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Research Article

Resilience of Antibiotic Usage and Vital Signs in COVID-19 Patients: A Post-Pandemic Analysis in Pakistan

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Abstract: COVID-19 has had a profound global impact, wreaking havoc on economies and causing a significant loss of lives. Pakistan has also faced severe consequences from the pandemic. To combat the virus, antibiotics such as Azithromycin, Ceftriaxone, Cefixime, Clarithromycin, Levofloxacin, Moxifloxacin, Meropenem, Tazobactam, Tienam, and Vancomycin have been administered to COVID-19 patients. Various vital signs such as temperature, respiratory rate, oxygen saturation, pulse rate, and blood pressure have been closely linked to the symptoms of COVID-19. This study examines the impact of antibiotic usage and vital signs on the survival and mortality of COVID-19 patients using a dataset collected from four major hospitals in Pakistan. The analytical approach includes descriptive analysis, a t-test, and a chi-square test of independence. The originality of this research lies in its comprehensive exploration of the relationship between specific antibiotics and the monitoring of vital signs in the context of COVID-19. It offers a systematic analysis of existing information to derive meaningful insights. Azithromycin emerged as the predominant antibiotic used to treat COVID-19 patients in Pakistan, with other antibiotics showing varying usage patterns. Strong, significant associations were identified between Azithromycin, Tazobactam (Tanzo), and the binary response variable (died/alive). Regarding vital signs, significant relationships were observed for patient age, systolic blood pressure, and diastolic blood pressure when compared to the response variable. This study's findings underscore the importance of Azithromycin and Tazobactam in COVID-19 treatment and highlight the role of vital signs in predicting patient outcomes.

Keywords: Antibiotic Levels, Vital Signs, Survival and Mortality, Post COVID Patients Analysis.

1. INTRODUCTION

The year 2020 is not as fanciful due to the spreading and overwhelming figures of Coronavirus disease (COVID-19) [1, 2]. Millions of people have been affected due to the horrible threat of COVID-19 around the world [3]. It is a drastic fact that the COVID-19 pandemic has remodeled the fabric of society, clipped the human psyche, influenced public policies, redefined business horizons, and redesigned interpersonal relations around the globe. The COVID-19 has severely affected the world economies. The outbreak of COVID-19 was first experienced in Wuhan, China at the end of December 2019 and then it rapidly spread worldwide in almost 209 countries in America, Europe, Australia, Africa, and Asia [4, 5]. Worldwide, COVID-19 is responsible for a huge no. of deaths. COVID-19 is also a heinous issue for the Pakistan's healthcare sector. Pakistan's economy was vulnerable to offer the high level of COVID-19 treatment set by the World Health Organization (WHO) [5, 6]. COVID-19 is a virus that most frequently attacks the human respiratory system. The WHO had classified the COVID-19 epidemic in Pakistan as the Sixth Public Health of Emergency Services (SPHEC). Pakistan has made strong efforts to eradicate the spread of COVID-19 by creating special laboratories, hospital wards, quarantine, awareness campaigns, and lockdowns.

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Coronavirus is a contagious disease attributed to the most recently discovered severe acute respiratory syndrome coronavirus-2 (SARs-COV-2). Arshad *et al.* [7] emphasized trials to study the combination impact of hydroxychloroquine and azithromycin for the treatment of positive COVID-19 patients and they reported that the combination of hydroxychloroquine and azithromycin was associated with reduced mortality. Miranda *et al.* [8] highlighted that the absence of reliable statistics on antimicrobial usage during the COVID-19 pandemic poses a significant challenge to effective public health policy formulation and strategic planning. Gautret *et al.* [9] reported that the COVID-19 virus was significantly eliminated when azithromycin was added to hydroxychloroquine in a clinical trial. Echeverria-Esnal *et al.* [10] revealed that azithromycin behaved well against a different viral cycle of SARS-CoV-2 and it reduced the risk of mortality as well as the ventilation period. Gonzalez-Zorn [11] reported that the use of four antibiotics i.e. amoxicillin, erythromycin, cefixime, and levofloxacin was significant in curing the COVID-19 pandemic. Langford *et al.* [12] reported that unnecessary use of antibiotics was likely to be high in COVID-19 patients. The different vital signs (physiological measurements) i.e. Temperature, Respiratory rate, Oxygen saturation, Pulse rate, blood pressure, and Level of consciousness are associated with the symptoms of COVID-19. Different antibiotics i.e. Azithromycin, Ceftriaxone, Cefixine, Chlathromycin, Levofloxacin, Moxifloxacin, Meranum, Tanzo, Tienum, and Vancomycin had been administered in Pakistan for the treatment of COVID-19.

In Pakistan, different antibiotics such as Azithromycin, Ceftriaxone, Cefixime, Clarithromycin, Levofloxacin, Moxifloxacin, Meropenem, Tanzo, Tienam, and Vancomycin were administered to treat COVID-19 patients in different hospitals. However, there is a lack of detailed post-COVID-19 studies in Pakistan showing which level/dose of antibiotics are significantly associated with survival and mortality of COVID-19 patients, which level can prevent the patient from major casualties, and which level/dose of antibiotics can be helpful for better treatment. Vital signs (physiological measurements) such as temperature, respiratory rate, oxygen saturation, pulse rate, and blood pressure are closely linked to COVID-19 symptoms. In Pakistan, no post-COVID-19 study has been carried out which is evident whether vital signs (physiological measurements) are statistically associated and helpful for detecting COVID-19 pandemic symptoms. The absence of post-COVID-19 studies in Pakistan focusing on antibiotic levels and vital signs makes this research highly original and impactful. This research seeks to address these critical gaps in understanding for more effective patient management and treatment. This study is based on cross-sectional statistical analysis to elaborate:

1. Which level/ dose of antibiotics are significantly associated with survival and mortality of COVID-19 patients, which level can prevent major casualties, and which level of antibiotics can ensure better treatment measures for the patients admitted in the hospitals of Pakistan?
2. Whether vital signs (physiological measurements) i.e. temperature, respiratory rate, oxygen saturation, pulse rate, and blood pressure are associated and helpful for detecting COVID-19 symptoms.
3. To layout some recommendations about the usefulness of different antibiotics and the effects of vital signs (physiological measurements) for detecting COVID-19 symptoms.

2. MATERIALS AND METHODS

2.1. Data Collection and Variables Descriptions

This study utilizes secondary data collected from four major hospitals in Rawalpindi and Islamabad, including the Pakistan Institute of Medical Sciences Hospital, Pakistan Air Force Hospital, Benazir Bhutto Shaheed Hospital, and Holy Family Hospital. The dataset comprises information from 1806 COVID-19 patients spanning from February to August 2020. The data includes vital medical signs such as temperature, respiratory rate, oxygen saturation, pulse rate, systolic blood pressure, and diastolic blood pressure, as well as the administration of various levels of antibiotics, including Azithromycin, Ceftriaxone, Cefixime, Clarithromycin, Levofloxacin, Moxifloxacin, Meropenem, Tanzo, Tienam, and Vancomycin. Patient status (alive/died) is also recorded for analysis. Vital medical signs are treated as quantitative measures, while antibiotics are categorized into three levels for examination.

A_0 = when no antibiotics are given to COVID-19 patients.

A_l = when a low dose of antibiotics is given to COVID-19 patients.

A_h = when a high dose of antibiotics is given to COVID-19 patients.

2.2. Statistical Data Analysis

The statistical analysis is carried out in the following steps:

1. Descriptive statistical analysis is performed using counts, percentages, mean, and standard deviation for the variables of interest.
2. The chi-square (χ^2) test is used to determine whether there is a significant association between two categorical variables i.e. died/alive against different antibiotics levels.

$$\chi 2 = \sum \frac{(O_i - E_i)^2}{E_i} \quad (1)$$

Where "O_i" defined the observed values and "E_i" defined the expected values in the datasets of interest. The hypothesis is set as:

H_0: There is no significant difference existing for died/alive against different levels of antibiotics applied.

H_1: There is a significant difference existing for dead/alive against different levels of antibiotics applied.

3. T-test is applied to measure the significance of died/alive against different vital signs (physiological measurements) i.e. respiration rate, body temperature, oxygen saturation level, pulse rate, and blood pressure.

$$t_{\bar{\theta}} = \frac{\phi - \theta}{\frac{s}{\sqrt{n}}} \quad (2)$$

Where "ϕ" is the mean of sample data, "θ" overall mean of the dataset, "s" is the standard deviation, and "n" stands for the sample size. The hypothesis set as:

H_0: There is no significant difference between dead/alive against different vital signs.

H_1: There is a significant difference between dead/alive against different vital signs.

3. RESULTS

3.1. Significance of Different Levels of Antibiotics and Died/Alive

Table 1 shows the association for different levels of antibiotics against the response variable died/alive. For azithromycin 208 (11.5%) patients were treated with "A_o", 113 (6.3%) with "A_l" and 1485 (82.2%) with "A_h". For azithromycin, 143 (69%) were alive and 65 (31%) have died for level "A_0", 74 (65%) were alive and 39 (35%) died from level "A_l", 1124 (76%) were alive and 361 (24%) were died of level "A_h". For the Ceftriaxone 1380 (76.4%) patients were treated with "A_0", 214 (11.8%) with "A_l" and 212 (11.7%) with "A_h". For Cefatriaxone, 1021 (74%) were alive and 359 (26%) died for level "A_0", 166 (78%) were alive and 48 (22%) died from level "A_l", 154 (73%) were alive and 58 (27%) were died for level "A_h". Figure 1 illustrates that the maximum number of patients are given high levels of antibiotics "A_h" for azithromycin, while it is found vice versa for all other antibiotics. The Chi-square and p-value found 9.44 and 0.009 for azithromycin, 7.32 and 0.026 for Tanzo. There is a strong association exist between the antibiotic Azithromycin and Tanzo with the binary response variable died/alive. For Tienum, Moxifloxacin, Cefixine, Levofloxacin, Vancomycin, Chlathromycin, and Meranum, the p-value reported as 0.322, 0.147, 0.446, 0.969, 0.712, 0.922 and 0.877. All these p-values found greater than 5% level of significance. There is no association exists between Tienum, Moxifloxacin, Cefixine, Levofloxacin, Vancomycin, Chlathromycin, and Meranum for response variable died/alive, while it is reported statistically strong associations between Azithromycin and Tanzo with response variable died/alive.

3.2. Significance of Different Vital Signs and Response Variable Died/Alive

Table 2 shows the degree of relation between different vital signs (physiological measurements) and the response variable died/alive. The mean age of patients was found to be 47.38 with a standard deviation of 17.17. For patients' age high value of standard deviation indicates a larger variation among the ages of COVID-19 patients, while found lowest for body temperature. For the respiratory rate, 24.14 breaths per minute indicates a very serious condition [13, 14]. The average temperature of the human body was found 99.15 with the lowest standard deviation of 1.20, which indicates the temperature of COVID-19 patients varies in the normal range. The 88.48% saturation oxygen level with a standard deviation of 12.54 is considered a low oxygen level.

Table 1. Significance of different levels of antibiotics and response variable died/alive.

Antibiotics	Levels	Count (%)	Alive	Died	Chi-Sq	p-Value
Azithromycin	None (A_0)	208(11.5)	143 (69)	65 (31)	9.44	0.009
	Low (A_l)	113(6.3)	74 (65)	39 (35)		
	High (A_h)	1485(82.2)	1124 (76)	361 (24)		
Cefatriaxone	None (A_0)	1380(76.4)	1021 (74)	359 (26)	1.57	0.456
	Low (A_l)	214(11.8)	166 (78)	48 (22)		
	High (A_h)	212(11.7)	154 (73)	58 (27)		
Tienum	None (A_0)	1643(91)	1227 (75)	416 (25)	2.26	0.322
	Low (A_l)	39(2.2)	29 (74)	10 (26)		
	High (A_h)	124(6.9)	85 (69)	39 (31)		
Tanzo	None (A_0)	1509(83.6)	1104 (73)	405 (27)	7.32	0.026
	Low (A_l)	97(5.4)	82 (85)	15 (15)		
	High (A_h)	199(11)	154 (77)	45 (23)		
Moxifloxacin	None (A_0)	1783(98.7)	1328 (74)	455 (26)	3.83	0.147
	Low (A_l)	16(0.9)	9 (56)	7 (44)		
	High (A_h)	7(0.4)	4 (57)	3 (43)		
Cefixine	None (A_0)	1798(99.6)	1336 (74)	462 (26)	0.58	0.446
	Low (A_l)	8(0.04)	5 (63)	3 (38)		
	High (A_h)	0	0	0		
Levofloxacin	None (A_0)	1785(98.8)	1325 (74)	460 (26)	0.06	0.969
	Low (A_l)	9(0.5)	7 (78)	2 (22)		
	High (A_h)	12(0.7)	9 (75)	3 (25)		
Vancomycin	None (A_0)	1794(99.3)	1331 (74)	463 (26)	0.68	0.712
	Low (A_l)	11(0.6)	9 (82)	2 (18)		
	High (A_h)	1(0.1)	1 (100)	0		
Chlathromycin	None (A_0)	1772(98.1)	1316 (74)	456 (26)	0.16	0.922
	Low (A_l)	17(0.9)	12 (71)	5 (29)		
	High (A_h)	17(0.9)	13 (76)	4 (24)		
Meranum	None (A_0)	1744(96.6)	1294 (74)	450 (26)	0.26	0.877
	Low (A_l)	48(2.7)	37 (77)	11 (23)		
	High (A_h) (	14(0.8)	10 (71)	4(29)		

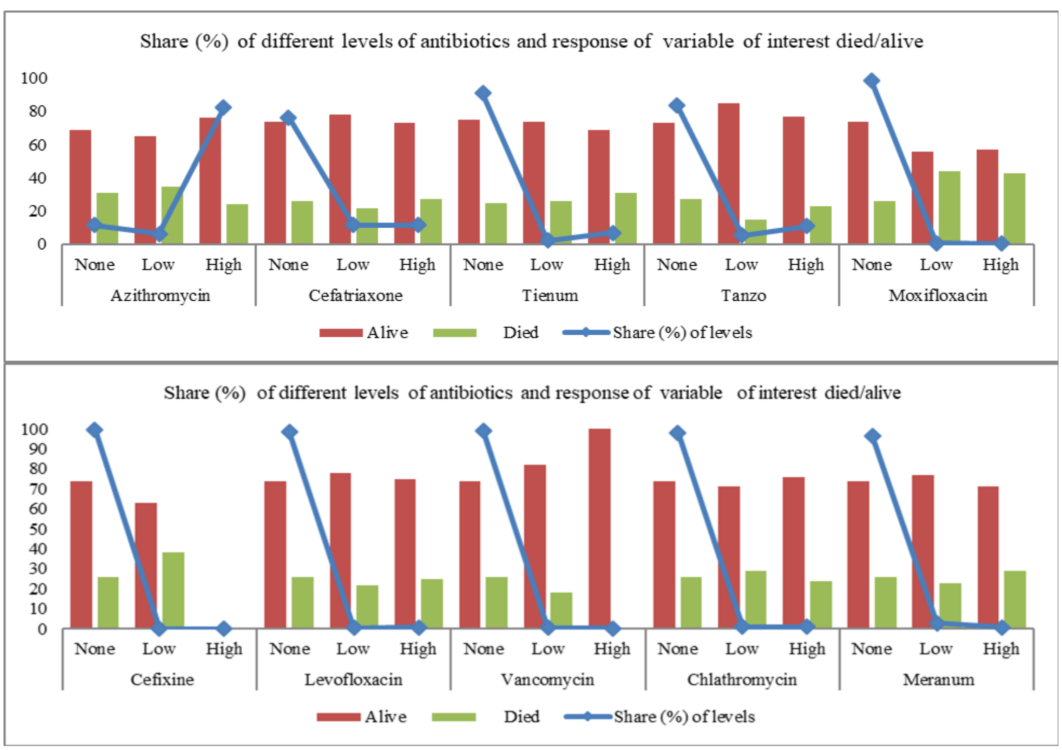

Fig. 1. Share (%) of different antibiotic levels and the response of variable died/alive.

Table 2. Relation between the vital signs and response variable died/alive.

Vital signs	Mean	Standard deviation	t-value	p-value
Age of patients	47.38	17.17	18.723	0.00
Respiratory Rate	24.14	8.95	-0.707	0.476
Body Temperature	99.15	1.20	0.717	0.476
Oxygen saturation level	88.48	12.54	1.344	0.179
Systolic blood pressure	120.09	18.70	-2.117	0.034
Diastolic blood pressure	77.28	12.53	-2.116	0.035
Pulse rate	89.48	14.74	0.559	0.576

The value of standard deviation was found 18.70, 12.53, and 14.74 respectively for systolic blood pressure, diastolic blood pressure, and pulse rate, which are considerably large variations. The p-value was found less than 0.05 for the age of the patient, systolic blood pressure, and diastolic blood pressure, which indicates there is statistically significant relation exists for these variables against response variables died/alive, while all other vital signs yield statistically insignificant relation for the response variable died/alive.

4. DISCUSSION

Several studies have examined the application pattern of antibiotics in COVID-19 patients. Estrada *et al.* [15], Fiol *et al.* [16], Akhtar *et al.* [17], Mansoor *et al.* [18], Saeed *et al.* [19], and Alvi *et al.* [20] conducted similar investigations. They found that bacterial co-infections were infrequent among COVID-19 patients, yet the utilization of antibiotics was widespread. There was promising evidence suggesting that azithromycin could serve as a potential treatment for COVID-19. Clear and specific guidelines are essential for establishing a targeted treatment to minimize associated risks and inappropriate use of antibiotics. Mustafa *et al.* [21], and Farooqui *et al.* [22] also confirmed the alarming issue of suboptimal antibiotic usage and its consequential contribution to antibiotic resistance. Their research reveals a worrisome trend of excessive antibiotic consumption among hospitalized patients with suspected or confirmed COVID-19 patients in Pakistan. Gul *et al.* [23] also emphasized the urgent need for pharmacist and pharmacy technician programs to curb antibiotic misuse and combat antimicrobial resistance (AMR). Urgent attention is needed to combat the unnecessary prescription of antibiotics in the context of COVID-19 infection. This research examined the three levels of ten different antibiotics and confirmed that the majority of patients received high level antibiotics in the case of azithromycin, while the pattern was reversed for all other antibiotics i.e. Ceftriaxone, Cefixine, Chlathromycin, Levofloxacin, Moxifloxacin, Meranum, Tanzo, Tienum, and Vancomycin Furthermore, a strong association was identified between the use of azithromycin and Tanzo with the binary response variable died/alive. Haq *et al.* [24] found that COVID-19 mortality in Pakistani hospitalized patients was linked to demographic factors, clinical lab characteristics, oxygen saturation, and late admission. Aksel *et al.* [25], and Qureshi *et al.* [26] applied a similar study and found that vital signs significantly influenced the survival and mortality of COVID-19. Similarly, Jeong *et al.* [27] identified that cough, fever, nasal congestion, and diarrhea are key symptoms for establishing comprehensive COVID-19 screening criteria. This study extended the vital signs (physiological measurements) to temperature, respiratory rate, oxygen saturation, pulse rate, and blood pressure with the survival and mortality of COVID-19 patients, which had not been studied earlier. The mean age of patients indicates a larger variation while the temperature of COVID-19 patients varies within the normal range. The 88.48% saturation oxygen level with a standard deviation of 12.54 was considered a low oxygen level. Large variations were found for blood pressure and pulse rate. The age of the patient and blood pressure were found to be statistically significant.

5. CONCLUSIONS

The year 2020 is not as fanciful due to the spreading figures of COVID-19. Worldwide, COVID-19 was responsible for significant casualties and posed a severe challenge for Pakistan. Different vital signs (physiological measurements) i.e. temperature, respiratory rate, oxygen saturation, pulse rate, and blood pressure are associated with the symptoms of COVID-19 and different antibiotics i.e. Azithromycin, Ceftriaxone, Cefixine, Chlathromycin, Levofloxacin, Moxifloxacin, Meranum, Tanzo, Tienum, and Vancomycin had been administrated to treat the COVID-19. No detailed post-COVID-19 research has been conducted in Pakistan to study the significance and associations of antibiotic levels and vital signs with survival and mortality in COVID-19 patients.

This study provides evidence of which antibiotic levels and vital signs significantly influence the survival and mortality of COVID-19 patients. The secondary data of 1806 COVID-19 patients are used and three levels of antibiotics are studied. Descriptive statistical analysis, chi-square, and t-test are applied to assess the significance of died/alive against antibiotics levels and vital signs. Maximum numbers of patients were given high levels of antibiotics for azithromycin, while it is found vice versa for all other antibiotics. The strong significant associations reported for Azithromycin and Tanzo with the binary response variable died/alive, while all other antibiotics levels yield statistically insignificant results. For vital signs, a high standard deviation was found for the ages of COVID-19 patients. The temperature of COVID-19 patients varies in a normal range. High standard deviations were found for systolic blood pressure, diastolic blood pressure, and pulse rate. Statistically significant relation exists for the age of the patient, systolic blood pressure, and diastolic blood pressure against response variables died/alive, while all other vital signs yield insignificant results. This study provides a foundation for formulating enhanced recommendations and identifying future research areas by leveraging predictive modeling through machine learning and statistical techniques. It focuses on the interplay between antibiotic levels and vital signs to effectively detect and monitor the deterioration of patients afflicted with various severe diseases.

6. CONFLICT OF INTEREST

All authors affirm that they have no conflict of interest.

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