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Research Article

Antibiotics, Vital Signs and Comorbidities as Predictors of COVID-19 Mortality: An Unadjusted and Adjusted Logistic Regression Analysis

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Abstract: This study explores the association between COVID-19 patients and antibiotic usage (Azithromycin, Ceftriaxone, Tanzo, Tienum) concerning vital signs and comorbidities (diseases) to enhance treatment efficacy, emphasizing mortality risk. Logistic regression is used for unadjusted model (M_0) links antibiotics, while adjusted models (M_1, M_2, M_3) incorporate vital signs and comorbidities, etc. Antibiotics are categorized into low (L_1) and high (L_2) doses. Models are classified as ILRM (insignificant with low risk of mortality), SLRM (significant with low risk of mortality), IHRM (insignificant with high risk of mortality) and SHRM (significant with high risk of mortality). Azithromycin exhibits IHRM at L_1 and SLRM at L_2 for M_0, M_1/M_2 show IHRM at L_1 and ILRM at L_2. M_3 shows IHRM. Ceftriaxone transitions from ILRM at L_1 to IHRM at L_2 (except M_3). Tanzo shows SLRM at L_1 (M_0) and ILRM in other models (except M_3 at L_2). Tienum indicates IHRM at both levels (M_0), while adjusted models associate it with ILRM at L_1 and IHRM at L_2. This research provides crucial insights for healthcare professionals to predict and manage vital signs and comorbidities variations, and to underline the mortality risk in COVID-19 patients.

Keywords: COVID, Antibiotic, Vital Signs, Comorbidities, Unadjusted and Adjusted Models, Mortality Risk.

1. INTRODUCTION

The Coronavirus disease (COVID-19) dramatically reshaped societal structures, impacted human psychology, influenced public policies and redefined interpersonal interactions through isolation and digital reliance [1, 2]. COVID-19 is a highly contagious respiratory illness caused by the severe acute respiratory syndrome [3-5]. The virus was first identified in December 2019 in the city of Wuhan, China. The global situation with COVID-19 has been dynamic, with various waves of infections.

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Vaccination campaigns have played a crucial role in mitigating the impact of the virus, providing immunity to individuals and reducing the severity of illness. Several vaccines have been developed and authorized for emergency use, contributing to a significant decrease in severe cases and mortality rates in many regions [6-7]. However, challenges persist, including the emergence of new variants of the virus, vaccine distribution disparities and ongoing public health measures [8, 9]. Some areas of world have experienced resurgences of COVID-19 cases, leading to fluctuations in containment efforts [10, 11]. Governments and health authorities continue to adapt strategies based on the evolving nature of the pandemic, balancing public health concerns with the need for economic stability and societal well-being. The virus has been responsible for a significant number of deaths worldwide and has presented a critical challenge for Pakistan's healthcare sector [12, 13]. Pakistan managed well to meet the high standards for COVID-19 treatment set by the World Health Organization [14-16].

Islam *et al.* [17], Gul and Yucesan [18] and Spangler *et al.* [19] reported that different vital signs play a vital role in monitoring the individuals, whether it is suspected or confirmed COVID-19 patient, and these vital signs, i.e., (temperature, respiratory rate, oxygen saturation, pulse rate, blood pressure and level of consciousness) are associated with the symptoms of a COVID-19 infection. Fever is a common symptom of COVID-19. Generally, normal body temperature for a healthy adult can range between 97.8 degrees Fahrenheit (36.5 degrees Celsius) and 99 degrees Fahrenheit (37.2 degrees Celsius) and body temperature above 100.4 °F (38 °C), is often observed in infected individuals [20, 21], Generally, normal respiration rates for an adult person at rest typically range from 12 to 16 breaths per minute and increased respiratory rate may be indicative of respiratory distress or pneumonia, which can be associated with severe cases of COVID-19 [22, 23]. COVID-19 can lead to respiratory issues and monitoring oxygen saturation levels is crucial. A decrease in oxygen saturation may indicate respiratory compromise or the development of acute respiratory distress syndrome [24]. American Heart Association (AHA) defined the accepted normal blood pressure as: a systolic blood pressure of less than 120 mm Hg and a diastolic blood pressure of less than 80 mm Hg, and monitoring pulse rate and blood pressure helps assess the cardiovascular impact of the infection [25, 26]. Generally, the normal resting heart rate for healthy adults typically falls within the range of 60 to 100 beats per minute [27, 28]. Monitoring vital signs is a crucial aspect of managing and providing care to individuals with COVID-19, especially in severe cases where prompt medical intervention may be necessary. Regular monitoring helps healthcare professionals assess the progression of the illness and adjust treatment plans accordingly. Different antibiotics, i.e., Azithromycin, Cefatriaxone, Tanzo, and Tienum had been applied in Pakistan for the treatment of COVID-19 [29-31].

In the healthcare domain, the standard practice involves administering various antibiotics, such as Azithromycin, Cefatriaxone, Tanzo, and Tienum, to treat bacterial infections. It is crucial to understand the potential impact of these antibiotics on essential indicators like temperature, respiratory rate, oxygen saturation, pulse rate and blood pressure. It is important to consider their effects on different comorbidities (diseases), i.e., diabetes, high blood pressure, heart, kidney, asthma, tuberculosis, cancer, nervous disorders, allergies, Chronic Obstructive Pulmonary Disease (COPD), etc. This understanding is essential for effective patient management and safety. The primary goal is to examine the dataset of post-COVID-19 patients and develop a robust and accurate logistic regression model that can predict the mortality risk of individuals with COVID-19. This involves developing various unadjusted and adjusted statistical models using different levels of antibiotics, vital measurements and diseases. The goal is to assist healthcare professionals in anticipating and effectively managing potential fluctuations in vital signs following antibiotic treatment. This research aims to contribute to the improvement of patient care by providing healthcare professionals with a reliable tool for managing antibiotic-related effects on vital signs and comorbidities.

2. MATERIALS AND METHODS

2.1. Data Collection and Variables Descriptions

The research gathered secondary data of COVID-19 patients, admitted to four hospitals, both public and private, located in Rawalpindi and Islamabad. These hospitals are Pakistan Air Force Hospital, Pakistan Institute of Medical Sciences Hospital,

Holy Family Hospital and Benazir Bhutto Shaheed Hospital. The study encompassed the timeframe spanning from February to August 2020. The statistical analysis was conducted using SPSS to ensure robust estimation and validation of results. The identification of variables is described as follows:

i. Antibiotics used are classified into two relative categories (levels) as: *"L_1"* = low dose is given, and *"L_2"* = high dose is given. Four antibiotics (Azithromycin, Cefatriaxone, Tanzo, and Tienum) are studied. Patients received Azithromycin as follows: 113 in L_1 and 1485 in L_2. Ceftriaxone was administered to 214 in L_1 and 212 in L_2. Tienum was provided to 39 in L_1 and 124 in L_2. Tanzo was prescribed to 97 in L_1 and 199 in L_2. The classification of antibiotic use into low (L_1) and high (L_2) levels is a relative categorization derived from four hospital records and does not represent standardized or guideline defined dosage thresholds. It is important to note that, in the context of COVID-19 management in Pakistan, antibiotic prescribing practices were heterogeneous and largely physician dependent, with dose variations influenced by clinical severity and institutional protocols rather than fixed benchmarks. Therefore, the L_1 and L_2 classifications represent comparative groupings derived from observed prescribing patterns across hospitals, rather than fixed or universally defined dosing standards.
ii. The presence and absences of various variables recorded, i.e., respiration rate, body temperature, oxygen saturation level, blood pressure, pulse rate, patient age, gender and survival outcome of individuals.
iii. The presence and absences of various comorbidities recorded, i.e., diabetes, blood pressure, heart disease, kidney disease, asthma, tuberculosis, cancer, nervous disorders, allergies, HCV, anemia, Chronic Obstructive Pulmonary Disease (COPD), etc.

2.2. Odds ratio, Un-adjusted and Adjusted Logistics Regression Models

Logistic regression is a statistical model used to forecast the likelihood of a binary outcome by considering one or more predictor variables (categorical or continuous) [32-35]. Logistic regression model (logistic function) is also known as the sigmoid function. The sigmoid function is useful for representing probabilities of any real value numbers to the range of 0 and 1. In logistic regression, the model predicts the probability of an event occurring as a function of one or more predictor variables. The coefficients of logistic regression represent the log-odds or logit transformation of the odds ratio for each predictor variable.

$$\log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 y_1 + \beta_2 y_2 + \beta_3 y_3 + \cdots + \beta_m y_m \quad (1)$$

Where "*p*" stands the probability of the event occurring, "*1-p*" stands the probability of the event not occurring and *"p/1-p"* stands the odds of the event occurring. *"β_0"* stands the intercept, and *"β_i"* (I = 1, 2, 3, … m) stands regression coefficients associated with independent variables *"y_i"*.

The odds ratio is a measure of association between an interest and outcome [36, 37]. In logistic regression, the odds ratio for a predictor variable is given by:

$$Odds\ Ratio = e^{\beta_i} \quad (2)$$

The odds ratio represents the multiplicative change in the odds of the event for a one-unit increase in the predictor variable [36, 37]. The logistic regression coefficients represent the change in the log-odds of the event per unit change in the corresponding predictor variable. The odds ratio is the exponential of the coefficient and represents the multiplicative change in the odds of the event for a one-unit change in the predictor variable [38-40]. Logistic regression coefficients are in the log-odds scale, while odds ratios provide a more interpretable measure of the effect of predictor variables on the odds of the event. The odds ratio (OR) measures the strength and direction of the association between two variables. It is calculated as the ratio of the odds of an event occurring in one group to the odds of it occurring in another group.

$$OR = \frac{OG_a/1 - OG_a}{OG_b/1 - OG_b} \quad (3)$$

Where *"OG_a"* stands the odds of the event of interest for group-a, and *"OG_b"* stands the odds of the event of interest for group-b. "*OR = 1"*, suggests that there is no association between the interest and the outcome. *"OR > 1"*, implies a positive association

between the interest and the outcome, and *"OR < 1"*, indicates a negative association between the interest and the outcome. The significance of the OR is often assessed through confidence intervals (CI), and if 95% CI does not include 1, suggests association is statistically significant. In logistic regression, both unadjusted (single predictor variables, without considering the effects of other variables) and adjusted models (multiple predictor variables) are commonly used to analyze the relationship between predictor variables and a binary outcome [41-44]. Various unadjusted and adjusted models are developed to predict the mortality risk (yes/no) of COVID-19 patients (Died/ Alive), incorporating with age, gender, antibiotics, vital signs and different comorbidities. The un-adjusted mode used as:

$$M_i = \log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_i y_i \quad (4)$$

Where *"M_i"* stands the dependent variable, as the mortality risk (yes/no) in COVID-19 patients (Died/Alive), *"β_0"* stands the intercept, and *"β_i"* stands coefficients associated with covariate antibiotics *"y_i"*. Three adjusted models used as:

i. "M_1" as dependent variable, as the mortality risk (yes/no) in COVID-19 patients (Died/ Alive) against with coefficients associated with covariate, antibiotics, age and gender.
ii. "M_2" applied with dependent variable, as the mortality risk (yes/no) in COVID-19 patients (Died/Alive) against with covariate antibiotic, age, gender, respiration rate, temperature, oxygen saturation, blood pressure and pulse rate.
iii. "M_3" used the dependent variable, as the mortality risk (yes/no) in COVID-19 patients (Died/Alive), against with covariate antibiotic, age, gender, respiration rate, temperature, oxygen saturation, blood pressure, pulse rate, diabetes, BP, heart disease, kidney disease, asthma, TB, cancer, nervous disorder, allergies, HCV, Anemia, COPD and others comorbidities.

2.3. Decision Analysis

The decision criteria for both adjusted and unadjusted models are as follows:

i. Statistically insignificant with low risk of mortality (ILRM).
ii. Statistically significant with low risk of mortality (SLRM).
iii. Statistically insignificant with high risk of mortality (IHRM).
iv. Statistically significant with high risk of mortality (SHRM).

2.4. Hypothesis Testing

This study explores the relationship between mortality risk in COVID-19 patients and various predictors. To ensure methodological clarity and reproducibility, the statistical framework of the study is explicitly defined through the following hypotheses.

The statistical hypotheses of this study are:

- **Null Hypothesis (H_0):** The estimated odds ratios are statistically insignificant for the risk of mortality at the 5% level of significance in COVID-19 patients for the predictors, i.e., antibiotics usage, vital signs and existing comorbidities.
- **Alternative Hypothesis (H_1):** There is a statistically significant association between the estimated odds ratios and the risk of mortality at the 5% level of significance in COVID-19 patients for the predictors, i.e., antibiotics usage, vital signs and existing comorbidities.

3. RESULTS

A distinct model is used simultaneously for each antibiotic. The coefficient represents the estimated change in the log-odds of the outcome variable associated with a one-unit change in the predictor variable. Positive coefficients suggest an increase in the odds, while negative coefficients suggest a decrease. The odds ratio (OR) represents the ratio of the odds of the event in one group to the odds of the event in another group. The 95% confidence interval provides a range within which we can be reasonably confident that the true value of the odds ratio lies. P-values and 95% confidence intervals (CI) is used to identified the significance of the results

3.1. Comparisons of Azithromycin Models

Table 1 provides coefficients, p-values, odds ratios (OR), and 95% confidence intervals (CI) for different models (M_0, M_1, M_2 and M_3) of the antibiotic Azithromycin across two levels (L_1 and

L_2). In the unadjusted model (M_0), the odds ratio (OR) for the exposure variable Azithromycin at a low dose (L_1) is determined to be 1.16, indicating an OR greater than 1. The corresponding 95% confidence interval (CI) ranges from 0.71 to 1.90 (inclusive of 1) and coefficient is found as 0.15. An odds ratio greater than 1 suggests a positive association between the exposure variable and the outcome. For the response variable mortality (yes/no), an OR greater than 1 implies that the odds of dying are higher in L_1 compared to the other group, and it could indicate an increasing risk associated with L_1. The odds of mortality risk are greater in the L_1 being compared to the L_2, and this might imply an increased likelihood of being died, but this association is statistically insignificant, as the reported p-value is 0.55. Similarly, in the case of a high dosage (L_2), the exposure variable Azithromycin yields coefficient as -0.35, odds ratio values of 0.71, accompanied by a 95% confidence interval (CI) ranging from 0.52 to 0.97. An odds ratio less than 1 suggests a negative association between the exposure variable Azithromycin at L_2 and the outcome. 1t implies that the odds of dying are lower in L_2 compared to the others group. It could indicate a protective effect (lower risk) of the mortality, and this association is statistically significant, as indicated by a p-value of 0.03.

In the case of model M_1, administering L_1 level of Azithromycin antibiotic yielded an odds ratio of 1.17, with a 95% confidence interval (CI) in the range of 0.69 to 1.99, and coefficient as 0.16. These findings suggest an increasing risk associated with the L_1, and it is statistically insignificant as p-value is found 0.56. For model M_1, employing L_2 level of Azithromycin, resulted in an odds ratio of 0.76, with a 95% CI of 0.54 to 1.08, p-v1lues of 0.13 and slop is -0.26. These results indicate a potential protective effect (lower risk) of the mortality, and this association is observed statistically insignificant.

In the case of M_2, the OR for the L_1 of the Azithromycin antibiotic is found as 1.17, with a 95%CI of 0.69 to 2.00 and slope coefficient as 0.16. These findings indicate a potential risk or high risk of mortality in L_1 compared with L_2 for M_2, and it is statistically insignificant as p-values are found as 0.56. Similarly, for the L_2 level of Azithromycin in M_2, the OR is 0.76, and the 95% CI is from 0.53 to 1.07) with p- value of 0.13, and slope coefficient as -0.27. These results suggest a potential protective effect (low risk of mortality), and this is statistical insignificant. In the case of model M_3, the administration of a L_1 level of Azithromycin antibiotic, yielded an odds ratio of 1.34, with a 95% CI of 0.74 to 2.43, p- values is found greater than 0.05 and coefficient as 0.29. These findings indicate a statistically insignificant risk. For model M_3 with a L_2 level of the Azithromycin, the resulting odds ratio is 1.09, the 95% CI is lies between 0.74 and 1.62, and slope as 0.09. These outcomes suggest a potential risk (high risk) both for L_1 and L_2, and it do not reach statistical significance as p-values > 0.05 in both cases L_1 and L_2.

The current statistical analysis suggests a statistically insignificant high risk of mortality (IHRM) for the unadjusted model (M_0) and all adjusted models (M_1, M_2 and M_3) for low dose. In the case of high dose, there is a potential protective

Table 1. Odd ratio, confidence interval (CI) and slope coefficient for Azithromycin models.

Antibiotics	Model	Levels	Coefficient	P-Value	OR	CI (95%)		Decision
						Lower Bound	Upper Bound	
Azithromycin	M_0	L_1	0.15	0.55	1.16	0.71	1.90	IHRM
		L_2	-0.35	0.03	0.71	0.52	0.97	SLRM
	M_1	L_1	0.16	0.56	1.17	0.69	1.99	IHRM
		L_2	-0.26	0.13	0.76	0.54	1.08	ILRM
	M_2	L_1	0.16	0.56	1.17	0.69	2.00	IHRM
		L_2	-0.27	0.12	0.76	0.53	1.07	ILRM
	M_3	L_1	0.29	0.33	1.34	0.74	2.43	IHRM
		L_2	0.09	0.66	1.09	0.74	1.62	IHRM

effect (low risk of mortality) for all models except M_3, where it falls into the high-risk. The statistically significant p-value for L_2 in the unadjusted model (M_0) indicates a statistically significant low risk of mortality (SLRM). However, for adjusted models M_1 and M_2, it is found to be a statistically insignificant low risk of mortality (ILRM), and for adjusted model M_3, it is an insignificant high risk of mortality (IHRM). The term insignificant implies that the observed effects may be due to random variability rather than a true association.

3.2. Comparisons of Ceftriaxone Models

Table 2 presents the results of the logistic regression analysis for the association between different levels of Ceftriaxone use and the odds of outcome, as indicated by the coefficients, p-values, odds ratios and corresponding confidence intervals (CI). For the antibiotic Ceftriaxone, at M_0, both levels L_1 and L_2 exhibit coefficients, which are not statistically significant with p-values 0.26 and 0.67, respectivrly, suggesting no significant impact of Ceftriaxone. Similar patterns are observed for M_1, M_2 and M_3, indicating no substantial change in the odds of the outcome with use of Ceftriaxone. The 95% confidence intervals (include 1), further supporting the lack of statistical significance and implies uncertainty.

In case of Model M_0 at L_1, OR value is found as 0.82, that suggests a possible protective effect (low risk of mortality). The slope is found negative -0.19. For the L_2, OR is reported as of 1.07, implies a possible risk (high risk of mortality). The positive slope coefficient is found as 0.06. For M_1 at L_1, OR is founds as 0.85, it is suggesting a potential protective effect (low risk of mortality). The slope is found negative with as values of -0.16. In similar case at L_2, OR value is 1.01 indicates a potential risk (high risk of mortality). The slope is found positive with as values of 0.003. M_2 shows the OR value is 0.84 at L_1, suggests a possible protective effect. The negative slope value is found as -0.16, while for L_2, the OR value is 1.06, indicating a possible risk, the coefficient is found as 0.06. The OR of 0.78, and 0.80 are found for M_3 at L_1 and L_2, respectively, suggests a possible protective effect.

In summary, both the unadjusted model (M_0) and all adjusted models (M_1, M_2 and M_3) show statistically insignificant results. The odds ratios and p-values consistently indicate an insignificant low risk of mortality (ILRM) at L_1 for the unadjusted model (M_0) and all adjusted models (M_1, M_2, and M_3). However, at L_2, the odds ratios and p-values reveal a statistically insignificant high risk of mortality (IHRM) for the unadjusted model (M_0) and adjusted models M_1 and M_2. In the case of adjusted model M_3, the results are reported as ILRM. The term insignificant implies that the observed effects may be due to random variability rather than a true association.

3.3. Comparisons of Tanzo Models

Table 3 shows the odd ratio, CI, and slope coefficient for Tanzo antibiotic. For model M_0, L_1 of Tanzo antibiotic yielded an OR of 0.50 with a 95% CI) in the range of 0.28 to 0.87. These findings indicate a protective effect (low risk of mortality) that is statistically significant with p-value is 0.01.

Table 2. Odd ratio, confidence interval (CI) and slope coefficient for Ceftriaxone models.

Antibiotics	Model	Levels	Coefficient	P-Value	OR	CI (95%)		Decision
						Lower Bound	Upper Bound	
Ceftriaxone	M_0	L_1	-0.19	0.26	0.82	0.58	1.16	ILRM
		L_2	0.06	0.67	1.07	0.77	1.48	IHRM
	M_1	L_1	-0.16	0.40	0.85	0.58	1.24	ILRM
		L_2	0.003	0.98	1.01	0.70	1.43	IHRM
	M_2	L_1	-0.16	0.39	0.84	0.58	1.24	ILRM
		L_2	0.06	0.74	1.06	0.74	1.53	IHRM
	M_3	L_1	-0.24	0.27	0.78	0.51	1.21	ILRM
		L_2	-0.22	0.30	0.80	0.52	1.22	ILRM

Table 3. Odd ratio, confidence interval (CI) and slope coefficient for Tanzo models.

Antibiotics	Model	Levels	Coefficient	P-Value	OR	CI (95%)		Decision
						Lower Bound	Upper Bound	
Tanzo	M_0	L_1	-0.70	0.01	0.50	0.28	0.87	SLRM
		L_2	-0.22	0.20	0.79	0.56	1.13	ILRM
	M_1	L_1	-0.57	0.06	0.56	0.31	1.03	ILRM
		L_2	-0.16	0.39	0.84	0.57	1.24	ILRM
	M_2	L_1	-0.52	0.08	0.59	0.32	1.08	ILRM
		L_2	-0.09	0.62	0.91	0.61	1.34	ILRM
	M_3	L_1	-0.38	0.26	0.68	0.35	1.33	ILRM
		L_2	0.25	0.26	1.28	0.82	1.99	IHRM

For model M_0, the L_2 resulted in an OR of 0.79 with a 95% CI of 0.56 to 1.13. These results suggest a potential protective effect (low risk of mortality), and not statistically significant as p-value is 0.20. All coefficients found negative except M_3 for L_2. In the case of model M_1, the L_1 and L_2 of Tanzo antibiotic produced an OR of 0.56, 0.84; 95% CI from 0.31 to 1.03 and 0.57 to 1.24 with p-values of 0.06 and 0.39, respectivrly. Similarly, for M_2, the L_1 and L_2 produced OR values of 0.59 and 0.91, 95% CI from 0.32 to 1.08 and 0.61 to 1.34 with p-values of 0.08 and 0.62, respectively. These results suggest a potential protective effect (low risk of mortality) for M_1 and M_2, and the findings are statistically insignificant. Concerning model M_3, the L_1 of Tanzo antibiotic generated an OR of 0.68 and the 95% CI is from 0.35 to 1.33. These findings suggest a potential protective effect, and it is not statistically significant as p-value is greater the level of significance and 95% CI includes 1. For model M_3, the L_2 of Tanzo antibiotic produced an OR of 1.28 with a 95% CI in the range of 0.82 to 1.99. These results indicate a potential risk (high risk of mortality), and it is statistically insignificant. All coefficients found negative except M_3 for L_2.

In summary, both the unadjusted model (M_0) and all adjusted models (M_1, M_2 and M_3) exhibit statistically insignificant results, except for the low dose (L_1) in the unadjusted model M_0, where a statistically significant low risk of mortality (SLRM) is observed. The odds ratios and p-values consistently indicate an insignificant low risk of mortality (ILRM) at L_1 for all adjusted models (M_1, M_2 and M_3). However, at L_2, the odds ratios and p-values reveal a statistically insignificant low risk of mortality (ILRM) for the unadjusted model (M_0) and adjusted models M_1 and M_2. In the case of adjusted model M_3, the results are reported as IHRM. The term insignificant implies that the observed effects may be due to random variability rather than a true association.

3.4. Comparisons of Tienum Models

Table 4 shows the odds ratio, 95% CI, and slope coefficient for Tienum antibiotic. For each level of Tienum (M_0, M_1, M_2 and M_3), the coefficients represent the change in the log-odds of the outcome variable found negative for L_1 (M_1, M_2 and M_3), and positive for L_2 (M_1, M_2 and M_3). OR values found greater than 1 for L_1 (M_0) and L_2 (M_0) with values of 1.02 and 1.35, respectively, indicating the possible risk, and found statistically insignificant. P-values of all models with 95% CI (includes 1), indicating that the results are statistically insignificant. For each level of Tienum (M_1, M_2 and M_3), the OR for L_1, is found 0.64, 0.66 and 0.51, respectively; while for L_2, it is found 1.22, 1.43 and 1.45, respectively. These results show that there is a possible protection (low risk of mortality) for each level of Tienum (M_1, M_2 and M_3) for L_1, while possible risk (high risk of mortality) for L_2 (M_1, M_2 and M_3).

In summary, both the unadjusted model (M_0) and all adjusted models (M_1, M_2 and M_3) exhibit statistical insignificance for the antibiotic Tienum. The odds ratios and p-values consistently indicate a statistically significant high risk of mortality (IHRM) at L_1 and L_2 for unadjusted model (M_0). For the low dose (L_1), all the adjusted models (M_1, M_2 and M_3) produced ILRM, while for L_2, it is reported

Table 4. Odd ratio, confidence interval (CI) and slope coefficient for Tienum models.

Antibiotics	Model	Levels	Coefficient	P-Value	OR	CI (95%)		Decision
						Lower Bound	Upper Bound	
Tienum	M_0	L_1	0.01	0.96	1.02	0.49	2.10	IHRM
		L_2	0.30	0.13	1.35	0.91	2.00	IHRM
	M_1	L_1	-0.45	0.27	0.64	0.28	1.42	ILRM
		L_2	0.20	0.35	1.22	0.79	1.89	IHRM
	M_2	L_1	-0.40	0.33	0.66	0.29	1.50	ILRM
		L_2	0.36	0.12	1.43	0.90	2.25	IHRM
	M_3	L_1	-0.66	0.17	0.51	0.20	1.32	ILRM
		L_2	0.37	0.16	1.45	0.85	2.46	IHRM

as IHRM. The term insignificant implies that the observed effects may be due to random variability rather than a true association.

4. DISCUSSIONS

The present study provides a comprehensive evaluation of antibiotic usage (Azithromycin, Ceftriaxone, Tanzo, and Tienum) in relation to mortality risk using unadjusted and adjusted logistic regression models. The findings contribute to the ongoing debate regarding the clinical effectiveness and risk implications of empirical antibiotic therapy in COVID-19 management in Pakistan. In line with earlier research, the findings reaffirm the central role of vital signs in determining disease severity and patient characteristics outcomes. Previous studies by Islam *et al*. [17], Gul and Yucesan [18] and Spangler *et al.* [19] have highlighted the importance of indicators such as oxygen saturation, respiratory rate and body temperature in monitoring and predicting COVID-19 progression. By incorporating these variables into the adjusted models, the present analysis provides a more reliable estimation of mortality risk, underscoring the limitations of relying solely on unadjusted associations. The results for Azithromycin reflect the inconsistency widely reported in the literature. While some investigations have suggested that its use may contribute to improved recovery or reduced mortality [45, 46], other studies have found no meaningful clinical benefit [47, 48]. In the present study, associations between Azithromycin and mortality were not statistically significant. Although a slight protective trend appeared in unadjusted models at higher doses, this effect weakened after controlling for confounding variables. This indicates that earlier observed benefits may be attributed more to patient characteristics than to the drug itself, reinforcing concerns about its routine use without clear clinical indication. For Ceftriaxone, the analysis consistently shows no statistically significant relationship with mortality across all model specifications. This observation aligns with broader evidence indicating that the widespread use of antibiotics during the pandemic often as a precaution against secondary infections did not necessarily improve patient survival [30, 31]. These findings emphasize the importance of promoting judicious antibiotic use, particularly in resource constrained settings where antimicrobial resistance is an increasing concern. The analysis of Tanzo presents an interesting pattern, where a significant protective effect is observed only in the unadjusted model at low doses. However, this significance disappears in adjusted models, indicating that the initial association was likely confounded by demographic or clinical factors. This pattern reinforces the methodological importance of multivariate adjustments in epidemiological modeling, as emphasized in logistic regression literature [41-44]. Tienum shows no statistically significant association with mortality risk across models, although a pattern of potential increased risk at higher doses is observed. These findings are important in the context of empirical antibiotic escalation strategies used during severe COVID-19 cases. The absence of significant benefits, combined with potential risks, underscores the need for evidence based prescription practices. Overall, the dominance of statistically insignificant results across antibiotics suggests that antibiotic

therapy alone is not a decisive factor in reducing COVID-19 mortality, particularly when adjusted for vital signs and comorbidities. This is consistent with global findings that COVID-19 is primarily a viral disease and antibiotics should be reserved for cases involving confirmed bacterial co-infections [30]. From a methodological standpoint, the study clearly demonstrates the value of progressive model adjustment. The transition from the unadjusted model to fully adjusted specifications illustrate how the inclusion of demographic characteristics, vital signs and comorbidities conditions refines the interpretation of associations. This approach is consistent with established statistical practices, which advocate for adjusted models to obtain more accurate and unbiased estimates [32-35]. The findings suggest that the prescription of antibiotics during COVID-19 should be undertaken with heightened caution, prioritizing decisions grounded in clinical evidence rather than routine or empirical use, especially during pandemic scenarios. The study further underscores the importance of integrating patients' vital signs and pre-existing health conditions into clinical risk assessments, as these factors have a significant influence on patient outcomes. From a healthcare policy standpoint, it is essential for authorities to strengthen formal antimicrobial stewardship programs, aiming to limit unnecessary antibiotic use and curb the potential development of antimicrobial resistance over time.

5. LIMITATIONS AND FUTURE RECOMMENDATIONS

This study provides insights into the role of antibiotics, vital signs and comorbidities as predictors of COVID-19 mortality using both unadjusted and adjusted logistic regression analyses, but it has some limitations. It relies on secondary data from the early pandemic period (February to August 2020), which may limit generalizability to later waves or different healthcare settings. The observational design prevents definitive conclusions about causality, as residual confounding and treatment selection bias may remain. Categorization of antibiotic doses use only in two steps as low and high groups, which may be extends in more dosing, standardized threshold and time span etc. Some models yielded non-significant results, possibly due to small sample sizes, measurement errors or unobserved patient heterogeneity. Key clinical factors, such as drug timing, infection severity and hospital level variations, were not considered. Future studies using larger, prospective datasets with more detailed clinical information are recommended.

6. CONCLUSIONS

This research studying the COVID-19 patients in association with antibiotics, i.e., Azithromycin, Cefatriaxone, Tanzo, and Tienum, in association with vital measurements and underlying comorbidities effects to layout the comprehensive patient management and better treatment efficacies for the mortality risk (yes/no). The logistic regression model for one unadjusted model (M_0) associated with antibiotics and three adjusted models as: M_1 associated with antibiotics, gender and age, M_2 associated with antibiotics, gender, age and vital measurements, and M_3 associated with antibiotics gender, age, vital measurement and comorbidities are applied. Odds ratios (OR), 95% confidence interval (CI) and p-value is used to examine determine the results using the secondary data of COVID-19 patients spanning from February to August 2020. Antibiotics are classified into two relative categories as: low dose (L_1) and high dose (L_2). The decision criteria for both adjusted and unadjusted models hinge on statistical significance and mortality risk. Insignificant models with low risk of mortality are categorized as ILRM, while significant models with low risk fall under SLRM. Insignificant models with high risk of mortality are termed IHRM and significant models with high risk are classified as SHRM.

For Azithromycin, the findings indicate IHRM for unadjusted model (M_0) and adjusted models (M_1, M_2 and M_3) for L_1. The unadjusted model (M_0) at L_2 has SLRM, but adjusted models M_1 and M_2 show ILRM, and M_3 shows IHRM. For ceftriaxone, at L_1, indicating ILRM for all models. However, at L_2, unadjusted model (M_0) and adjusted models M_1 and M_2 suggest an IHRM, while adjusted model M_3 shows ILRM. In Tanzo, all models show statistically insignificant results, except for the unadjusted model (M_0) at low dose (L_1), which indicate SLRM. However, at L_2, all models exhibit ILRM, except for adjusted model M_3, where results are IHRM. The unadjusted model (M_0) and adjusted models (M_1, M_2 and M_3) show statistically insignificance for the antibiotic Tienum. The unadjusted model (M_0) indicates a statistically insignificant high risk

of mortality (IHRM) at L_1 and L_2. The adjusted models (M_1, M_2 and M_3) consistently reporting statistically insignificant high risk of mortality (IHRM) at L_2, while at L_1, they show statistically insignificant low risk of mortality (ILRM). This study can be extended to include others antibiotics and its various levels of doses. The research is supporting to healthcare professionals in predicting and managing vital signs and comorbidities variations for COVID-19 patient.

7. CONFLICTS OF INTEREST

The authors declare no conflict of interest.

8. ETHICAL STATEMENT

The research utilized secondary data of COVID-19 patients admitted to four hospitals, i.e., Pakistan Air Force Hospital, Pakistan Institute of Medical Sciences (PIMS), Holy Family Hospital and Benazir Bhutto Shaheed Hospital, located in Rawalpindi and Islamabad, covering the period from February to August 2020. The data were used in National College of Business Administration and Economics (NCBA&E), Multan, as part of the M.Phil. Thesis of Imtiaz Ahmed in Statistics, titled as: "Validation of early warning scores for detecting deteriorating patients in Pakistani hospitals during pandemic: A multicenter study" in 2023. As this study involved anonymized secondary data without any direct interaction with patients or human subjects, therefore no ethical approval was required.

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11. AUTHORSHIP CONTRIBUTION STATEMENT

All authors have equal contributions.

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