Original Research

Antimicrobial prescribing and clinical outcomes in patients with COVID-19 infection: Experience of a single center in an upper middle-income country

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Abstract

Objectives: The aim of this study was to describe antimicrobial prescribing patterns in hospitalized adult patients with confirmed diagnosis of COVID-19 infection, and to determine the relationship between antimicrobial agent used and non-survival amongst the studied COVID-19 patients. **Methods:** This is an observational, retrospective study. Specialty Clinic Hospital in Jordan is selected as the study setting for this conducted study. The study comprised of all hospitalized adult patients with confirmed diagnosis of COVID-19 infection who were admitted to the hospital between October 2020 and December 2020. **Findings:** A total of 216 hospitalized patients with confirmed COVID-19 were included in the analysis. The majority of patients were prescribed antibiotic agents (n=149, 69.0%). Almost half of the patients have been prescribed antivirals agent (n=111, 51.4%). Survivals were significantly more likely to have been prescribed third generation cephalosporin (19.8% vs 3.4%, p=0.02). Non-survivals were significantly more likely to be older in age (mean age: 70.5 vs 62.7 years, p=0.009), have higher mean Charleston Comorbidity Index Score (3.7 vs 2.7, p=0.01), have at least one comorbidity (93.1% vs 71.1%, p=0.008), had shortness of breath at admission (72.4% vs 50.8%, p=0.023) and were admitted to the ICU during current admission (96.6% vs 18.7%, p<0.001) compared to survivors. Non-survivals were significantly more likely to had increased levels of WBC count (41.4% vs 19.7%; p=0.034), increased neutrophiles count (72.4% vs 39.4%; p=0.004) and higher mean C-reactive protein (167.2 vs 103.6; p=0.001) at admission. **Conclusions:** The results of this study demonstrated factors are associated with the non-survival, and additionally benchmarked the mortality rate, amongst the studied COVID 19 patients.

Keywords: Antimicrobial; Prescribing; COVID-19; Infection; Jordan

INTRODUCTION

In December 2019, the first case of coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China. Although, most individuals infected with COVID-19 experience mild symptoms; there is around 14% of cases that experience sever disease, requiring hospitalization and respiratory support and 5% of cases that required admission to the intensive care unit (ICU). In severe cases, COVID-19can be complicated by the acute respiratory distress syndrome (ARDS), sepsis and septic shock, multiorgan failure, including acute kidney injury and cardiac injury.[1,2]

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The World Health Organization (WHO) has initially recommended the use of empirical antibiotics in cases of COVID-19 pneumonia with emphasis on early antimicrobial de-escalation.[2] Nonetheless, early antimicrobial de-escalation might not be easily implemented in practice, especially due to overcrowded hospitals and overloaded laboratories in addition to lack of evidence on effective antimicrobial agent against COVID-19. This may have led to widespread and excessive prescribing of broad-spectrum antimicrobials around the world, which could contribute to the existing epidemic of antimicrobial resistance.[3] Many have suggested that antimicrobial stewardship approaches are highly needed during the COVID-19 pandemic.[3,4]

Detailed data about antimicrobial use in treatment of COVID-19 patients and prescribing patterns in COVID-19 patients is lacking in most countries around the world. An international web-based survey aimed to investigate the pattern of antibiotic use for treatment of COVID-19 patients in 23 countries found that 52.4% of physicians prescribed a combination of β-lactams and macrolides or fluoroquinolones in inpatient settings, where 50.3% of physicians prescribed piperacillin/tazobactam combination in ICU settings. The mean duration of antibiotic treatment was 7.12 (SD = 2.44) days.[5]

In china, where COVID-19 has first emerged, several studies have described antimicrobial used in COVID-19 patients. In one study, among 99 patients hospitalized between 1 January to 20 January, 2020, 76% received antiviral treatment, including oseltamivir, ganciclovir and lopinavir and ritonavir tablets with a median duration of antiviral treatment of 3 (range:

3–14) days and 71% received antibiotic treatment, including cephalosporins, quinolones, carbapenems, tigecycline against methicillin-resistant Staphylococcus aureus and linezolid with a median duration of antibiotic treatment of 5 (range: 3–17) days. A total of 23 patients (23%) were admitted to the ICU and 11 patients died (11%) during the study.[6]

In another hospital in china, among 102 patients hospitalized between 3 January and 1 February 2020, 98% received antiviral therapy, including oseltamivir (64.7%), cludedArbidol (34.3%), and lopinavir (27.5) in addition 99% received antibiotic treatment, including quinolones (85.3%), cephalosporins (33.3%) and carbapenems (24.5%). The mean length of hospitalization was 11 days. Of these, 18 patients (17.6%) were admitted to the ICU and 17 patients died (16.7%) during the study.[7]

Several studies in the United states (US) have also described antimicrobial used in COVID-19 patients. One study of 242 patients hospitalized between March 1 and April 24, 2020 found that antibiotics were administered in 67% of patients, including ceftriaxone (54%), vancomycin (48%), azithromycin (47%) and cefepime (45%).Mortality was documented in 21.5% of patients.[8] Another study in the US of 39 patients hospitalized between March 1 and April 28, 2020 found that antimicrobials were administered in 59% of patients. The mean duration of antimicrobial treatment was 5.4 (SD = 2.9) days and mean length of stay was 8.5 (SD ± 5) days.[9]

Interestingly, to date, only one study was found in the literature from the Arab world. A case series of COVID-19 hospitalized patients between February 24 and April 24, 2020, from two hospitals in Oman, reported that among 63 patients, 97% received either chloroquine or hydroxychloroquine and 59% received lopinavir/ritonavir combination. The three most commonly prescribed antibiotics were ceftriaxone (79%), azithromycin (71%) and piperacillin/tazobactam combination (49%). The median length of stay was 4 days. Twenty four patients were admitted to the ICU (38%) and 5 patients died (8%) during the study.[10] Therefore, we aimed in this study to describe antimicrobial prescribing patterns in hospitalized adult patients with confirmed diagnosis of COVID-19 infection in a single center in Jordan. In addition to determine the relationship between antimicrobial agent used and non-survival amongst the studied COVID-19 patients.

MATERIAL AND METHODS

Compliance with ethical standards

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For the purposes of conducting this study, approvals were obtained from the Institutional Review Board (IRB) at Specialty Hospital (Reference No: 103773/T/1/5). For this type of study (retrospective in design), formal individual patient consent was not required by Institutional Review Board.

Study setting

Specialty Clinic Hospital is selected as the study setting for this conducted study. This hospital is serving one of the fastest-growing areas in Jordan due to its unique location as it is located at center of the capital Amman. Specialty Hospital has around 300 professional staff aligned with different clinical service lines; and specialties that includes: medicine, obstetrics, pediatrics, surgical, critical care services that support the trauma program; in addition to the largest burn unit in the country.

Study population

The study comprised of all hospitalized adult patients with confirmed diagnosis of COVID-19 infection (by a positive real-time polymerase chain reaction [RT-PCR] assay for severe acute respiratory coronavirus virus 2 [SARS-CoV-2]) who were admitted to the hospital between October 2020 and December 2020.

Inclusion and exclusion criteria

The following inclusion and exclusion criteria were applied:

Inclusion criteria:

- Patient aged ≥ 18 years

- Patient has confirmed diagnosis of COVID-19 infection by PCR

Exclusion criteria:

- None

Study design

This is an observational, retrospective study. All electronic medical records of patients with confirmed diagnosis of COVID-19 infection who meets the inclusion criteria were included in the study.

Data collection

The study comprised of all hospitalized adult patients diagnosed with COVID-19 infection in Specialty hospital for a period of three months between 01 October 2020 and31 December 2020.Medical records of adult patients with confirmed diagnosis of COVID-19 infection by PCR admitted to the hospital in the period between 01 October 2020 and 31 December 2020 werere viewed. A pre-designed data collection form was completed based on the data in the patient electronic file and other sources in the hospital electronic medical records Software.

The following data were collected in the data collection form: baseline demographic characteristics (gender, age, smoker, BMI), medical service, date of COVID- 19 diagnosis, risk factors and underlying co-morbidities, previous hospitalization or ER visits in the last 14 days, clinical symptoms and signs on admission, disease severity (i.e. need for respiratory support and/or ICU admission), laboratory parameters, microbial sensitivity, previous antimicrobial therapy in the last 14 days, current antimicrobial therapy including antibiotics, antiviral agents and non-survival amongst the studied COVID-19 patients.

DEFINITIONS

Acute Respiratory Distress Syndrome (ARDS): is acute-onset hypoxemia (the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxy- gen [Pao2:Fio2], <300) with bilateral pulmonary opacities on chest imaging that were not fully explained by congestive heart failure.

Severe pneumonia: a fever or suspected respiratory infection plus one of the following: respiratory rate of >30 breaths/min, severe respiratory distress and SpO2 of <90% on room air.

Mild disease: when no additional oxygen requirement is needed.

Moderate disease: when new or increased need for supplemental oxygen is needed.

Severe disease: when invasive or noninvasive ventilation or ICU admission is needed.

Duration of antibiotic therapy (DOH): The number of days of antibiotic therapy is defined in this study as the total number of days of all antibiotics administered to the patient both while in hospital and after discharge.

OUTCOME MEASURES

Primary outcome measures

The first outcome measure was prescribing patterns of antimicrobial agents for treatment of COVID-19. The second outcome was the association relationship between antimicrobial agent and non-survival amongst the studied COVID-19 patients.

Data analyses

Descriptive statistics were used to describe the data. For categorical variables, frequencies and percentages were reported. For continuous variables, mean and standard deviation were used to summarize the data. Several tests were used to identify individual relationships between the data collected on potential risk factors and the non-survival amongst the studied COVID-19 patients: (i) the Mann-Whitney U-test was employed with non-normally distributed scale variables; and (ii) Pearson's Chi-square test was used with categorical variables (Fisher's exact test was used when the data does not fit the criteria of the Chi-square test). All the statistical analysis procedures were performed using the Statistical Package for Social Sciences, Windows Version 25.0 (SPSS, Chicago). Microsoft Excel 2010 was used in order to display statistical data and figures.

RESULTS

Demographic and clinical characteristics

A total of 216 hospitalized patients with confirmed COVID-19 were included in the analysis. Mean age was 63.8 years (SD 14.8) and 55.6% of patients were males (n=120). Ninety patients (42.9%) were obese with a Body Mass Index (BMI) more than 30.0 kg/m² and only 5 patients were smokers (2.3%). Sixteen patients (7.4%) had a previous history of hospitalization or Emergency room (ER) visit in the last 14 days and 16 patients (7.4%) had previous history of antibiotic prescription in the last 14 days. A total of 63 patients (29.2%) were admitted to the Intensive Care Unit (ICU) and 29 patients (13.4%) died during current hospitalization (Table 1).

Table 1. Demographic and clinical characteristics of hospitalized COVID-19 patients stratified by survival				
Characteristics n (%)	**Full Cohort 216 (100)**	**Non-survival 29 (13.4)**	**Survivals 187 (86.6)**	**P-Value***
Male Gender, n (%)	120 (55.6)	20 (69.0)	100 (53.5)	0.086
Age, mean (SD), years	63.8 (14.8)	70.5 (14.5)	62.7 (14.6)	**0.009**
Smoker, n (%)	5 (2.3)	0 (0.0)	5 (2.7)	0.479
BMI, n (%), kg/m²				
< 18.5	1 (0.5)	1 (3.4)	0 (0.0)	
18.5 - 29.9	119 (56.7)	17 (58.6)	102 (56.4)	**0.040**
≥ 30.0	90 (42.9)	11 (37.9)	79 (43.6)	
Previous hospitalization or ER visit in last 14 days, n (%)	16 (7.4)	2 (7.1)	14 (7.5)	0.653
Antibiotic use in last 14 days, n (%)	16 (7.4)	4 (13.8)	12 (6.4)	0.150
Charleston Comorbidities Index Score, mean (SD)	2.8 (1.8)	3.7 (1.6)	2.7 (1.8)	**0.010**
Comorbidities, n (%)				
Any Comorbidity, n (%)	161 (74.5)	27 (93.1)	134 (71.7)	**0.008**
Cardiovascular diseases	131 (60.6)	21 (72.4)	110 (58.8)	0.116
Diabetes Mellitus	105 (48.6)	18 (62.1)	87 (46.5)	0.087
Chronic kidney disease	16 (7.4)	4 (13.8)	12 (6.4)	0.150
Cerebrovascular diseases	11 (5.1)	2 (6.9)	9 (4.8)	0.449
Respiratory system disease	3 (1.4)	1 (3.4)	2 (1.1)	0.353

Nervous system disease	4 (1.9)	0 (0.0)	4 (2.1)	0.559
Liver disease	1 (0.5)	0 (0.0)	1 (0.5)	0.866
Connective tissue disease	1 (0.05)	1 (3.4)	0 (0.0)	0.134
Malignant tumor	1 (0.05)	0 (0.0)	1 (0.5)	0.866
Others	27 (12.5)	3 (10.3)	24 (12.8)	0.493
Clinical symptoms and Signs on admission, n (%)				
Cough	116 (53.7)	16 (55.2)	100 (53.5)	0.513
Shortness of breath	116 (53.7)	21 (72.4)	95 (50.8)	**0.023**
Fever	115 (53.2)	14 (48.3)	101 (54.0)	0.353
Muscle ache	88 (40.7)	10 (34.5)	78 (41.7)	0.299
Nausea and vomiting	27 (12.5)	3 (10.3)	24 (12.8)	0.493
Diarrhea	20 (9.3)	2 (6.9)	18 (9.6)	0.478
Chest Pain	15 (6.9)	2 (6.9)	13. (7.0)	0.674
Headache	13 (6.0)	0 (0.0)	13 (7.0)	0.145
Sore throat	3 (1.4)	0 (0.0)	3 (1.6)	0.647
Rhinorrhea	2 (0.9)	0 (0.0)	2 (1.1)	0.749
Confusion	1 (0.5)	0 (0.0)	1 (0.5)	0.866
Others	25 (11.6)	0 (0.0)	25 (13.4)	**0.022**
White Blood Cell count, n (%)				
Decreased (< 4.0)	17 (8.0)	2 (6.9)	15 (8.2)	
Normal (4.0 - 11.0)	147 (69.3)	15 (51.7)	132 (72.1)	**0.034**
Increased (> 11.0)	48 (22.6)	12 (41.4)	36 (19.7)	
Neutrophils count, n (%)				
Decreased (< 50)	3 (1.4)	0 (0.0)	3 (1.7)	
Normal (50-80)	114 (54.5)	8 (27.6)	106 (58.9)	**0.004**
Increased (> 80)	92 (44.0)	21 (72.4)	71 (39.4)	
C-reactive protein count, mean (SD)	112.4 (90.1)	167.2 (93.6)	103.6 (87.1)	**0.001**
Microbial sensitivity Test	8 (3.7)	2 (6.9)	6 (3.2)	0.292
ICU admission, n (%)	63 (29.2)	28 (96.6)	35 (18.7)	**<0.001**

*Variables with P<0.05 were presented in bold

Mean Charleston Comorbidity Index score was 2.8 (SD 1.8). The majority of patients (n= 161, 74.5%) had at least one co-morbidity with cardiovascular diseases (n= 131, 60.6%) and diabetes mellites (n= 105, 48.6%), as the most common co-morbidities followed by chronic kidney disease (n= 16, 7.4%) and cerebrovascular diseases (n= 11, 5.1%), respectively. The most prevalent symptoms at admission were cough (n=116, 53.7%), shortness of breath (n=116, 53.7%) and fever (n = 115, 53.2%), followed by muscle ache (n= 88, 40.7%) and nausea and vomiting (n=27, 12.5%; Table 1).

Non-survivals were significantly more likely to be older in age (mean age: 70.5 vs 62.7 years, p=0.009), have higher mean Charleston Comorbidity Index Score (3.7 vs 2.7, p=0.01), have at least one comorbidity (93.1% vs 71.1%, p=0.008), had shortness of breath at admission (72.4% vs 50.8%, p=0.023) and were admitted to the ICU during current admission (96.6% vs 18.7%, p< 0.001) compared to survivors (Table 1).

Laboratory findings at admission

A total of 48 patients (22.6%) and 92 patients (44.0%) had increased White Blood Cell (WBC) count and increased neutrophiles count at admission, respectively. Mean C-reactive protein count was 112.4 (SD 90.1) at admission. Microbial sensitivity test was done in only 8 patients (3.7%).

Non-survivals were significantly more likely to had increased levels of WBC count (41.4% vs 19.7%; p = 0.034), increased neutrophiles count (72.4% vs 39.4%; p = 0.004) and higher mean C-reactive protein (167.2 vs 103.6; p = 0.001) at admission (Table 1).

Antibiotic prescription during hospitalization

The majority of patients were prescribed antibiotic agents (n=149, 69.0%); 81 of which were prescribed a single antibiotic (37.5%) and 68 were prescribed a combination antibiotic (31.5%). The most frequently prescribed antibiotic classes were fluoroquinolone (n= 69, 31.9%) and macrolide (n= 54,

25.0%) followed by third generation cephalosporin (n= 38, 17.6%), penicillin (n= 30, 13.9%) and carbapenem (n= 25, 11.6%), respectively. Only 17.5% of patients were prescribed antibiotics for a duration of less than 3 days (n=26), 44.3% for a duration of 3-5 days (n=66) and 38.2% for a duration of 6-10 days (n=57; Table 2).

In general, non-survivals were significantly more likely to have been prescribed antibiotics compared to survivors (93.1% vs 65.2%, p =0.001). They were also significantly more likely to have been prescribed a single antibiotic compared to survivors (55.2% vs 34.8%, p= 0.03). More specifically, non-survivals were significantly more likely to be prescribed fluoroquinolone (48.3% vs 29.4%, p =0.037) and penicillin (41.4% vs 9.6%, p <0.001), where survivals were significantly more likely to have been prescribed third generation cephalosporin (19.8% vs 3.4%, p =0.02; Table 2).

Antiviral prescription during hospitalization

Almost half of the patients have been prescribed antivirals agent (n=111, 51.4%); 110 of which were prescribed Favipiravir and only one patient were prescribed Remdesivir. More than half of the patients were prescribed antiviral for a duration of 6-10 days (n=60, 54.1%; Table 2).

In general, non-survivors were significantly more likely to have been prescribed antiviral compared to survivors (72.4% vs 48.1%, p =0.012). More specifically, they were significantly more likely to have been prescribed Favipiravir compared to survivors (69.0% vs 48.1%, p= 0.022) and have been prescribed antiviral treatment for a longer duration 6-10 days (55.1% vs 53.8%, p= 0.008; Table 2).

DISCUSSION

In this study, we describe the clinical characteristics, antimicrobial treatment, and outcomes of hospitalized patients with confirmed COVID-19 infection admitted to a single hospital in Jordan. To our knowledge, our study is the first in the country and one of the few in the region. Our data can be used to guide local guidelines and treatment protocol, much needed in the current time.

In our study, more than half (55.6%) of hospitalized patients were males, 42.9% were obese and 74.5% had at least one comorbidity. Only five patients were smokers, and mean age was 63.8 years. When stratified by survival, older age, male

Table 2. Antibiotic and Antiviral prescription of hospitalized COVID-19 patients stratified by survival				
Characteristics n (%)	**Full Cohort** **216 (100)**	**Non-survival** **29 (13.4)**	**Survivals** **187 (86.6)**	**P-Value***
Antibiotic prescription, n (%)				
Any, n (%)	149 (69.0)	27 (93.1)	122 (65.2)	**0.001**
Single Antibiotic, n (%)	81 (37.5)	16 (55.2)	65 (34.8)	**0.030**
Combination Antibiotic, n (%)	68 (31.5)	11 (37.9)	57 (30.5)	0.255
Antibiotic Class, n (%)				
Fluoroquinolone, n (%)	69 (31.9)	14 (48.3)	55 (29.4)	**0.037**
Macrolide, n (%)	54 (25.0)	5 (17.4)	49 (26.2)	0.213
Third Generation Cephalosporin, n (%)	38 (17.6)	1 (3.4)	37 (19.8)	**0.020**
Penicillin, n (%)	30 (13.9)	12 (41.4)	18 (9.6)	**<0.001**
Carbapenem, n (%)	25 (11.6)	6 (20.7)	19 (10.2)	0.096
Fourth Generation Cephalosporin, n (%)	1 (0.5)	0 (0.0)	1 (0.5)	0.866
Duration of Antibiotic treatment, n (%), days				
< 3	26 (17.5)	6. (22.2)	20 (16.4)	
3-5	66 (44.3)	7 (25.9)	59 (48.4)	0.090
6-10	57 (38.2)	14 (51.9)	43 (35.2)	
Antiviral prescription, n (%)				
Any, n (%)	111 (51.4)	21 (72.4)	90 (48.1)	**0.012**
Antiviral type, n (%)				
Favipiravir, n (%)	110 (50.9)	20 (69.0)	90 (48.1)	**0.022**
Remdesivir, n (%)	1 (0.5)	1 (3.4)	0 (0.0)	0.134
Duration of Antiviral treatment, n (%), days				
< 3	17 (15.3)	7 (35.0)	10 (11.0)	
3-5	34 (30.6)	2 (10.0)	32 (35.2)	**0.008**
6-10	60 (54.1)	11 (55.1)	49 (53.8)	

*Variables with P<0.05 were presented in bold

gender, obesity and having comorbidities more specifically cardiovascular disease and DM were associated with non-survival, which is consistent with several meta-analysis.[11-19]

Higher COVID-19 infection prevalence among males can be related to the higher intensity of immune related genes and regulatory elements in the X chromosome, which lead to a higher infectious disease susceptibility in males.[20] Associations between severity and mortality of COVID-19 patients and obesity, DM, cardiovascular disease and hypertension can be related to the way the COVID-19 virus binds and enters the host cell via the angiotensin-converting-enzyme-2 (ACE2) receptor.[21] Expression of ACE2 receptor in DM is high in adipose tissue and circulating levels of ACE2 is higher in DM, meaning more ACE2 receptors are available for binding and entry of the virus to the cell.[22]

In hypertension, angiotensin-converting enzyme (ACE) inhibitors are one of the key agents used and many guidelines recommend its use as a first line treatment,[23] some studies have suggested that their use might increase the ACE2 expression,[24,25] this may result in increased number of ACE2 receptors available for the virus to bind to. Further studies are needed to support such evidence.

In our study, no strong association was found between smoking and survival, as only five patients were smokers. Several meta-analyses showed a significant association between smoking and severity and mortality of hospitalized COVID-19 patients.[26-29] Nonetheless, some other meta-analysis has showed that nicotine might have a protective effect,[30] or low prevalence of smokers among hospitalized COVID-19 patients,[31] which is similar to our result.

Most common symptoms at admission in our cohort were cough, shortness of breath and fever. These symptoms have been described as the most common symptoms in COVID-19 patients.[17,32] Although this shows a similar host immune response in most COVID-19 patients, nonetheless, based on these common symptoms alone, it's harder to distinguish between a COVID-19 infection and other viral or bacterial infections. Fever can also be a leading cause for inappropriate prescription of antibiotic treatment in this patient group.

When stratified by survival, shortness of breath was associated with non-survival. This is consistent with a meta-analysis[33] that found shortness of breath were associated with severity and mortality of COVID-19 patients. This suggest that difficulty breathing should be an alarming sign that need immediate intervention and close monitoring. Furthermore, this can relate to the need of ICU admission in this patient group for mechanical oxygenation and support. The ICU admission rate was 29.2% in our study, which is in the range of that reported in some meta-analysis (20.3% - 34.6%).[17,33]

In our study, non-survivals were more likely to have increased WBC count and neutrophils count and higher mean C-reactive protein at admission compared to survivals. This consistent with several meta-analyses[18,34,35] and is the result of the acute inflammation state caused by the COVID-19 infection. This suggest that such laboratory findings along with others not reported in our study (i.e., lactate-dehydrogenase, procalcitonin, creatine kinase, D-dimer, alanine aminotransferase and aspartate transaminase) can play a vital role in monitoring the prognosis of hospitalized COVID-19 patients.

In our study, nearly three-quarters of patients (69.0%) were prescribed antibiotics and the most frequently prescribed antibiotic classes were fluoroquinolone (31.9%) and macrolide (25.0%) followed by third generation cephalosporin (17.6%), penicillin (13.9%) and carbapenem (11.6%), respectively. This is consistent with antibiotic use percentages reported in several meta-analysis 62.4%,[36] 63.9%[37] and 76.8%.[38] The most common antibiotic classes prescribed reported in one of the meta-analysis were fluoroquinolones (20.0%), macrolides (18.9%) followed by β-lactam/β-lactamase inhibitors (15.0%) and cephalosporins (15.0%).[36]

Interestingly, when antibiotic prescribing was analyzed by region, a considerable heterogeneity was detected (I2 = 99%). East/Southeast Asia (excluding China) ranked first in the use of antibiotics (87.5%), followed directly by the Middle East (two studies from Iran and Turkey) (86.0%) and China (76.2%). Europe (63.1%) and in North America (USA) (64.8%) reported the lowest percentages, respectively.[36]

Although bacterial co-infection has not been reported in our study, literature showed the rate of bacterial co-infection to be 8.6%.[36] This suggest that a very large proportion of patients are being prescribed unnecessary antibiotics, increasing the risk of antimicrobial resistance and that such practice seems to be universal. The future impact of the COVID-19 on universal antimicrobial resistance is yet not known, but growing concern has been reported. After more than a year and a half of the pandemic and widespread use of antibiotic, more effort to raise awareness on microbial steward ship is needed, especially in regions where the problem has been witnessed even before the pandemic including the middle east. More tailored and updated treatment guideline on appropriate use of empirical antibiotic in COVID-19 patient is highly needed, especially at a time where new information on the new virus is becoming available every day.

The coronavirus disease-2019 (COVID-19) outbreak all over the world has led the researchers to strive to develop drugs or vaccines to prevent or halt the progression of this ailment. To hasten the treatment process, repurposed drugs are being evaluated. Recent findings suggest that Remdesivir and favipiravir are antiviral agents that might show the potential to combat COVID-19 in short term.[39] Favipiravir has shown promising results in clinical studies in China, Russia, and Japan, and more trials are underway in multiple countries, including USA, UK, and India. Recently, treatment guidelines from many countries have included favipiravir in the treatment protocol.[40] However, in our study non-survivors were significantly more likely to have been prescribed Favipiravir compared to survivors.

STRENGTHS AND LIMITATIONS OF THE STUDY

This study has several strengths. Firstly, to the best of our knowledge, our study is the first of its kind in the country

and one of the few in the region. Secondly, the data used were primarily recorded for another purpose, i.e. data were recorded as part of routine practice, which, in turn, minimised information bias. Thirdly, the data regarding antimicrobial prescription were collected from highly reliable databases, i.e. health services systems of the Specialty Hospital.

Despite these strengths, the study had a number of limitations. No adjustment was possible for any variation of infection control practices that were in the place in the study site hospital during the study period. The performance indicator reports generated by the infection control team within the studied hospital, however, showed that the monthly compliance rate to hand hygiene and environmental decontamination among the hospital staff was high respectively across the study period. These data present confidence that cross-contamination rates were likely to be low in the study site hospital over the study period, i.e. the rate of COVID 19 infection transmission (from patient to patient) was low.

CONCLUSION

The results of this study demonstrated factors are associated with the non-survival across the studied COVID 19 patients. The study also benchmarked the mortality rate amongst the studied COVID 19 patients in a Jordanian medium sized hospital over the study period.

DECLARATIONS

Funding

Conflicts of interest

The authors declare no competing interests.

Consent to participate

For this type of study (retrospective in design), formal individual patient consent was not required by Institutional Review Board.

Consent for publication

Not applicable.

Availability of data and material

The datasets generated during the current study are available from the corresponding author on reasonable.

Code availability

Not applicable.

Authors' contributions

All authors have contributed significantly to the publication. Their contributions meet the criteria for authorship. M. A. contributed to conceptualization, methodology, writing original manuscript and supervision. A. T.: participated in writing original manuscript and conceptualization. S. B.: participated in conceptualization and methodology. S. A. & D. S.: contributed to conceptualization, methodology, reviewing the main manuscript and analysis. A. B: contributed to data collection and resources.

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