risk of infection and less confident about treating Covid-19 patients due to a dearth of guidelines and insufficient diagnostic availability[18]. On chest X-ray, nearly all Covid-19 patients had symmetrical lung infiltration; however, only a few had significant sputum production for culture sensitivity or gram stain[19]. Consequently, the choice to start an antimicrobial was influenced by the presence of elevated inflammatory markers and any infiltrate on an x-ray[20].

The World Health Organization (WHO) has released Covid-19 guidelines for the clinical management of Covide-19patients. In general, treatment in Patients with mild illness is primarily supportive and symptomatic. Antimicrobial therapy against possible pathogens causing severe acute respiratory distress or sepsis is recommended for patients hospitalized with suspected Covid-19 [21].

During the initial wave, antimicrobials such as Azythromycin, Doxycycline, Ivermectin, and others were abused in the community, but when treatment guidelines were established, consumption declined[22,23]. On the top of that, world health organization identified Ceftraixone, Vancomycin, Azythromycin, Carbepenems, tigecycline and linezolid as critically essential antibiotics (CIA) for humans[24].

Due to the misuse of ceftriaxone, a variety of non-enteric bacteria and enterobacteriaceae have evolved resistance to third-generation cephalosporin[25]. If this massive use continues, there will be few alternatives available, all of which will be incredibly expensive for developing countries[26].

According to a systematic review, two-thirds of Covid-19 patients received antimicrobial therapy on average, while only a tiny percentage had bacteriologically proven coinfections[27]. Surprisingly, the rate of antimicrobial prescription does not vary with the severity of the illness[28]. The higher the usage of empiric antimicrobials in Covid patients, the greater the risk of clostridium difficile infection and the emergence of multidrug-resistant organisms[29].

However, to reduce irrational antimicrobial usage, it is necessary to investigate trends and factors related to empiric antimicrobial therapy from the perspective of Covide-19. This research may shed light on antimicrobial resistance and prescribing practices. Henceforth, we conducted a brief online survey to learn more about antimicrobial prescribing behavior in Covid-19 Patients. Evaluating the trends and predictors of antimicrobial prescribing practices in Covid-19 can aid in identifying intervention opportunities to improve rational use.

Materials and methods

Study design and population: A cross-sectional, multi-centered, web-based questionnaire survey was conducted among physicians working in the Covid unit of government and non-government medical colleges in the Chittagong division of Bangladesh during June, 2021 to December 2021. Ethical approval was obtained from the institutional review board of BGC Trust Medical College. The physicians were notified that their participation was entirely voluntary and that anonymity would be maintained to protect confidentiality. Cronbach's alpha was used to assess the validity and internal consistency of the study questionnaire, and the questionnaire had good internal consistency (Cronbach's alpha = 0.81).

Study Procedure: We designed an 11-question questionnaire. The questionnaire gathered information about the participants' backgrounds, what factors influenced the administration of Covid-19 patients with antimicrobials, and the availability of local antimicrobial guidelines about Covide-19. Finally, participants were recommended to choose empirical antimicrobial therapy for Covid-19 Patients both in the clinical ward and ICU setting. They were also asked how long they usually stayed on antimicrobials. The questionnaire was created with the assistance of prior research[11]. The questionnaire was tested on ten participants to ensure it was clear and understandable. The questionnaire was sent to 120 physicians by email, WhatsApp, and Facebook Messenger. A few young physician volunteers were enrolled from different medical colleges to distribute the questionnaire and adequately address the study. To maintain confidentiality, the response was sent over Google Drive and was anonymous. The automated Google form received only one response from one email address to avoid repeated or multiple responses. Using the survey platform, two reminders were sent.

Results and discussion

The survey was completed by 74 participants from 12 university-affiliated government and non-government hospitals at Chittagong division, Bangladesh. Majority of the respondents worked in government hospitals (76%, n = 56/74). Over the half of the participants was medical officer (47%, n=35) and only 3% was professor. About half of the participants (49%, n=36) worked directly with Covide-19 patients and only 7% of participants (n= 5) were related with developing local Covid-19 care guidelines (Table-1).

Table-1: Demographics and Information of the Study Participants (N=74).

Item	Variable	Frequency (*n*) & percentage (%)
Gender	Male	57/74 (77%)
	Female	17/74 (23%)
Type of Hospital	Govt.	76% (56/74)
	Non- govt.	24% (18/74)
Designation	Medical Officer	47% (35/74)
	Registrar	37% (19/74)
	Assistant Professor	16% (12/74)
	Associate Professor	8% (6/74)
	Professor	3% (2/74)
Role in managing Covid-19 Patient	Direct care of patients with Covid19	49% (36 /74)
	Management/supervision of direct Covid-19 patient care	29% (29/74)
	Development of local Covid-19 guidelines	7 (5/74)
	Others	20% (15/74)

The presence of local guidelines for antimicrobial use in Covid-19 patients was reported by 31% (n =23) participants, and 69% (n =51) did not have local guidelines. The severity of the disease was identified as the most crucial reason for the initiation of antimicrobials by nearly 87% (n =64) of participants, followed by radiological findings 64% (n=47), laboratory markers of inflammation 60% (n=44). The participants recognized that the most important laboratory biomarkers were C reactive protein 48% (n=35), D-dimer% (n =26), and Procalcitonin 23% (n=31).

In response to a question on the empirical use of antimicrobials in Covid-19 Patients, only 14% of physicians stated that they did not routinely prescribe antimicrobials. 69% of respondents chose to prescribe any antimicrobial while the Patient was admitted to the hospital, followed by on diagnosis in the outpatient department (26%, n=19), ICU (58%, n=43), and Patient in ventilator (42%, n=32).

In reply to the question asked about empiric antimicrobial prescribing in Covid-19 Patients, the majority of the participants stated that empiric treatment was necessary with activity against the specific microbes such as Pseudomonas aeruginosa (n=51, 68%), Klebsiella Pneumoniae (n=48, 65%), Staphylococcus aureus (n=33, 45%), Atypical Pathogen (n=30, 40%), and Acinetobacter (n=17, 23%).

Meropenem was the most common antimicrobial prescribed in Patients in the Covid ward, reported by 54% (n=40) of participants, followed by Azithromycin 42% (n=31), ceftriaxone 41% (n=30) (Table-2).

Table-2: Percentage of Physician-recommended specific class of antimicrobials in Covid ward (N=74).

Name of Antimicrobial	Responses Frequency (n) & percentage (%)
Azithromycin	31/74 (42%)
Meropenem	40/74 (54%)
Co-Amoxyclav plus Macrolid	20/74 (27%)
Co-Amoxyclav plus fluroquinolone	13/74 (18%)
Moxifloxacin	20/74 (27%)
Ceftriaxone/Cefotaxime	30/74 (41%)
Pipercilin/Tozabactum	8/74 (11%)
Linezolid	9/74 (12%)
Ceftaroline	4/74 (6%)
Clindamycin	6/74 (8%)
Vancomycin	1/74 (1%)

In Covid ICU, Meropenem (84%, n=62), Piperacillin/ tazobactam (42%, n=31), Linezolid (44%, n=32), and Ceftriaxone (32%, n=23) were the routinely prescribed antimicrobials (Table-3). In response to the duration of therapy, 66% and 42% responded that the stated duration of antimicrobial therapy was 7 and 14 days, respectively.

Table-3: Percentage of physician-recommended specific class of antimicrobials in Covid-19 ICU (N=74).

Name of antimicrobial	Responses Frequency (n) & percentage (%)
Meropenem	62/74 (84%)
Linezolid	32/74 (44%)
Pipercilin/Tozabactum	31/74 (42%)
Co-Amoxyclav plus Colistin	7/74 (10%)
Cefipime	7/74 (10%)
Co-Amoxyclav plus fluroquinolone	13/74 (18%)
Ceftriaxone/Cefotaxime	23/74 (32%)
Ceftaroline	1/74 (2%)

In the present study, two-thirds of the participants (69%) claimed that their hospital did not have local guidelines. In a survey among European clinicians conducted by Beović B et al., the majority of respondents reported that their hospital had a local guideline for antimicrobial therapy for Covid patients but mainly followed their existing guideline of community-acquired pneumonia[11].

Another study in Pakistan showed that most hospitals lacked local institution-based clinical guidelines for Covid-19 patients[12].

The dearth of local clinical guidelines for managing Covid patients may lead to inappropriate antimicrobial use, thus exacerbating the AMR problem[18].

According to the current study, the severity of the disease (87%), radiological findings (64%), elevated C reactive protein (48%), and Procalcitonin (31%) were the most critical determinants of initiating antimicrobial therapy. Several studies revealed similar results[20,28].

Antimicrobials are often prescribed empirically in Covid-19 patients, like most other illnesses[19]. In this survey, more than half of physicians mentioned that empiric antimicrobial treatment is necessary for the treatment of secondary infection, mostly with Pseudomonas aeruginosa (69%), Klebsiella Pneumonae (65%) and Staphylococcus aureus (45%) in Covid patient. A concordant result revealed by Hayat et al study stated that two-thirds (79.4%) of antimicrobials are prescribed in Covid-19 Patients empirically infected with methicillin-resistant Staphylococcus aureus[18].

However, for the treatment of a probable Covid-19 patient[4], mostly broad-spectrum antimicrobials were given as a preventative approach or to treat subsequent bacterial infection and pneumonia[30]. In the present study, Meropenem is the most widely recommended antibiotic for Covid-19 ward reported by 54% of the physician, followed by Azythromycin 42%, ceftriaxone 41%. The majority of the physician mentioned that Meropenem (84%), Piperacillin/tazobactam (42%), linezolid (44%) ceftriaxone (32%) were the most regularly recommended antibiotic in the ICU of Covid-19. Similar findings were revealed in Molla MMA et al. study conducted in a Covid-19 dedicated hospital of Bangladesh[31]. In contrast to the current study, Beovic et al. found that more than half of the physicians in the Covid-19 ward used Beta-lactams in conjunction with macrolides or fluoroquinolones. At the same time, piperacillin/tazobactam was the most commonly used antimicrobial in the Covid-19 ICU[11].

The most likely reason for the increase in Meropenem prescribing in the Covid ward could be the recommendation of Meropenem by clinical management guidelines recommended by the Ministry of health and family welfare of Bangladesh in severely ill Covid-19 Patients. However, insufficient antiviral drug availability and anxiety and uncertainty contribute to antimicrobial overuse worldwide[32].

In this study, more than half of the participants (67%) stated that the extent of antimicrobial therapy was 7 days. The findings are comparable to those of O'Kelly et al.[27]. According to research by Boevic et al. the extent of antimicrobial therapy was 5 days in North America and the United Kingdom and 7 to 8 days in Italy and other unspecified regions[11].

This study has significant shortcomings. It only included physicians working at tertiary healthcare facilities and was conducted on a small sample size. As a result, the findings have limited generalizability.

Conclusion

Unguided and pointless use of antimicrobials throughout the Covid-19 period in Bangladesh conceived a circumstance where the future of antimicrobials is at stake, and the world already stands at the margin of emerging antimicrobial resistance. Therefore the findings of this survey can create an impulse to launch a successful antimicrobial stewardship program that will allow physicians to prescribe judiciously. In order to reduce unnecessary antimicrobial prescriptions, interventional measures should include strict adherence to Covid-19 clinical treatment guidelines. Active educational strategies, such as academic details and workshops, should be implemented in each hospital based on its specific resources.

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