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Review Article

Antibiotic Prescription and Its Impact on COVID-19 Patient Recovery: A Cross-sectional Study

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Abstract

Background: COVID-19, a newly discovered infectious disease, with a wide range of intensity, has recently become the primary global health issue. Antibiotics are medications designed against microorganisms that are typically not effective in viral infections such as COVID-19. Considering that more than a third of physicians prescribe antibiotics for COVID-19 patients, it was essential to examine the efficacy of these medications.

Methods: This cross-sectional study was conducted on 128 hospitalized COVID-19 patients in Iran and performed appropriate statistical tests, including the Chi-square test, and regression analyses, using SPSS 26 (IBM, USA). The missing data were managed properly.

Results: The study included 128 COVID-19 patients with a mean age of 58.7 years, and 46.9% were male. Age was the only factor significantly associated with mortality and hospitalization. However, patients with abnormal potassium, prothrombin, partial thromboplastin time, urea, creatinine, and albumin levels had significantly different hospitalization periods and mortality rates. The most commonly prescribed antibiotics were ceftriaxone, hydroxychloroquine, and azithromycin. In addition, patients who took vancomycin had a significantly higher mortality rate.

Conclusion: Our findings revealed that age and gender could significantly impact hospital stay duration and mortality rates. Considering that certain antibiotics were linked to prolonged hospital stays, bacterial infection during COVID-19 was not significantly related to increased mortality, which questions the necessity of antibiotics for all patients. The study identified age, gender, and certain lab parameters as associated factors with COVID-19 outcomes. Since its retrospective nature and small sample size limit the findings' applicability, larger studies are needed to confirm the findings and explore other potential risk factors.

Keywords: COVID-19, Antibiotic, Recovery

Introduction

The emergence of the coronavirus as a pandemic in December 2019 posed a unique challenge for the healthcare community worldwide. SARS-CoV-2 was first detected during the examination of an unknown type of pneumonia in Wuhan, China. Since then, it has rapidly spread across the globe, infecting millions of people and causing widespread disruption to daily life. COVID-19 is highly contagious and can cause severe respiratory illness, leading to hospitalization and even death.[1,2]

The severity of the COVID-19 infection can vary widely, with some patients experiencing mild symptoms and others becoming critically ill. Studies of previous influenza pandemics have shown that bacterial co-infection and secondary bacterial infection are important risk factors for patients' severity and mortality rate. In the case of COVID-19, the prevalence of bacterial infection in intensive care unit patients has been reported to range from 14% to 100% and to be associated with a higher risk of death.[3-5]

Antibiotics are a group of drugs prescribed to suppress microorganisms. While antibiotics are not effective against viral infections such as COVID-19, they may be used to treat bacterial co-infections that could occur. There is concern that the increased use of antibiotics during the COVID-19 pandemic could exacerbate the current global epidemic of antimicrobial resistance. An online survey conducted at the end of March 2019 revealed that 33% of an international group of physicians reported prescribing hydroxychloroquine (or chloroquine) to COVID-19 patients, and 41% had prescribed azithromycin or similar antibiotics.[6,7]

A study by Liu et al showed that antibiotic treatment is associated with increased mortality, and most patients gain no benefit from antibiotics. They further found that only 3.2% of COVID-19 patients with bacterial co-infection or secondary bacterial infection had benefited from antibiotic treatment, while 57.1% of patients who received antibiotics did not have experiences of bacterial co-infection or secondary bacterial infection.[8]

In addition to the use of antibiotics, other treatments have been used to manage COVID-19 patients, including antiviral drugs, steroids, and immunomodulators. The World Health Organization recommends corticosteroid use in patients with severe and critical COVID-19, as they have been shown to reduce mortality in these patients.[9]

Given that over a third of physicians prescribe antibiotics for COVID-19 patients, it was necessary to investigate their effectiveness in hospitalized COVID-19 patients in Maragheh hospitals.[10] Accordingly, this study aims to contribute to the understanding of the use of antibiotics in the treatment of COVID-19 patients. The study evaluated the effectiveness of antibiotics in COVID-19 patients' recovery.

Methods

This cross-sectional study utilized archived data from all three university hospitals in Maragheh, Iran, to investigate the effectiveness of prescribed antibiotics in hospitalized COVID-19 patients. The study population included all patients admitted to these hospitals between March 20 and September 20, 2020. The sample size was estimated at 128, using appropriate statistical methods, with a margin of error of 5% and a 95% confidence interval.

Descriptive and analytical statistics, including an independent sample t-test, Chi-square test, and logistic regression analyses, were performed using SPSS 26 (IBM, USA) to identify any significant relationships between variables and outcomes. The significance level was set at 0.05.

To ensure ethical considerations were met, the Ethical Committee of Maragheh University of Medical Sciences approved the study protocol. We also followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline to ensure that the study was properly reported. This guideline provides a checklist of 22 items that authors should address when reporting observational studies, including study design, participant characteristics, statistical methods, and results.

In addition to the used statistical methods, it is important to note that data collection was performed retrospectively. This implies that the study was limited by the data available in the records. The missing data were managed by proper methods; however, any missing or incomplete data may have influenced the results.

Results

A total of 128 patients were included in this study. The mean age of the patients was 58.7 years (SD = 17.76), and 46.9% were male. The two most common comorbidities among the patients were high blood pressure and diabetes. Out of all the patients, though only 5.5% indicated bacterial infection (white blood cell > 10 000, C-reactive protein > 50, and Temperature > 38), 82.8% received antibiotics during their hospitalization. The average duration of hospitalization was 6.96 days (SD = 3.83) (Table 1). The overall mortality rate among the patients was 12.5%. Among those who received antibiotics, the mortality rate was 14.2%.

Logistic regression analysis demonstrated that except for age ($P = 0.02$, odds ratio = 0.954), factors such as gender, type of residence, a history of underlying diseases,

Table 1. Demographic Profile of the Study Participants (N = 128)

	No.	%
Gender		
Female	68	53.1
Male	60	46.9
Age (y)	Mean: 58.69	SD: 17.76
Residence		
Urban	85	66.4
Rural	43	33.6
Hospitalization period (day)	Mean: 6.96	SD: 3.83
Discharge		
Recovery	112	87.5
Death	16	12.5
Underlying disease		
Yes	48	37.5
No	80	62.5
Diabetes	14	10.9
High blood pressure	33	25.8
Asthma	6	4.7
Heart disease	7	5.5
Cancer	1	0.8
Neurological disease	6	4.7
Antibiotic consumption		
Yes	103	80.5
No	25	19.5
CT scan		
Clear	3	2.3
Not definitive	98	76.6
Suspected	20	15.6
Infected	7	5.5
PCR test		
Positive	68	53.1
Negative	4	3.1
Not definitive	56	43.8

Note. SD: Standard deviation; CT: Computed tomography; PCR: Polymerase chain reaction.

and bacterial co-infection were not significantly associated with mortality (Table 2).

In addition, according to linear regression analysis, except for age and gender ($P = 0.004$ and 0.006, respectively), type of residence, history of underlying diseases, and bacterial co-infection had no association with the hospitalization period. Older people and women had more hospital stays (Table 3).

Based on the patients' computed tomography (CT) scan and polymerase chain reaction (PCR) results since they were tested during admission, patients with different CT scan results (not definitive, doubtful, infected, and healthy) demonstrated a significant difference in the hospitalization period ($P = 0.002$) but not in mortality ($P = 0.854$). On the other hand, there were no significant differences in the hospitalization period or mortality in patients with different PCR results (Table 4).

Patients with abnormal potassium, prothrombin, and partial thromboplastin time results during admission blood tests had a significantly different hospitalization period ($P = 0.023$, 0.001, and 0.045, respectively). In addition, patients with abnormal potassium and urea results had significantly different mortality rates ($P = 0.008$ and 0.016, respectively). Furthermore, there were significant differences in the hospitalization period and mortality between patients with abnormal urea ($P = 0.001$ and 0.001), creatinine ($P = 0.001$ and 0.044), and albumin ($P = 0.011$ and 1.000) in blood tests during discharge and patients with normal results (Table 4).

According to archived data, the most commonly prescribed antibiotics were ceftriaxone, hydroxychloroquine, and azithromycin (52.3%, 45.3%, and 35.9%, respectively). Significant differences were found in the hospitalization period between patients who took vancomycin and gentamycin ($P = 0.003$ and 0.015, respectively). Moreover, in patients who took vancomycin, the mortality rate was significantly higher than in other patients ($P = 0.002$, Table 5).

Despite the missing data, there was a significant relationship between ceftriaxone prescribed dosage and hospitalization period ($P = 0.006$, Table 6).

Discussion

Our findings indicated that age and gender are two important factors that have significant associations with both a longer duration of hospital stay and higher mortality rates among COVID-19-infected patients. This is in line with the findings of previous studies, which have shown that older individuals and those with underlying medical conditions, such as hypertension, diabetes, and cardiovascular diseases, are at increased risk of poor outcomes following COVID-19 infection.[11]

Additionally, it was revealed that the presence of bacterial co-infection was not significantly associated with increased mortality rates; this finding leads us to the conclusion that administering antibiotics may not be necessary for all patients infected with COVID-19, especially those with non-severe illnesses. However, the impact of antibiotics may remain uncertain because 82.8% of patients in our study received antibiotic therapy, and 14.2% of them died. Based on the findings of Akbariqomi et al, antibiotic treatment was associated with adverse

Table 2. Logistic Regression Analysis: Examining Mortality as an Outcome*

	B	SE	Wald	df	Sig.	Exp (B)
Gender	-1.052	0.620	2.880	1	0.090	0.349
Age	-0.048	0.021	5.308	1	0.021	0.954
Type of residence	0.367	0.633	0.335	1	0.563	1.443
Underlying disease	0.175	0.638	0.076	1	0.783	1.192
Bacterial co-infection	-1.020	0.950	1.153	1	0.283	0.361
Constant	5.306	1.660	10.217	1	0.001	201.454

Note. B: Estimated logit coefficient; SE: Standard error; df: Degree of freedom; Sig.: Significance level; Exp (B): Exponential value of B.
*Dependent variable: Mortality.

Table 3. Linear Regression Analysis: Hospitalization Duration as the Dependent Variable*

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
	B	SE	Beta			Lower Bound	Upper Bound
Constant	2.032	1.611		1.261	0.210	-1.163	5.226
Gender	2.040	0.732	0.256	2.785	0.006	0.587	3.492
Age	0.062	0.021	0.275	2.926	0.004	0.020	0.104
Type of residence	0.703	0.823	0.081	0.854	0.395	-0.930	2.336
Underlying disease	-0.087	0.755	-0.011	-0.115	0.908	-1.585	1.410
Bacterial co-infection	-0.161	1.514	-0.010	-0.106	0.916	-3.162	2.841

Note. Sig.: Significance level; SE: standard error.
*Dependent variable: Hospitalization period (day).

Table 4. Test Results During Admission and Discharge[a]

	No. (%)		Hospitalization Period		Mortality	
	Admission	Discharge	*P* Value[b]		*P* Value[c]	
			Admission	Discharge	Admission	Discharge
WBC	Mean: 7300.43 (SD: 3424.63)	Mean: 7865.44 (SD: 5344.8)	0.580	0.727	0.350	0.002
CRP	Mean: 282.90 (SD: 1833.67)	Mean: 47.82 (SD: 21.98)	0.422	0.285	0.259	0.538
CT scan						
Not definitive	98 (76.6)	-	0.002	-	0.854	-
Doubtful	20 (15.6)	-				
Infected	7 (5.5)	-				
Healthy	3 (2.3)	-				
PCR						
Not definitive	56 (43.8)	-	0.121	-	1.000	-
Positive	68 (3.1)	-				
Negative	4 (53.1)	-				
Blood pressure	20 (15.6)	2 (1.6)	0.550	0.270	1.000	1.000
Hct	23 (18)	10 (7.8)	0.245	0.085	0.164	0.612
Hb	5 (3.9)	0	0.088	-	0.117	-
RBC	4 (3.1)	0	0.081	-	0.418	-
Na	5 (3.9)	1 (0.8)	0.617	0.187	1.000	0.125
Mg	7 (5.5)	1 (0.8)	0.912	0.291	0.595	1.000
K	17 (13.3)	11 (8.6)	0.023	0.963	0.008	0.628
P	9 (7)	0	0.525	-	0.601	-
Ca	12 (9.4)	2 (1.6)	0.348	0.324	1.000	1.000
Urea	14 (10.9)	9 (7)	0.390	0.001	0.016	0.001
Albumin	7 (5.5)	8 (6.3)	0.230	0.011	1.000	1.000
Prothrombin	3 (2.3)	3 (2.3)	0.001	0.718	1.000	0.332
Creatinine	18 (14.1)	12 (9.4)	0.237	0.001	0.050	0.044
Cholesterol	3 (2.3)	0	0.850	-	1.000	-
ALP	4 (3.1)	1 (0.8)	0.545	0.802	1.000	1.000
PT	8 (6.3)	6 (4.7)	0.232	0.834	1.000	0.163
PTT	4 (3.1)	2 (1.6)	0.045	0.499	0.418	1.000
ESR	35 (27.3)	2 (1.6)	0.720	0.864	1.000	1.000
SGPT	6 (4.7)	5 (3.9)	0.278	0.424	0.559	1.000
LDH	17 (13.3)	10 (7.8)	0.479	0.393	0.446	0.612
CPK	1 (0.8)	2 (1.6)	0.992	0.472	1.000	1.000
INR	1 (0.8)	1 (0.8)	0.992	0.187	1.000	1.000
MCH	2 (1.6)	0	0.493	-	1.000	-
AST	6 (4.7)	0	0.169	-	0.559	-
ALT	5 (3.9)	0	0.979	-	0.493	-

Note. SD: Standard deviation; WBC: White blood cell; CRP, CT: Computed tomography; PCR: Polymerase chain reaction; Hct: Hematocrit; Hb: Hemoglobin; RBC: Red blood cell; Na: *Sodium*; Mg: *Magnesium*; K: *Potassium*; P: Phosphorus; Ca: Calcium; ALP: Alkaline phosphatase; PT: Prothrombin; PTT: Partial thromboplastin time; ESR: Erythrocyte sedimentation rate; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase; LDH: Lactic dehydrogenase; CPK: *Creatine phosphokinase*; INR: International normalized ratio; MCH: Mean *corpuscular* hemoglobin; AST: Aspartate aminotransferase; ALT: Alanine transaminase; ANOVA: Analysis of variance.

[a] Based on frequencies of abnormalities, [b] Pearson's correlation, one-way ANOVA, and independent sample t-test, [c] Independent sample t-test, chi-square, and Fisher's exact test.

Table 5. Effects of Antibiotic Usage on Hospitalization Duration and Mortality in COVID-19 Patients

	N	%	Hospitalization Period		Mortality	
			Day (SD)	*P* Value[a]	Count	*P* Value[b]
Ceftriaxone	67	52.3	7.15 (3.58)	0.564	7	0.594
Ciprofloxacin	2	1.6	7.5 (0.71)	0.456	0	1.000
Clindamycin	8	6.3	6.75 (2.44)	0.814	1	1.000
Metronidazole	3	2.3	7 (5.29)	0.991	0	1.000
Meropenem	4	3.1	9 (2.83)	0.234	1	0418
Vancomycin	6	4.7	11.5 (6.83)	0.003	4	0.002
Azithromycin	46	35.9	8.13 (4.3)	0.015	6	1.000
Gentamicin	1	0.8	Missing	-	0	1.000
Hydroxychloroquine	58	45.3	7.41 (3.73)	0.222	8	0.791

Note. SD: Standard deviation.
[a] Independent sample t-test, [b] Chi-square (Fisher's exact test for tests that have an expected count less than 5).

Table 6. Correlation of Antibiotic Dosage With Hospitalization Duration and Mortality in COVID-19 Patients

	Mean Dosage mg (SD)			Mortality	Hospitalization Period
	All	Recovered	Died	*P* Value[a]	*P* Value[b]
Ceftriaxone	30.56 (23.1)	31.86 (22.9)	21 (24.33)	0.340	0.006
Ciprofloxacin	Missing	Missing	Missing	-	-
Clindamycin	101.6 (120.22)	123 (127.35)	16	0.507	0.054
Metronidazole	25 (10.54)	25 (10.54)	-	-	-
Meropenem	63 (12.73)	63 (12.73)	-	-	-
Vancomycin	105 (69.52)	-	105 (69.52)	-	0.400
Azithromycin	36.43 (53.82)	36.43 (53.82)	-	-	0.263
Gentamicin	Missing	Missing	Missing	-	-
Hydroxychloroquine	Missing	Missing	Missing	-	-

Note. SD: Standard deviation. [a] Independent sample t-test, [b] Spearman's correlation.

drug reactions in a significant proportion of patients who did not have a bacterial co-infection.[12] The other alternative reason could be that bacterial infections are a sign of severity, and these patients are more likely to die.

Abnormal levels of electrolytes (potassium, prothrombin, and partial thromboplastin time) and renal function tests (urea, creatinine, and albumin) during admission were significantly associated with a longer duration of hospital stay and higher mortality rates. This finding, which conforms to the findings of Vihinen et al, suggests that monitoring these laboratory parameters could be useful in predicting the severity of disease and outcomes among COVID-19-infected individuals.[13]

According to our analysis, there was a significant association between the use of certain antibiotics (vancomycin and gentamycin) and the prolonged length of hospital stay among COVID-19-infected individuals. However, there was no significant association between the use of ceftriaxone, azithromycin, and hydroxychloroquine and either length of hospital stays or mortality rates.

The limitations of this study include the retrospective nature of the data collection, which may have led to incomplete or missing data. Despite this limitation, the use of archived data allowed researchers to study a large number of patients over a relatively long period of time, providing valuable insights into the effectiveness of antibiotics in COVID-19 patients. Further studies with larger sample sizes and the inclusion of other potential risk factors are warranted to confirm these findings.

Conclusion

Our findings confirmed that age, gender, and laboratory parameters such as electrolytes and renal function tests influence clinical outcomes in COVID-19 patients. However, the study has limitations, including its retrospective nature and relatively small sample size. The call for further studies with larger sample sizes and the inclusion of other potential risk factors indicates that this is an area of research that is still evolving and that there's much more to learn about how different factors affect COVID-19 outcomes.

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Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

The Ethical Committee of Maragheh University of Medical Sciences approved the study protocol (IR.MARAGHEHPHC.REC.1400.005).

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