ORIGINAL ARTICLE

Patterns of In-patient Antibiotic Use among COVID-19 Patients in a Tertiary Government Hospital: A Retrospective Cross-sectional Survey

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ABSTRACT

Background. The occurrence of the COVID-19 pandemic resulted in increased risk of developing antimicrobial resistance due to the high utilization of antimicrobial agents. Since antimicrobial utilization is a crucial driver in the development of antimicrobial resistance, the need for antimicrobial use surveillance is crucial in identifying prescription patterns that would help provide proper interventions.

Objective. To determine the antibiotic use and prevalence of prescription quality indicators among COVID-19 patients admitted at a tertiary government hospital.

Methods. A retrospective cross-sectional survey was conducted to provide data on antibiotic use and the prevalence of prescription quality indicators among COVID-19 patients in a tertiary-level hospital from June 2021 to June 2022.

Results. A total of 342 patient medical records were surveyed. The majority (119, 34.8%) of the patients were in the age group 41-60 years old and there were more male patients (52.34%) than female patients (47.66%). About 88.99% of the patients were considered to have community-acquired COVID-19 infections. Co-morbidities among patients were seen in more than half of the surveyed population (64%). These include hypertension, diabetes mellitus, chronic kidney disease, coronary artery disease, chronic lung disease, and hematologic disorders.

Empiric antibiotic therapy was high at 88.88%, while definitive treatment with confirmed bacterial infection was only at 11.11%. The most frequently prescribed antibiotic therapies are azithromycin (250, 45.9%), ceftriaxone (188, 32.2%), and cefuroxime (58, 9.9%). Patterns of antibiotic use are attributed to the similarities of respiratory bacterial infections with COVID-19 cases.

Prescription quality indicators assessed in the study include documentation of indication for prescriptions, guideline compliance, collection of culture before antibiotic therapy, and stop/review documentation. Out of 583 antibiotic prescriptions, 464 (79.58%) were properly documented with an indication. Non-compliance to guidelines reached 39.11%, while the stop and review date documentation rate was 20.41%. The collection of culture before the start of antibiotic therapy was at 50.2%.

Conclusion. The results from the study highlighted the need for antimicrobial surveillance and stewardship efforts among COVID-19 and other viral infections.

Keywords: COVID-19, antibiotic, stewardship, coronavirus, prevalence survey

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INTRODUCTION

Over the previous decades, the increasing percentage of antimicrobial resistance (AMR) has been largely recognized as an imperative health concern, causing severe health and economic effects worldwide.[1] In an estimation, about 10 million deaths worldwide can possibly occur by 2050 due to the development of drug-resistant infections. The economic impact of AMR is catastrophic, forcing up to 24 million people to suffer poverty.[2] The increasing overuse of antibiotics is a major contributor to the global development of AMR. Much of the literature on AMR have shown a direct link between antimicrobial consumption and the dissemination of resistant bacterial strains.[3] Since the discovery of antimicrobials, a massive improvement in medical practice has been seen due to the rapid and specific treatment of infectious diseases. This remarkable development has led to the widespread practice and belief that antimicrobials should be applied empirically to all ailments.[4]

Hospitals are among the healthcare facilities with the highest antibiotic use due to the high density of infectious disease patients requiring immediate care and attention. The influx of patients with life-threatening symptoms prompts immediate action requiring multiple antimicrobials to cover the unidentified pathogen. A multicenter prevalence study in the United States found that 59.6% of antimicrobial treatments are unsupported by medical data and deemed inappropriate.[5] A similar study in Japan showed that about 38% of antimicrobial therapy is inappropriately prescribed. Among the most common reasons for inappropriateness were the drug's spectrum and lack of microbial indication.[6] Healthcare practitioners' practices have turned hospitals into breeding grounds for antibiotic-resistant microorganisms. To prevent the rise in antimicrobial resistance, antibiotic drugs must be used more effectively. The occurrence of COVID-19 pandemic has intensified the risk for AMR due to the increasing number of antibiotic use in various healthcare facilities.[1] The US Center for Disease Control has reported an increase in antibiotic utilization among agents commonly prescribed for respiratory infections due to the difficulties in distinguishing COVID and community-acquired pneumonia in patients arriving at healthcare institutions.[7] The inability to accurately and quickly diagnose infectious diseases in diverse healthcare settings adds to the indiscriminate use of antibiotic. Inadequate diagnostic capacity, differences in local resistance patterns, and the limited access of infectious disease specialists are among the factors that contribute to misuse of antibiotic agents. Most general practitioners prefer to prescribe empirical antimicrobials based on local epidemiology and previous experience rather than testing for culture and antimicrobial sensitivity. This strategy frequently leads to incorrect antibiotic use and the development of antimicrobial resistance. An accurate and rapid diagnostic tool in infectious diseases is critical for establishing proper antibiotic use and preventing antimicrobial resistance.[3] Previous investigations have observed that COVID-19 patients are given antibiotics despite the fact that bacterial co-infections are uncommon.[8] Several studies have shown variations in prescription patterns and antibiotic utilization across various healthcare settings.[9,10]

A meta-analysis by Langford et al. has shown that about 74.6 % of admitted COVID-19 cases have been prescribed with broad-spectrum antibiotics.[11] The various studies that analyzed antibiotic use of COVID-19 patients have shown different patterns of antibiotic utilization based on geographical location and prescribing practices of professionals. One published study on multicenter antimicrobial use reports among seven hospitals in Croatia, Italy, Serbia, and Slovenia was conducted by Papst et al. This study has shown a 52.7 % antibiotic prescribing rate among COVID-19 patients. and the most commonly prescribed antibiotics were classified under the "Watch" classification of the World Health Organization.[12] However, a prevalence study conducted by Ng et al. in a tertiary hospital in Singapore has seen a decrease in antibiotic usage despite the occurrence of the pandemic. The prevalence of antibiotic prescribing in the said hospital last 2015 was 55% which significantly decreased to 47% last 2020. The study also noted an improvement in the antimicrobial prescribing quality indicators, highlighting the importance of stewardship interventions in the hospital setting.[9]

Quality indicators (QIs) are measurable elements of practice performance for which there is evidence or consensus that can be used to assess the quality of antibiotic care provided.[13] The variations in antibiotic use among healthcare institutions were seen globally due to diverse guidelines and investigational protocols in managing the novel disease. Educational background and antimicrobial use or resistance was determined as contributing factors that affect the development of prescribing practices among healthcare professionals.[14] These elements vary from institution to institution and require continuous evaluation to improve management and prescribing practice.[15]

In the Philippines, it was reported that antimicrobial use prevalence on COVID-19 wards was 85.6% and 73.8% on intensive care and medical wards, respectively.[16] Due to the large prevalence of antimicrobial use, several medical organizations and health professionals have advocated for rational and judicious use of antimicrobial agents in COVID-19 cases.[16] Most healthcare institutions within the country lack antimicrobial use surveillance programs to monitor local antimicrobial consumption. The importance of local data on the pattern of antimicrobial use and the prescribing practice of healthcare professionals greatly affects the development of antimicrobial resistance.[17] Since antimicrobial utilization is a crucial driver in the development of antimicrobial resistance, the need for antimicrobial use surveillance is crucial in identifying prescription patterns that would help provide proper interventions.[2] Data on antimicrobial use will guide antimicrobial stewardship

programs of institutions to customize strategies for mitigating the development of antimicrobial resistance.[18]

To further build upon the antimicrobial use surveillance among novel infectious diseases like COVID-19 cases, an analysis of antimicrobial use and prescribing patterns are needed to be conducted within the Philippines. This study aims to determine the antibiotic use and prevalence of prescription quality indicators among COVID-19 patients admitted at Jose B. Lingad Memorial General Hospital. The World Health Organization has cited that antimicrobial use surveillance and monitoring as one of the five strategic priorities in the Global Plan on AMR.[19] This information will help the institution provide essential insights and evidence into the specific influences of particular use patterns on resistance and help identify areas needing specific initiatives in the prescribing practices of healthcare professionals.[17]

METHODS

Research Design

The study utilizes a retrospective cross-sectional survey to investigate the antibiotic utilization and presence of prescription quality indicators among COVID-19 inpatients admitted at Jose B. Lingad Memorial General Hospital (JBLMGH) from June 2021 to June 2022. A retrospective cross-sectional survey enables analysis of existing medical data from the source of the information without the need of direct intervention. The JBLMGH is a Department of Health-designated End-referral training hospital in Region III with a wide array of basic and comprehensive specialty and subspecialty health services. The institution was also designated by the DOH as one of COVID-19 Treatment Centers in Central Luzon.

Study Population

The target population includes COVID-19 patients admitted from June 2021 to June 2022. Inclusion criteria for the study population include patients 18 years old and above with suspect, probable, or confirmed cases of COVID-19 infections and who are prescribed with at least one systemic antibiotic during the course of the treatment period. The definition of suspected and probable cases is based on the Philippine Department of Health COVID-19 Surveillance System.[20]

The suspected case is defined as a patient with the following conditions:

- Patients with severe acute respiratory illness (SARI: acute respiratory infection with history of fever or measured fever >38 C, and cough with onset within the last 10 days and who require hospitalization).
- Patients with influenza-like illness that are:
    - Residing or working in an area with high risk of transmission of the virus: for example, closed residential settings and humanitarian settings such as camp and camp-like settings for displaced persons, any time within the 14 days prior to symptoms onset; OR
    - Residing in or travel to an area with community transmission anytime within 14 days prior to symptoms onset; OR
    - Working in health settings including within health facilities and within households, anytime within the 14 days prior to symptoms onset

Probable cases are defined as a suspected case that fulfills the following criteria:

- Suspect case whom testing for COVID-19 is inconclusive
- Suspect who tested positive for COVID-19 but whose test was not conducted in a national or subnational reference laboratory or officially accredited laboratory for COVID-19 confirmatory testing

Confirmed cases are defined as a positive result from SARS-CoV-2, using laboratory-based polymerase chain reaction or serologic assay.[20]

Sampling Method

The study utilized a simple random sampling design in which COVID-19 patients admitted from June 2021 to June 2022 were subjected to sampling. The minimum sample size requirement of this study was 293 COVID-19 patients admitted at Jose B. Lingad Memorial General Hospital. This was computed using the sample size formula for estimating the population proportion based on the following information: (1) population size of 5270, (2) the confidence level was set at 95%, (3) the expected prevalence of antibiotic use in COVID-19 patients was around 72%, and (4) margin of error of 5%.[21] Open epi website was utilized in the sample size calculation.

$$\text{Finite population: } n' = \frac{n}{1+\frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2 N}}$$

Data Collection

The research instrument used in the study is a patient data collection form from the Global-Point Prevalence Survey of Antimicrobial Consumption and Resistance. It is divided into three domains: clinico-demographic information, antibiotic therapy, and antibiotic quality indicators. Two independent data collectors conducted chart reviews from the eligible medical records.

The antibiotic therapy of each patient was assessed and categorized based on compliance with the hospital's Standard Treatment Guidelines and the DOH National Antibiotic Guidelines.

The independent data collectors were tapped to perform collection of needed data for the study. The data collector was trained on chart review procedures and the use of the data collection tools. Data collection was done from June to-July

2023 and performed after working hours or during day-off of selected data collectors to ensure adequate time and focus on the assigned task.

Data collectors used simple random sampling to select patient records, ensuring unbiased representation. Inclusion and exclusion criteria were also used to determine eligible patient records for data collection. Two data collectors were assigned per patient record for independent verification following the procedure of data collection:

- Verify demographic and clinical data per record
- Extract antibiotic therapy per patient case
- Note documentation status for quality indicators

All collected patient data were de-identified by using specific survey codes during the data collection process. Physical and digital data were kept securely and accessible only to authorized personnel to ensure confidentiality of data

Data Entry and Analysis

All patient data collection forms were validated for consistency and accuracy before data entry. The investigators conducted a random audit of 34 patient data collection forms to ensure accuracy and completeness of the data collected. All collected data were entered into a web-based tool for data entry and validation designed by the University of Antwerp (http://global-pps.com) by two independent data collectors. All discrepancies detected by the system were resolved through consensus of the data collectors and investigators.

Validated data were exported and analyzed with Microsoft Excel 2019. All antibiotic utilization and compliance to prescription quality indicators were examined. Data such as clinico-demographic characteristics, antibiotic prescribed, and antimicrobial quality indicators were presented using percentage and weighted mean.

Ethical Approval

Ethical approval was obtained from Saint Louis University-University Research and Innovation Center: Research Ethics Committee (SLU-REC 2023-008). Before data collection, permission was sought from respective hospital administration. Collected data were de-identified during data collection and data were analyzed in aggregate to maintain confidentiality and anonymity of information.

RESULTS

Demographic Characteristics of Patients

The medical records of all 342 COVID-19 patients who were admitted to the hospital were examined. Table 1 summarizes the clinic-demographic characteristics of COVID-19 patients admitted from June 2021 to June 2022 at Jose B. Lingad Memorial General Hospital. The mean age of the patients was 50.43 ±1.8 years and the majority (34.8%) of the patient were in the age group 41-60 years old. There were more male patients (52.34%) than female patients (47.66%). About 86.84% of the COVID-19 cases were diagnosed with positive laboratory-based polymerase chain reaction assay. Severe cases were predominant in the institution which constituted about 57.61% of the total cases surveyed. Moreover, 80.99% of the cases were categorized

Table 1. Clinico-demographic Characteristics of Hospitalized COVID-19 Cases at JBLMGH in Pampanga, Philippines, June 2021 to June 2022

	(N) (%)
Age (years)	
18-20	0 (0.0)
21-40	110 (32.2)
41-60	119 (34.8)
61-80	104 (30.41)
>80	9 (2.6)
Sex	
Male	179 (52.34)
Female	163 (47.66)
COVID-19 classification	
Probable	18 (5.26)
Suspect	27 (7.89)
Confirmed	297 (86.84)
Severity of the disease	
Mild	40 (11.69)
Moderate	105 (30.70)
Severe	197 (57.61)
Type of infection	
Community-acquired infection	277 (80.99)
Hospital-acquired infection	65 (19.01)
Laboratory findings	
White Blood Cell count	
>10,000 cells/m^3	44 (12.86)
5,000-10,000 cells/mm^3	298 (87.14)
C-reactive proteins	
>1 mg/dL	44 (12.86)
Procalcitonin	
>2 ng/mL	11 (3.22)
Culture and sensitivity	
Blood culture	161
Urine culture	1
CSF culture	1
Wound culture	4
BAL culture	2
Sputum culture	8
Type of treatment	
Empiric Treatment	518 (88.88)
Definitive Treatment	65 (11.11)
Comorbidities	
With Co-Morbidities	219 (64%)
Chronic kidney disease	56
Chronic lung disease	21
Hypertension	129
Coronary artery disease	33
Diabetes Mellitus (type 1 or type 2)	90
Hematologic disorders	5

Table 2. Quality Indicators for Antibiotic Prescriptions of COVID-19 Patients at JBLMGH Pampanga, Philippines, June 2021-June 2022

	(N) (%)
Documentation of indication for antibiotic therapy	
Yes	464 (79.58)
No	119 (20.42)
Culture before antibiotic therapy	
Yes	293 (50.29)
No	290 (49.71)
Compliance to guidelines	
Compliant	355 (60.89)
Non-compliant	228 (39.11)
Presence of stop/review date	
Yes	119 (20.41)
No	464 (79.53)

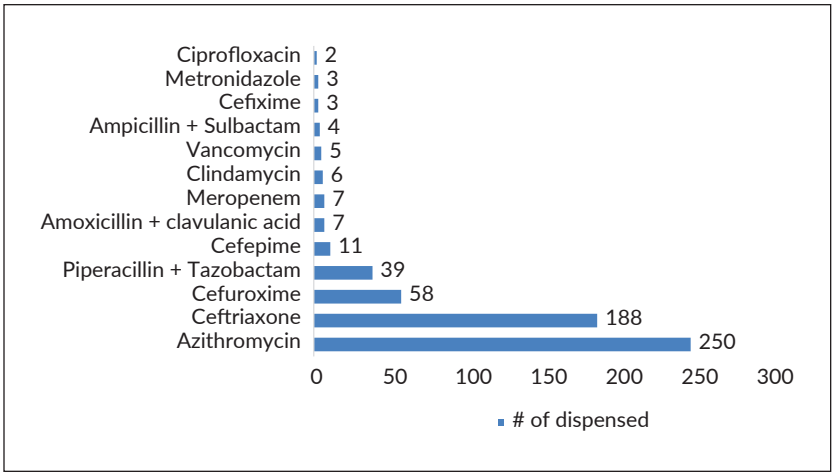

Figure 1. Commonly prescribed antibiotic among COVID-19 patients at JBLMGH, June 2021- June 2022.

under community-acquired infections while hospital-acquired infections were only 19.01%. Co-morbidities among patients were seen in more than half of the surveyed population (64%). These include hypertension, diabetes mellitus, chronic kidney disease, coronary artery disease, chronic lung disease, and hematologic disorders.

One hundred sixty-one patients (46.9%) underwent blood culture and sensitivity testing. With regard to white blood cell count and c-reactive proteins, 44 patients (12.86%) were assessed with elevated laboratory results. Out of 342 patients, only 11 patients were measured for procalcitonin level of whom all of the patients were documented to have results above 2 ng/mL. Empiric treatment was predominant in the population accounting to 518 (88.88%) cases while definitive treatment was only seen on 65 cases (11.11%).

Antibiotic Use among Hospitalized COVID-19 Patients

Antibiotic use among admitted COVID-19 patients involves various antimicrobial agent. Figure 1 highlights the most commonly prescribed antibiotic agents being prescribed to COVID-19 cases from June 2021 to- June 2022 at Jose B. Lingad Memorial General Hospital. Azithromycin (250, 45.9%), ceftriaxone (188, 32.2%), and cefuroxime (58, 9.9%) were among the most prescribed antibiotics prescribed to COVID-19 cases. Other antibiotics that were prescribed include antipseudomonal beta-lactam antibiotics, carbapenems, and glycopeptide.

Antibiotic Quality Indicators

Table 2 shows the summary of the presence of quality indicators for antimicrobial prescriptions among COVID-19 patients at Jose B. Lingad Memorial General Hospital from June 2021 to- June 2022. Out of 583 antibiotic prescriptions, 464 (79.58%) were properly documented with an indication. Culture and sensitivity testing were requested on 293 (50.29%) patients before starting an antibiotic therapy. Prescribers' compliance to guidelines were at 60.89% with 355 prescriptions assessed in compliance to the standard treatment guideline. However, the presence of the stop or review date for antimicrobial therapy were only documented in 119 (20.41%) prescriptions.

Patterns of Antibiotic Quality Indicators among Empiric and Definitive Antibiotic Treatment

Two types of treatment that were seen among the surveyed population were empiric and definite therapies. Table 3 shows the comparison between empiric and definitive antibiotic treatments and the patterns of antimicrobial quality indicators of each treatment. Empiric treatment for COVID-19 cases

Table 3. Patterns of Antibiotic Quality Indicators among Empiric and Definitive Antibiotic Treatment of COVID-19 Patients at JBLMGH Pampanga, Philippines, June 2021-June 2022

Quality Indicators	Empiric treatment N (%)	Definitive treatment N (%)
	518 (88.88)	**65 (11.11)**
Documentation of indication for antibiotic therapy		
Yes	412 (79.5)	52 (80)
No	106 (20.5)	13 (20)
Culture before antibiotic therapy		
Yes	228 (44)	65 (100)
No	290 (66)	0
Compliance to guidelines		
Compliant	315 (60.8)	40 (61.5)
Non-compliant	202 (39.2)	26 (38.5)
Presence of stop/review date		
Yes	106 (20.5)	13 (20)
No	412 (79.5)	52 (80)

were prominent in the study population which accounted for 88.88% of the total antimicrobial prescriptions while definitive treatment was only 11.11 %. Documentation of the indication for antibiotic therapy were seen on more than 50% of prescriptions for both types of antibiotic treatment. About 80% of both empiric and definitive treatment showed proper documentation of the reason for using antimicrobial agents. Collection of culture in empiric therapy were only seen on 44% of the treatment options in contrast with definitive therapy which showed 100% collection of culture samples before starting antibiotic therapy. In terms of compliance to guidelines, more than half of both antibiotic treatments were seen to be in compliance with guidelines. Stop and review dates documentations were relatively low showing 80% of both treatments lacking antibiotic review dates in the medical charts.

DISCUSSION

The occurrence of COVID-19 cases is greatly affected by several conditions and demographic factors present in the population. In our study, the most common age group was 41-60 years old which was followed by patients in the 21-40 age group. This pattern of cases is attributed to the working population which are commonly exposed to the community during the pandemic. Patients in study have similar age patterns with the retrospective cohort study conducted in China[22], while a study in India by Soni et al. showed different age patterns of admitted COVID-19 patients within the hospital institution with a mean age of 33.5 years old[23]. These results are evident since risk of multimorbidity among individuals starts around the age group of 40-60 years old. A study by Barnett et al. showed that 30.4% of individuals age 45-64 years old reported at least two chronic conditions.[24] In relation to this, the Centers for Disease Control has cited that age remains to be the strongest risk factor for severe COVID-19 outcomes.[7] This is supported by a large cross-sectional study that was conducted by Kompaniyets et al. which showed a 2.2 risk ratio for age groups between 40-49 years old and a 4.3 risk ratio for ages 50-64 years old for severe COVID-19 outcomes. The presence of comorbidities among individuals were also associated with increased risk for severe COVID-19 infections.[25] In our study, 64% of the study population had underlying conditions which includes hypertension, diabetes mellitus, and chronic kidney disease. These patterns of co-morbidities were also similar with the study of Kompaniyets et al. which showed hypertension as the most frequent underlying condition among COVID-19 patients.[25]

The prevalence of empiric antibiotic treatment within the hospital institution is high, with 88.8% of the patients being given antibiotic therapy despite the lack of evidence of bacterial co-infections. Only 11.2% of the COVID-19 patients were under definitive treatment with positive culture and sensitivity results. These results are similar to several studies showing a prevalence rate of antibiotic use between 72%-100%. A retrospective cohort study by Zhou et al. showed that almost all admitted COVID-19-confirmed cases in the infectious disease specialty hospital were given empiric antibiotics. The prevalence of antibiotic use between non-survivor and survivor groups were 98% and 93%, respectively. The study showed non-conclusive evidence on the relation of antibiotic use and survival status of the COVID-19 cases.[22] Antibiotic use for COVID-19 cases was based on the WHO interim guidelines for treatment of possible bacterial co-infection. In the study conducted by Rawson et al. showed that about 72% of COVID-19 patients were given antibiotic treatment though the prevalence of confirmed bacterial co-infections was very low at 8%.[21] These are parallel to the prevalance of antibiotic use and confirmed bacterial co-infection in our study. These similarities underscore the prescribing behaviors of clinicians among COVID-19 cases. Another study from Jiangsu showed that three hospitals within the province had a 91% prevalence of antibiotic use.[26] This is mainly due to the difficulty of clinicians in distinguishing viral from bacterial infections due to similar clinical presentations of patients.[27] In a global survey conducted by Beovic et al. showed that clinicians are more inclined to the clinical manifestations of COVID-19 cases for starting antibiotic therapy. This highlights the possible antibiotic misuse of professionals, and the need for following antimicrobial stewardship principles in infectious disease management which is crucial to prevent the emergence of resistance.[28]

In this study, macrolides such as azithromycin were the most prescribed empiric antibiotic therapy. It was postulated that azithromycin possessed antiviral activity and immunomodulatory effects in relation to its potential efficacy against COVID-19.[29] However, its benefits were disproven after further investigation due to lack of evidence supporting the claim.[30] Other antibiotics that were also prescribed in our study include cefuroxime and ceftriaxone. A study in Sierre Leone also showed azithromycin and ceftriaxone as the most frequently prescribed antimicrobials among COVID-19 patients.[31] In contrast with our study, a meta-analysis by Langford et al. showed that fluoroquinolones were the most prescribed antibiotic among COVID-19 infections.[11] This data shows the differences in antibiotic guidelines and resistance patterns among healthcare institutions which greatly affects the prescribing practices of clinicians. These prescribing patterns may be associated with the empirical antibiotic treatment for bacterial pneumonia due to the difficulty of distinguishing viral and bacterial respiratory infections during the pandemic. The most common manifestations of COVID-19 cases include dry cough and bilateral chest X-ray changes. These symptoms and common clinical findings are often similar with atypical bacterial pneumonia.[22] Therefore, most of the antibiotics used such as macrolides and broad-spectrum beta-lactam antimicrobials were in line with the Philippine Clinical Practice Guidelines for Bacterial Pneumonia.[32] However, concerns on the increasing use of azithromycin and ceftriaxone were observed

and projected to increase extended-spectrum beta-lactamase (ESBL)-producing multidrug resistant microbes.[33] These antibiotics were categorized by the WHO under the "Watch" classification for the potential risk for resistance from their overuse.[34] Close antibiotic use monitoring of ceftriaxone and azithromycin are needed and stewardship interventions should be focused on improving prescribing practices of antibiotics with potential abuse among healthcare settings. Broad-spectrum antimicrobials were also seen to be used in the study which included antipseudomonal agents such as piperacillin + tazobactam, cefepime, and meropenem. These patterns are often associated with prevalence of the severe cases within the institution. About 57.6% of cases were classified under the severe category. These cases are often presented with acute respiratory distress, severe hypoxia, and signs of sepsis. Thus, broad-spectrum antibiotics are often prescribed due to assumption of the presence of polymicrobial infections. These practices potentially increase the risk of antibiotic overuse in the absence of confirmed infections. Efforts are needed for routine antibiotic review and rapid de-escalation practices to ensure optimal and rational use of antibiotics especially when COVID-19 infection is confirmed and culture results are available.

Antibiotic quality indicators are described as measurable elements for which there is evidence of their use to assess the appropriateness of antibiotic use.[35] These elements are formulated to help in the assessment of antibiotic therapies among institutions. In the study, the quality indicators that were included and collected were documentation of indications for prescriptions, guideline compliance, and stop/review documentation. In general, the indications for antibiotic use were recorded for 79.58% of the prescriptions, while stop/ review date documentation were only seen in 20.41% of the total prescriptions. This result showed a much higher compliance rate compared to a study conducted by Saleem, which showed a low rate of documentation with only 10.2% of the prescriptions were documented with an indication.[36] While the stop/ review dates documentation was only seen at 9.9% of the total prescription. In contrast, the results of a prevalence survey conducted in a tertiary hospital in Singapore recorded higher documentation rate ranging from 90-100% for indication and stop/review date.[37] Incomplete documentation would lead to suboptimal antibiotic therapies and may increase risk for antimicrobial resistance. The lack of clear indication correlates to inappropriate prescribing which leads to suboptimal antibiotic choices and compromises patient safety.

Documentation of indication and stop/review date has been a standard of care for antimicrobial stewardship programs in various institutions. Documenting these indicators allows clinicians to consider the reason for antimicrobial use, enhances continuity of care, and enables prescribing review from clinical pharmacists and AMS teams.[38] The presence of indication for use provides justification for antimicrobial use and helps in assessment of antimicrobial treatment. Increasing the number of documentations of both indication, and stop and review dates are important aspects of antimicrobial prescribing which help reduce inappropriate prescribing and optimize antibiotic use. These would help in providing essential information in guiding health professionals to practice rational antimicrobial use and help formulate interventions needed for antimicrobial therapies within the institution.[39] Poor documentation often leads to consequences of misguided treatment and prolonged antimicrobial therapy therefore it is important and beneficial to document important data in order to determine the reason for starting or continuing antibiotics.[40] Several studies have cited the importance of quality documentation of indication and stop/ review date as a basis for assessing appropriateness of antimicrobial therapies. These studies have shown variations in documentation rates and prompted stewardship initiatives to improve quality prescribing of professionals.[41,42] The results of the study highlight the need for further education and training on antimicrobial prescribing to standardize healthcare practices and improve proper documentation especially on definitive antibiotic treatment. Emphasis on stewardship interventions and reorientation to antibiotic policy is needed to improve the documentation practice of clinicians.

Initial guidelines for COVID-19 management recommend culture and sensitivity testing and empiric antimicrobial therapy for severe cases.[43] The overall compliance rate of culture collection before antibiotic therapy was at 50.89%. In empiric antibiotic treatment, only 44% (228) were compliant to collection of culture samples before starting an antibiotic therapy while definitive antibiotic treatment showed 100% compliance rate for culture collection. Half of the patients in the study were predominantly classified under severe COVID-19 infections. This would be mainly due to the fact that the hospital is one of the end-referral COVID-19 treatment facilities in the province. Compliance to culture collection in severe cases of COVID-19 were lower compared to the documented severe cases of COVID-19 in our study. This prompts the need for evaluating the implementation of protocols of culture collection before the start of antibiotic therapies within the institution.

Collection of microbiological specimens before initiation of antimicrobial therapy has been a standard principle of antimicrobial therapy. Several societies and health experts have stated that obtaining specimens prior to the administration of antimicrobials is a key part of stewardship programs.[44,45] Sterilization of culture and less accurate microbiological examination are consequences of early antibiotic use within our culture sample collection. A study conducted by Montravers and Aldeyab showed that starting antibiotic therapy before sample collection may result in detecting less-sensitive microorganisms.[33,46] The importance of collecting microbiological samples before antibiotic therapy is to obtain an accurate microbiological diagnosis of infections. This practice standard is supported by a diagnostic study conducted by Cheng, which showed a 12 % absolute difference in the proportion of positive blood cultures between pre- and post-

antimicrobial testing.[47] The results of the study emphasize that collecting blood cultures before delivering the various antimicrobials will give significant benefits in determining the actual organism that is causing the infection.

Compliance to guidelines for both empiric and definitive treatment was only at 60-61%, which is relatively low compared to several studies that have a 70-90% compliance rate for antibiotic prescriptions among COVID-19 cases.[48,49] The relatively low rate of guideline compliance contributes to inappropriate antibiotic use which may contribute to the acceleration of the development of AMR. Clinical practice guidelines are key antimicrobial stewardship strategies and play an important role in supporting appropriate antibiotic prescribing. A cohort study by Wathne showed lower 30-day-mortality and in-hospital mortality in the guideline adherent group. It showed favorable patient outcomes and shortens length of stay with adhering to antibiotic guidelines when treating infections in hospital inpatients.[50] Therefore, analyzing patterns on guideline compliance are important for assessing prescribing behaviors of health professionals and help tailor training of health professionals in antimicrobial stewardship principles for more optimal prescribing. The compliance rates seen within the study show gaps in the implementation of the stewardship program. These could include inadequate training and lack of real-time interventions. The need for additional training and orientation to COVID-19 guidelines on the use of antibiotic agents is evident. A 38.5% non-compliance to guidelines was seen among definitive treatments despite the presence of active cultures that can help guide in choosing the appropriate antimicrobial therapies. Results from the study show concerns on compliance to guidelines which are seen as a good quality indicator for antibiotic prescribing.[51,52] A review of prescribing practice and formulation of protocol for Infectious Diseases specialist consultation regarding antibiotic use in moderate and severe cases of COVID-19 is needed.

This study has some notable limitations. Firstly, it was a single center study which implied that findings should be read cautiously as they were anticipated to represent patterns of a specific geographic region. Analysis of patient characteristics only included patients receiving antimicrobials and may not provide an evaluation of all hospitalized patients with COVID-19 patients within the hospital institution. The assessment of antimicrobial therapy utilized the institution's standard treatment guidelines which may influence the review of the treatments in the COVID-19 cases. The study also used a retrospective survey in which assessment of antimicrobial therapies and quality indicators were dependent to the documented clinical record of each patient.

CONCLUSION

In conclusion, the assessment of COVID-19 cases revealed critical insights into the prescribing practices in a high-burden, referral hospital during the pandemic. Most of the COVID-19 cases in the JBLMGH were classified under severe cases with majority of the patients within the age of 40-60 years old. Hypertension was seen as the most common comorbidity among admitted COVID-19 cases. The utilization of antibiotics was shown to be extensive among COVID-19 patients within JBLMGH. The predominant finding showed high prevalence of empiric treatment (88.88%), despite low number of confirmed bacterial co-infections. This suggested the possibility of antibiotic misuse among COVID-19 cases. These were consistent global trends due to the difficulty in distinguishing viral and bacterial infections. Macrolides, third and second-generation cephalosporins, and antipseudomonal penicillin were widely used within the institution. The patterns of antimicrobial use were attributed to the similarities of respiratory symptoms of bacterial infections with COVID-19 patients. The presence of comorbidities (64%) and proportion of severe cases (57.61%) contributed to the complexities of the treatment decisions resulting in the use of broad-spectrum antimicrobials.

Antibiotic quality indicators are critical elements of antimicrobial stewardship programs which are used to assess the quality of antibiotic prescriptions. Significant gaps were seen in the adherence of stewardship standards, particularly in the documentation process. The stop/review dates documentation were only seen in 20.41% of all antibiotic prescriptions, citing the need for further training and education on clinicians on proper antimicrobial prescribing. Culture testing before starting antibiotic therapy was only at 50.29% of all cases. This underscores the need for the improving culture collection practices in the institution to ensure antibiotic treatments are based on microbial evidence and not just clinical assumptions. Compliance to guidelines of COVID-19 antibiotic prescriptions have relatively low compliance rates (60-61%) which signals the need for continuous antimicrobial surveillance and stewardship efforts among COVID-19 and other viral infections to prevent the spread of antimicrobial resistance.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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