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RESEARCH ARTICLE

Ali et al: Predicting CAP outcomes using ML

Unveiling etiology and mortality risks in community-acquired pneumonia: A machine learning approach

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ABSTRACT

Community-acquired pneumonia (CAP) is associated with high mortality, and accurate diagnosis and risk prediction are essential for improving patient outcomes. Traditional diagnostic methods have limitations, prompting the use of machine learning (ML) to enhance diagnostic precision and treatment strategies. This study aims to develop ML models to predict CAP etiology and mortality using clinical data to enable early intervention. A retrospective cohort study was conducted on 251 adult CAP patients admitted to two Jordanian hospitals between March 2021 and February 2024. Various clinical data were analyzed using ML techniques, including linear regression, random forest, SHapley Additive exPlanations (SHAP), lasso regression, mutual information analysis, logistic regression, and correlation analysis. Key predictors of CAP survival included zinc, vitamin C, enoxaparin, and insulin bolus. Mutual information analysis identified neutrophils, alanine transaminase, mean corpuscular volume, hemoglobin, and platelets as significant mortality predictors, while lasso regression highlighted meropenem, arterial blood gases, PCO_2, and platelet count. Logistic regression confirmed intensive care unit (ICU) stay, pH, pulmonary severity index, white blood cell (WBC) count, and bicarbonate levels as crucial variables. Interestingly, lymphocyte count emerged as the strongest predictor of bacterial CAP, conflicting with established knowledge that associates neutrophils with bacterial infections. However, findings related to HCO_3, blood urea nitrogen, and WBC levels were consistent with clinical expectations. SHAP analysis highlighted basophils and fever as key predictors. Further investigation is needed to resolve conflicting findings and optimize predictive models. ML offers promising applications for CAP prognosis but requires refinement to address discrepancies and improve reliability in clinical decision-making.

Keywords: Community-acquired pneumonia; CAP; machine learning; ML; mortality prediction; risk assessment; clinical predictors; SHAP analysis; logistic regression.

INTRODUCTION

Community-acquired pneumonia (CAP) poses a significant public health challenge worldwide, contributing to considerable morbidity and mortality across different age groups [1]. Defined as pneumonia contracted outside of a hospital or healthcare setting, CAP remains a leading cause of death, not only in underdeveloped regions but also in the developed world [2]. Effective management of CAP, crucial for improving patient outcomes, depends heavily on the accurate and timely identification of its etiology and assessing potential mortality risks.

Machine learning (ML), as an integral part of artificial intelligence (AI), has shown promising results in enhancing diagnostic precision, optimizing therapeutic strategies, and predicting clinical outcomes in various fields of medicine [3]. The potential of ML to transform the clinical approaches to CAP has not been completely realized, particularly in terms of integrating diverse datasets to predict disease etiology and outcomes [4].

By focusing on employing ML techniques to predict the causes and mortality associated with CAP, this study aims to address a significant gap in the current research landscape. The integration of ML tools in CAP management holds the potential to significantly enhance diagnostic accuracy, put treatment plans, and ultimately improve the prognostic outcomes for patients [5] . This research tries to explore these possibilities and aims to reinforce the evidence base by reliably correlating clinical data with patient prognosis using sophisticated algorithmic analysis.

The success of implementing this research could revolutionize the approach to handling CAP, leading to more personalized healthcare and better resource distribution in treating this prevalent disease.

CAP remains a significant healthcare challenge, ranking globally as a major cause of morbidity and mortality [1]. Each year, CAP leads to numerous hospital admissions, placing a heavy burden on medical staff, especially in high-risk groups such as the elderly and those with immune-compromising conditions [6]. The variability in clinical presentations—an attribute of CAP—ranges from mild respiratory symptoms to severe cases requiring intensive care. This variability is primarily due to the vast kinds of pathogens that can cause CAP, including a spectrum of bacteria, viruses, and atypical organisms [7].

The current tools for diagnosing CAP, which typically include chest X-rays, microbial cultures, and molecular tests, often fail to immediately and accurately identify the etiological agent. This limitation impacts the selecting of an appropriate treatment regimen, significantly impacting patient outcomes [8]. Additionally, resistance to antimicrobial agents among common respiratory pathogens further complicates the management of CAP, underscoring the crucial role of effective and accurately targeted initial empirical therapy [9].

Predicting outcomes for patients with CAP also has challenges arises from the heterogeneity in patient responses to CAP, influenced by factors such as underlying health conditions and age. Current predictive models lack the precision necessary to guide critical decisions regarding treatment intensity or hospitalization needs [10, 11].

Given these challenges, there is a pressing need for enhanced diagnostic and predictive capabilities in managing CAP. ML presents a promising solution because of its ability to process complex and huge data, potentially uncovering patterns that improve diagnostic accuracy, treatment personalization, and outcome prediction [12]. These advancements could significantly improve clinical decision-making processes, ultimately reducing the incidence of treatment failures and minimizing CAP-associated health burdens.

The study of ML applications in predicting etiology and mortality in CAP is important for several reasons. First, enhancing diagnostic accuracy has direct implications for treatment efficacy. Accurate early diagnosis enables timely and targeted treatment, which is critical in reducing the progression severity and improving patient recovery rates.

Second, by improving mortality prediction, healthcare providers can make more informed decisions about the level of care required. Patients with a poor prognosis could be prioritized for intensive interventions, potentially improving survival rates. Conversely, with reliable predictors indicating lower risk, patients could avoid unnecessary hospital admissions, reducing healthcare costs and minimizing the risk of hospital-acquired infections [13].

Furthermore, integrating ML into medical practices addresses the challenge of clinical variability in CAP treatment, aligning with precision medicine objectives. This not only aids in achieving better health outcomes but also in personalizing patient care, leading to more satisfactory patient experiences and adherence to treatment plans.

Lastly, the healthcare industry stands to gain from improved resource distribution, ensuring that the right staffing, equipment, and medications are available when needed, thereby enhancing the overall efficiency of healthcare delivery systems [14].

This research tries to use ML comprehensively within the healthcare sector, demonstrating how technology can intersect with clinical expertise to make significant differences in patient outcomes and healthcare systems operations.

Despite the extensive use of ML in medical diagnostics, its application in predicting the etiology and mortality of CAP remains underexplored. Existing studies predominantly focus on diagnosis and treatment outcomes but rarely combine ML techniques to predict the causal pathogens and associated mortality rates based on a huge data input. This gap is particularly significant given that timely and accurate determination of CAP etiology and prognosis could improve treatment strategies and outcomes.

The intersection of CAP management and ML offers significant potential for enhancing healthcare outcomes, yet there is a marked lack of research focusing on integrating these disciplines. The existing literature comprehensively addresses CAP's diagnostic procedures and treatment methods [2], and the applicative spans of ML in medical diagnostics separately [12]. Nevertheless, few studies have the specific application of ML techniques to predict the etiology and mortality associated with CAP.

The current landscape in clinical prediction models for diseases like CAP reveals a critical gap in using predictive modeling to anticipate disease etiology and outcomes [15]. While studies have shown the feasibility of using ML to predict outcomes in pneumonia cases [16], there is a notable lack of focus on directly correlating these outcomes with causative pathogens, which is essential for putting therapeutic approaches [15]. Research in cardiology and oncology has made significant progress in utilizing ML technologies [17]. However, similar advancements in infectious diseases like CAP are not as advanced [18]. Studies have demonstrated the potential of ML approaches in predicting mortality and disease progression in coronavirus disease of 2019 (COVID-19) pneumonia cases [19], and in developing models to predict adverse outcomes in CAP [20].

Efforts have been made to predict the outcome of SARS-CoV-2 pneumonia based on laboratory findings [20], and to develop models for predicting the severity of COVID-19 and mortality in pneumonia patients [21].

In the context of pneumonia, where up to 50% of cases lack identified causative pathogens [21], ML can offer a promising way for predicting outcomes and designing treatments. By integrating comprehensive patient histories, clinical signs, and diagnostic data with predictive modeling techniques, it is possible to enhance the understanding and management of diseases like CAP. Further research and development in this area could lead to more personalized and effective therapeutic interventions for patients with pneumonia.

The primary aim of this study is to develop, validate, and implement ML models specifically to predict the etiology and mortality of CAP. This involves designing models that utilize clinical data with diverse symptomology and outcomes associated with CAP. Ultimately, the purpose is to provide healthcare professionals with advanced, data-driven tools that enhance decision-making processes, potentially leading to more accurate and timely interventions, personalized treatment regimens, and overall improved patient prognosis.

MATERIALS AND METHODS

Study design and participants

This is a retrospective cohort multicentric study, with 251 adult patients included, involving Prince Hamza Hospital and the Islamic hospital, to ensure a diverse patient demographics and clinical variables and a comprehensive dataset. The participants were adults diagnosed with CAP admitted to the participating hospitals from March 10, 2021, to February 15, 2024. This timeframe allows for the inclusion of a substantial number of cases to enhance the statistical power and validity of the study.

Inclusion criteria included patients with a precise diagnosis of CAP confirmed by chest radiography or CT scan, if they were conducted. Alongside symptoms consistent with pneumonia, such as cough, fever, sputum production, and dyspnea. And microbiological laboratory results if they were available. Patients in ICU and ward were included to encompass various disease severities.

Patients with hospital-acquired pneumonia (HAP), patients transferred from outside hospitals after 48 hours of admission, and patients with incomplete medical records were excluded. Human Immunodeficiency Virus Acquired/ Immunodeficiency syndrome (HIV/AIDS) and long-term immunosuppressive therapy were likewise excluded in order to avoid possible confounding effects with different immune responses.

In compliance with laws and regulations governing the conduct of medical research, the study maintained the privacy and confidentiality of participants' data. The Institutional Review Board (IRB) of each clinical site approved the study, whereby all data were de-identified and kept in secure databases to protect patient confidentiality. This study complies with the Declaration of Helsinki. The approval of the study was gained from the Applied Science Private University, Jordan, the Islamic Hospital ethical committee in Amman, Jordan, and the Prince Hamza Hospital, Amman, Jordan (2021-PHA-35, IRB: 101/2021/1053, and 6-11-2021-129 respectively).

Data collection

The data for the participants was gathered from the medical records and electronic databases, the dataset, originally recorded in Excel, contained information about CAP patients, encompassing vital signs, physical and laboratory findings, length of stay (LOS), and in-hospital mortality sourced from electronic medical records. In addition to partnerships with hospitals and healthcare providers that treat CAP patients. The key elements of the data collection process include:

1. **Demographic Information**: Age, gender, and other relevant demographic factors that can influence disease outcomes.
2. **Clinical Data**: Detailed records of symptoms, duration of illness, previous health conditions, and clinical findings during physical examinations.
3. **Radiological Data**: The radiological data (Chest X-rays, and CT scans) were interpreted by two clinicians, who provided standardized findings such as the presence of pulmonary infiltrates, consolidation, or effusion
4. **Microbiological Data**: Results from respiratory sample cultures, blood tests, and other relevant microbiological investigations like the molecular methods (the real-time polymerase chain reaction (PCR)) used to determine the etiology of pneumonia.
5. **Laboratory Results**: Complete blood counts, C-reactive protein levels, arterial blood gases, and other relevant laboratory tests performed during hospitalization.
6. **Treatment Details**: Information on the medications prescribed, including type, dosage, and duration.
7. **Outcome Data**: Details of the patient's recovery, mainly in-hospital mortality.

Data preparation

Before starting ML modeling, we cleaned the medical files records that we collected. At the beginning we had 587 patient files with pneumonia diagnosis. After we removed the files with HAP, ventilator-associated pneumonia (VAP) and duplicated CAP files we reduced the number to 412 cases.

The files at the beginning had multiple lab results and vital signs records taken over the length of stay in the hospital of the patients. In our study the aim is to make a rapid decision about the clinical situation of the patients within few hours of the admission, so we had got only the first records for the lab results and vital signs reading (the number of features reduced from 3562 to 665 features).

We conducted data preprocessing steps over the left CAP files after cleaning, involved handling missing values- some files had high percentage of missing data, so we dropped them and finally reached 251 patients files. Other files with low percentage of missing, we normalized continuous variables and encoding categorical variables. Libraries such as Pandas and NumPy were employed to make data manipulation more efficient, ensuring consistency and accuracy. The normal ranges were used to handle missing values.

To optimize the dataset, columns with a single value or where 95% or more of the entries were identical were removed. These columns provided little to no meaningful information when analyzing correlations with the target variable. Their inclusion would have unnecessarily increased the dimensionality of the data, introducing low variance, adding noise, and potentially leading to biased results or overfitting. By eliminating these columns, the dataset was simplified, reducing noise and improving its overall quality for subsequent analysis. The number of features now is 132 features. This step is called features selection.

Machine learning techniques and feature evaluation

Several advanced ML techniques were applied to analyze the collected data and develop predictive models for CAP's etiology and mortality outcomes. The selection of appropriate ML algorithms is crucial for handling the complexity and variety of the data involved. The techniques have been chosen based on their proven performance in similar healthcare datasets [22].

This section details the methodology used to evaluate the impact of the top features on the target variable using seven distinct approaches: linear regression, random forest, mutual

information analysis, Lasso regression, Logestic regression, SHapley Additive exPlanations SHAP values, and correlation analysis. Each method provides unique insights into the relationship between the features and the target variable.

The dataset was randomly divided into training and testing subsets using an 80:20 split ratio. Furthermore, model performance and generalizability were assessed using 5-fold cross-validation within the training data. The average performance metrics across folds were reported to ensure robustness.

Linear regression coefficients

Linear regression was employed to understand the linear relationships between each feature and the target variable. The coefficients derived from the model indicate the direction and magnitude of the feature's impact [23, 24]:

This analysis provides a straightforward interpretation of feature contributions in a linear framework.

Random forest

A Random Forest model was used to assess the relative importance of features in predicting the target variable. Feature importance scores were computed, which indicate how critical each feature is for model predictions [25-27], where higher importance are features with higher scores and play a more significant role in predictions. Whereas, lower importance are features with lower scores and have a minor impact on predictions.

Unlike linear regression, Random Forest captures complex, non-linear relationships, providing a complementary perspective on feature importance.

Mutual information analysis

Mutual information analysis is a statistical technique used to measure the mutual dependence between two variables. It quantifies how much information knowing one variable provides about the other [28]. Mutual information is a concept from information theory and is widely used in fields such as machine learning, data analysis, and bioinformatics.

In the medical field, mutual information is a valuable tool for analyzing the relationship between medical predictors (such as biomarkers, test results, demographic data) and health outcomes (such as disease presence, survival rates, or treatment effectiveness). By quantifying

the dependency between predictors and outcomes, mutual information helps in feature selection, diagnostic modeling, and risk stratification [29]

Lasso regression (Least absolute shrinkage and selection operator)

Lasso is a type of linear regression that performs both feature selection and regularization to enhance prediction accuracy and interpretability. It is a statistical technique that can be used to study the effects of clinical variables in outcome prediction [30].

Logistic regression

Logistic regression is a widely used statistical and machine learning technique in clinical research for predicting binary outcomes, such as disease presence (yes/no), treatment success (effective/ineffective), or survival (alive/deceased). It estimates the probability that a given input belongs to a particular class based on clinical predictors (e.g., age, blood pressure, cholesterol levels).

SHAP (shapley additive explanations) values

SHAP values were used to explain the contribution of individual features to the model's predictions. SHAP analysis was employed not as a standalone predictive model but as a post hoc interpretability tool to explain the output of the trained random forest model. The SHAP values allowed to quantify the contribution of individual features to the model's predictions, thereby enhancing the interpretability and transparency of the decision-making process. This method provides detailed insights into both the magnitude and direction of feature impact: Blue points represent lower feature values contributing less to the target. Whereas, red points represent higher feature values contributing more to the target.

A SHAP summary plot was generated to visualize the overall influence of each feature on the target variable. This method is particularly useful for verifying the impact direction indicated by linear models and for uncovering interactions and non-linear relationships [31].

Correlation with the target

Correlation analysis was conducted to measure the linear relationship between each feature and the target variable [24]**.** Positive correlation indicates that as the feature increases, the target variable also increases. Whereas, negative correlation indicates that as the feature increases, the target variable decreases.

While correlation provides a simple measure of association, it does not account for non-linear relationships or interactions between features [24].

Each model was trained and validated on separate data splits to assess their performance accurately. Cross-validation techniques ensure that the models generalize well on unseen data. The performance of each method was measured using appropriate metrics such as accuracy, sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve.

To have an accurate and unbiased model, we made sure that our dataset is balanced. A balanced dataset with an equal number of observations for both recovered and dead patients was created to train and test our model. The data samples (patients) in the training dataset have been selected randomly and they were completely separated from the testing data (Figure 1).

Prior to balancing, the dataset exhibited a class imbalance with a higher proportion of survivors compared to non-survivors. To solve this issue, a random oversampling of the minority group (survivors) was performed to achieve a 1:1 class distribution in the training set. This resampling was conducted exclusively on the training data to avoid information leakage and ensure a fair evaluation of the model's performance.

Tools and software

Analysis was conducted using Python programming language in a Jupyter Notebook environment. Key libraries utilized include:

Pandas: For data manipulation and cleaning.

NumPy: For numerical operations.

Matplotlib/Seaborn: For data visualization.

These tools ensured the efficient handling of large datasets and the generation of high-quality visualizations to identify patterns and outliers.

Data transformation

After removing unnecessary columns, the dataset was further refined by encoding categorical variables. Columns containing string values were identified, and a LabelEncoder was applied to convert them into numeric values. Given the large number of columns—reduced from 665 to 132—LabelEncoder was chosen for its simplicity and efficiency, particularly for columns

with only two categories. This approach avoided further increasing dataset complexity, which could have introduced challenges in analysis and modeling.

Exploratory data analysis (EDA)

EDA was performed to understand the distribution of variables, detect anomalies, and assess correlations between features. Statistical summaries were computed to identify key trends, and graphical methods such as bar charts, heatmaps and sHAP Summary Plots were generated.

Feature selection

There were 132 features taken - in a step called features selection -from the original dataset. All relevant features were extracted. The primary aim of features selection can be regarded as searching for the most significantly informative features and removing redundant ones to decrease the dimension of the model and its complexity.

Selected features included demographic data, clinical characteristics and laboratory data that were taken at the admission moment. The features included in the predictor variables were age, gender, vital signs (ex: blood pressure, heart rate, respiratory rate, temperature), number of medical comorbidities (such as hypertension, diabetes mellitus), laboratory data (such as Complete Blood Count, Comprehensive Metabolic Panel and arterial blood gas (ABG) tests) and clinical scores (PSI, CURB-65). Table (1)

Statistical analysis

Statistical analyses were performed, followed by the development of predictive models to forecast key variables

The statistical analysis starts with examining the data collected through descriptive statistics to identify the central tendencies, normality distribution (using Shapiro-wilk test, Q-Q, and distribution plots), and variability. Continuous variables were summarized using means and standard deviations (SD) or medians and interquartile ranges (IQR), depending on normality assessment, in addition to frequencies and percentages for categorical variables. The statistical analysis was conducted using JASP 18.3.0 (Jeffreys's Amazing Statistics Program) and IBM SPSS statistics 25.

RESULTS

Demographic and clinical characteristics

A sample of 251 participants was included in this study. The median for their age was 60 years (IQR=25). Most were male 146 (58.2%) and 105 (41.8%) were female. The majority of patients were admitted to ICU 221 (88.0%) versus Ward 30 (12.0%). with median of LOS was 10 days (IQR 13), and for pateints were in ICU the ICU length of stay (ICU_LOS) the median was 4.77 days (IQR=1.77).

Regarding COVID-19 status, 18 (7.2%) had a current SARS-CoV2 infection, and 9 (3.6%) had a previous history of COVID-19. Table (2).

Participants had a high prevalence of comorbidities, with Diabetes Mellitus being the most prevalent (30.3%), followed by septic shock (25.5%), hypertension (13.1%), and cardiac diseases (8.8%). Other reported conditions were Alzheimer's disease (6.8%), chronic kidney disease (4.8%), anemia (2.8%), asthma (2.4%), and COPD (2.0%). Table (2).

Treatment background characteristics

The chronic treatments varied, vitamin C and zinc supplements showed the highest percentage of drug intake due to COVID-19 recommendations at that time for their prophylactic and supportive effects (29.1 % , 27.5 %) respectively . Insulin therapy also was used, with 24.7% on insulin bolus and 15.9% on basal insulin. This alongside DM as the most chronic conditions found. Omeprazole (19.1%), Bisoprolol (17.9%), and B complex (16.3%) were among the other most commonly used medications. Table (3).

The most common short-term treatments were antibiotics (80.1%), anticoagulants (78.1%), and Enoxaparin (77.7%). Antiviral agents were utilized by few patients (8.0%), and only 4.8% were given supportive drugs, including albumin, favipiravir, and norepinephrine injections (Table 6).

Characteristics specific to pneumonia

Among the included participants, the majority were classified as Class 2 (40.6%) and Class 3 (23.1%) according to the Pneumonia Severity Index (PSI), indicating moderate severity. Based on CURB-65 scores, 41.8% of patients had a score of 1, and 24.7% had a CURB-65 score of 2, indicating differences in pneumonia risk levels.

The majority of patients got bacterial CAP with 215 (85.7%), most of patients were survived 169 patients (67.3%) Table (4).

The most common initial clinical symptoms were dyspnea (38.6%) and fever (16.3%). Other symptoms were productive cough (6.8%), dry cough (6.4%), pleuritic chest pain (6.4%), headache (4.4%), vomiting (4.4%), and abdominal pain (4.0%). Notably, 4.0% of patients required intubation or mechanical ventilation. Table (4).

Machine learning analysis results to predict mortality

Global feature correlation structure

A comprehensive correlation heatmap (Supplementary Data) visualized the interdependence across all features. This analysis revealed a dense correlation structure, indicative of overlapping information among variables. Redundancy necessitates preprocessing steps, including features selection to ensure model robustness and reduce overfitting.

This step is performed after cleaning the columns; data cleaned excludes columns with all null values, leading to a more accurate and reliable correlation matrix for data cleaned.

The diagonal of the heatmap typically contains values of 1, representing the perfect correlation of each feature with itself. The color intensity in each cell indicates the strength and direction of correlation between the corresponding features on the axes. The heatmap uses a color gradient from blue to red, Positive correlations (closer to 1) are often shown in warm colors (e.g., red), while negative correlations (closer to -1) appear in cool colors (e.g., blue).

Certain feature groups exhibit noticeable correlations, suggesting potential multicollinearity or shared variance. For instance, tightly clustered red squares suggest high correlations between related clinical markers or treatment variables, while patches of blue indicate negative associations between certain variables. This matrix highlights the importance of addressing multicollinearity in model development and suggests that specific feature groups may have overlapped predictive power. Identifying and managing these relationships can enhance model performance and interpretability.

Feature correlation analysis

A correlation matrix is often calculated before building predictive models in Python (or any other programming language) to gain insights into the relationships between features. Highly correlated features could cause multicollinearity, requiring dimensionality reduction

techniques like principal component analysis (PCA) or the elimination of redundant features to enhance model performance and interpretability.

Sometimes, as in our study, the correlation matrix helps in identifying the relationships between different features in the dataset. It shows how strongly each feature is related to the others, which is crucial for understanding the underlying structure of the data.

The correlation matrix was used to find pairs of features with a correlation score of 0.8 or higher (highly correlated features). These pairs were then saved into a CSV file for easier inspection.

To evaluate the internal structure of the dataset and identify potential predictors of mortality, Pearson correlation heatmaps were generated. In our results high coefficient means high survival rate with the variables, as in encoding process for categorical variables we gave number one for survival outcome and number two for non-survival outcome. The correlation was between the variables and number one outcome, high correlation value means high correlation with the survival rate. This correlation with survival rate only for this step. Figure 2 shows the intercorrelation matrix among all features, revealing strong positive correlations between inflammatory markers (eg, C-reactive protein [CRP], ferritin), and between white blood cell count and neutrophil count ($r > 0.7$). These findings suggest potential collinearity among markers of systemic inflammation, which may influence model stability and necessitate variable selection or regularization strategies.

Top correlated features with the mortality target

Figure 3 shows the correlation between individual features and the target outcome of mortality. Age ($r \approx 0.45$), neutrophil count ($r \approx 0.41$), CRP ($r \approx 0.39$), and ferritin ($r \approx 0.36$) were among the strongest positive correlates with mortality, indicating their potential as high-risk predictors. Conversely, lymphocyte count ($r \approx -0.42$), oxygen saturation ($r \approx -0.38$), and hemoglobin level ($r \approx -0.33$) showed the strongest negative correlations, suggesting a protective role. These patterns underscore the prognostic relevance of age and markers of inflammation and hypoxia in predicting adverse outcomes. The identification of these features supports their prioritization in model development and interpretability analysis.

A focused heatmap (Figure 3) showed the variables most correlated with the mortality Notably, vitamin C, zinc, enoxaparin (CLEXAN) and insulin bolus exhibited the highest correlations.

Zinc and Vitamin C exhibited the highest positive correlation (r = 0.90), suggesting a strong relationship between these two variables with survival rate. Whereas, Insulin Bolus and Enoxaparin demonstrated a moderate correlation (r = 0.59), highlighting a potential interaction. LOS Showed minimal correlation with most variables, with the highest being a weak negative correlation with Vitamin C (r = -0.0066). Diastolic blood pressure shows low correlations with other variables, with the maximum being a weak positive correlation with Vitamin C (r = 0.15).

Mutual information analysis

The mutual information scores (Figure 4) quantify the dependency between each feature and the target variable (mortality), providing a ranking of the most informative predictors. Key findings include creatinine concentration, WBC including eosinophils, and neutrophils count. Number of previous hospitalizations is also a top contributor. RDW and ALT are other significant features reflecting their clinical relevance. This analysis underscores the critical role of inflammatory markers (eosinophils, neutrophils, and basophils count) in mortality outcome prediction, highlighting their importance in clinical decision-making.

Feature coefficients from lasso regression

The Lasso regression analysis (Figure 5) refined the list of predictors by identifying the magnitude and direction of their contributions to the mortality target. Culture demonstrated the highest positive coefficient (0.15). not clinically important as culture variable just gives indication if the patient did culture or not. Meropenem Showed a significant positive coefficient, suggesting its importance in predicting mortality.

ABGs BE, PCO_2, and platelet count contributed positively to the prediction model.

This analysis underscores the critical roles for meropenem, ABGs, pH and PCO2 in mortality outcome prediction.

Feature importance from logistic regression

The logistic regression-based feature importance analysis (Figure 6) provided an additional perspective on variable significance. For instance, pH identified as the most impactful predictor with the strongest negative impact (coefficient approximately -1.0). ICU_LOS and LOS: Showed a substantial positive impact with a coefficient around 0.6, and 0.4 respectively, suggesting that longer stays are associated with higher mortality. This analysis underscores the critical roles for pH, LOS, ICU_LOS, PCO2, diastolic blood pressure, WBC, HCO_3 and ABGs in predicting mortality rate.

SHAP analysis of medication and laboratory influence on model predictions

The SHAP summary plot shown in Figure **7** illustrates the impact of individual features—primarily medications and laboratory findings—on the predictive model for the survival outcome outcome. Features are ranked by their average absolute SHAP values, representing their overall contribution to the model's output.

The most influential feature was antibiotic usage, which had a strong negative SHAP value (impact < –0.6), indicating that antibiotic administration strongly decreased the predicted risk of the mortality outcome.

Basophil count and initial fever presentation also showed negative SHAP values, suggesting a modest inverse association with the predicted risk. Other features such as enoxaparin, ciprofloxacin susceptibility, and piperacillin/tazobactam susceptibility were associated with lower predicted risk, possibly reflecting effective treatment or underlying microbial sensitivity.

In contrast, meropenem susceptibility, imipenem susceptibility, and amikan susceptibility had the largest positive impacts, potentially reflecting resistance to critical antibiotics or associations with more severe infections requiring these drugs. Among medications, tocilizumab, prednisolone, and anticoagulant use were positively associated with the outcome, suggesting these therapies may be markers of greater disease severity or higher baseline risk.

Machine learning results for predicting etiology of CAP

Correlation analysis for predicting bacterial infection

A heatmap was generated to assess the correlation between clinical variables and bacterial infection (increasing coefficeints reading means higher opportunity for getting bacterial infection as the correlation was between the variables and positive bacterial infection result - Encoding bacterial infection with number one and no bacterial infection with number two) (Figure 8).

Enoxaparin, and other anti-coagulant treatments exhibited the strongest positive correlations with bacterial infection, with correlation coefficients of 0.99. Vitamin C supplementation showed also high correlation with Zinc (r = 0.90).

Feature importance analysis using logistic regression analysis for predicting bacterial infection

Logistic regression analysis was conducted to evaluate feature importance (Figure 9). Lymphocytes were the most influential predictor, with a coefficient value of approximately 0.11,

HCO_3, WBCs, and MCV, each contributing significantly to the prediction model.

Features such as BUN, neutrophils count and ABGs had significant negative relationship.

SHAP analysis

SHAP values were employed to interpret model predictions (Figure 10). Antibiotics, Basophils, and initial finding fever emerged as key variables influencing the model's output.

The correlation coefficients between selected features and the target variable

Figure 11 presents the correlation coefficients between selected features and the target variable. Antibiotics demonstrated the strongest positive correlation with the bacterial infection target. Enoxaparin and Anticoagulant suggesting that these treatments are significantly associated with the bacterial infection. The initial fever finding and Basophils also showed moderate positive correlations.

Conversely, features such as mAb of tocilizumab and susceptibility of Amikasin demonstrated weak negative correlations with the target.

Other antibiotic susceptibility variables, including susceptibility of Cefepime and susceptibility of Ciprofloxacin, had minimal or near-zero correlations, indicating limited direct association with the outcome.

The predictive performance of the logistic regression models for both outcomes is summarized in the Table 5. The mortality outcome model achieved robust performance, with AUROCs of 0.90 (95% CI: 0.85–0.95) in the training set and 0.88 (95% CI: 0.83–0.93) in the test set, indicating strong discriminative ability. The bacterial infection outcome model demonstrated even higher predictive power, with AUROCs exceeding 0.96 in both training and test sets, accompanied by perfect sensitivity (1.00) in both cases.

Table 6 reports a comparative summary of the top predictors identified by four variable-importance methods—mutual information, LASSO coefficients, logistic regression odds ratios, and mean SHAP values—highlighting both overlaps and divergences in feature ranking. Variables such as zinc, vitamin C, enoxaparin, and neutrophils consistently emerge as key predictors across multiple methods, reinforcing their clinical relevance in predicting mortality among patients with CAP. Meanwhile, other variables such as meropenem, pH, and platelet count show importance only in selected methods, underscoring the need for careful interpretation of variable-importance results depending on the statistical approach.

Table 7 shows forest plot data for key predictors of both investigated outcomes in this study. Variables such as ICU stay, pH, WBC, and platelets exhibit significant associations with mortality risk, with odds ratios ranging from 0.6 (pH) to 2.5 (ICU stay). Regarding bacterial infection outcome, predictors such as lymphocytes, HCO_3, WBC, and neutrophils, with odds ratios between 0.8 and 2.5. These forest plots give us important information about how important and accurate these predictors are compared to each other. This analysis supports the possible utility of these variables in clinical decision-making and model interpretability.

DISCUSSION

Authors should discuss the results and how they can be interpreted in the perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Limitations and future research directions may also be highlighted.

The primary aim of this study was to develop, validate, and implement ML models specifically tailored to predict the etiology and mortality of CAP. Among the 251 included patients, 215 (85.7%) had bacterial CAP and most of them survived (67.3%). Extensive treatment regimens

were noted, including high utilization of antibiotics and anticoagulants. Pneumonia was of variable severity.

Predicting mortality of CAP

In the Feature Correlation Analysis Regarding Mortality step, the results showed that zinc, vitamin C, enoxaparin and insulin bolus had high correlation with CAP in hospital survival rate.

Regarding zinc supplement; The clinical studies show same results as increasing zinc intake will decrease the mortality or increase the survival rate. One study result was : Zinc deficiency, common in developing countries, is linked to increased CAP morbidity and mortality. Zinc levels were lower in older patients, those with high CURB-65 scores, and smokers [32].

The feature correlation also showed high correlation for vitamin C supplement and in hospital survival rate, the clinical findings also agree with . In one systematic review showed that vitamin C supplementation had potential benefits on CAP management [33].

These nutrients are often studied for their potential benefits in supporting the immune system and improving outcomes in respiratory infections [34]. in our study they were taken as a chronic treatment emphasizing their role as immunity supporters.

The Feature Correlation Analysis also showed a high correlation between enoxaparin and in - hospital survival rate , this result is alongside the clinical findings. One study conducted, they found that Enoxaparin is associated with lower rates of mortality. Enoxaparin is often used as a preventative measure in hospitalized CAP patients to reduce the risk of venous thromboembolism, a serious complication that can worsen outcomes the pateints [35].

About insulin bolus treatment ; Severe infections like CAP trigger a stress response, leading to increased levels of cortisol, catecholamines, and inflammatory cytokines [36]. These factors contribute to insulin resistance and hyperglycemia, even in non-diabetic patients. In diabetic patients, CAP can cause poor glycemic control, increasing the risk of complications. Persistent hyperglycemia weakens the immune response, impairing neutrophil function and increasing infection severity [37]. Also high blood sugar levels are linked to higher mortality rates, prolonged hospital stays, and increased risk of complications such as sepsis and respiratory failure [38].

Insulin therapy in adult patients hospitalized for a critical illness, other than hyperglycemic crises, may decrease mortality in certain groups of patients [39]. And this result also right for insulin bolus treatment that decrease the mortality rate and LOS. [40].

The next step in ML modeling regarding CAP mortality predictors was Mutual information analysis. It's scores quantified the dependency between each feature and the target (mortality), providing a ranking of the most informative predictors. Neutrophils count, ALT, MCV, HGB and platelet count emerged as the top contributors. These findings underscore the importance of these variables , as these markers are often indicative of systemic inflammation.

High Neutrophil/Lymphocyte Ratio (NLR) and Neutrophil Count Percentage (NCP) are reliable predictors of mortality [41]. Overactive neutrophils release pro-inflammatory cytokines, which can cause tissue damage and thrombosis [42].

About ALT result, one study showed that; circulating liver function biomarkers showed diverse nonlinear correlations with mortality [43]. CAP triggers a systemic inflammatory response, which can elevate ALT levels due to liver stress.

Regarding MCV one study showed that large MCV was associated with all-cause mortality, cardiovascular disease mortality, and infection-associated mortality [44]. Elevated MCV may contribute to venous thromboembolic disease through increased hematocrit, which promotes platelet margination, or by increasing blood viscosity, reducing flow in large vessels and predisposing to clot formation. This imbalance in blood rheology can lead to thrombosis [45].

Patients with abnormal platelet count thrombocytopenia (19%) or thrombocytosis (28%) had a higher length of hospital stay, more in need for ICU admission, more use of mechanical ventilation invasive or noninvasive and more 30 days mortality rate [46].This agree with our model results.

An increase in hemoglobin level predicts an increased in mortality, ICU hospitalization, and extrapulmonary complications in COVID-19 patients [47]. Elevated hemoglobin increases blood viscosity, slowing circulation and raising the risk of thrombosis, stroke, and cardiovascular disease [48]. These clinical findings align the result regarding the mutual information analysis.

Feature selection through Lasso regression further refined list of predictors by identifying the magnitude and direction of their contributions to the mortality target. Features such as

Meropenem, ABGs, PCO_2, and platelet count demonstrated strong positive coefficients, suggesting their importance in predicting the mortality target. Conversely, features such as location and cardiovascular disease were negatively associated with the mortality outcome.

Regarding meropenem empirical treatment (in our data records meropenem used as empirical treatment). Empiric meropenem-based regimen appeared to be associated with lower mortality.[49]. But in recent study they found that meropenem increases mortality rate; 50 patients (14.12%) experienced treatment failure, and ICU mortality was 48.02% (120 patients). Predictors of meropenem failure included a higher APACHE (acute physiology and chronic health evaluation) score and shorter treatment duration. Predictors of mortality were high APACHE and SOFA scores, initiation of antibiotics more than 72 hours after sepsis onset, shorter treatment duration, and renal dose adjustments of meropenem [50]. The last study align with our model result.

Regarding ABGs , one study related to COVID-19 mortality, ABGs was found as a predictor of mortality in COVID pneumonia patients initiated on noninvasive mechanical ventilation [51].

Regarding the positive relationship with PCO2, clinical findings have same result with higher PCO2 being associated with worse survival [52]. Platelet count results also agree with the clinical findings. Findings among patients with mild thrombocytosis suggested that high-normal platelet count is associated with the occurrence of thrombotic events [53].

We had negative or inverse relationships (CVDs, COVID 19 and location) that may need more focusing on features or model selection as these findings should have positive impacts. The patient with severe CAP needs monitoring of an ICU where, if necessary, they can receive specialized support connected to a mechanical ventilator and/or hemodynamic support [54]. Also, patients can get pneumonia when infected with $SARS\text{-}COV_2$. The virus that causes COVID-19 can infect the lungs, causing pneumonia [55]. Finally CAP is a significant risk factor for all major cardiovascular disease events, including acute coronary syndrome, stroke, and mortality [56]. These clinical findings (CVDs, COVID-19 and location) have opposite relationship regarding our modeling results, so farther processing and handling must be needed regarding lasso regression model. Regarding pH, one study showed metabolic acidosis (low pH) is associated with higher mortality in ICU [57]. This inverse relationship agreed with our model results.

The last step used was Logistic regression. It provided an additional perspective on variable significance. Variables such as pH, ICU_LOS, LOS, age, PCO_2, O_2 saturation, and diastolic blood pressure were identified as the most impactful predictors of the mortality target outcome. Regarding pH, inverse relationship emphasized by clinical finding [57].

Regarding length of stay as mentioned earlier ; the patient with severe CAP needs monitoring of an ICU where, if necessary, they can receive specialized support connected to a mechanical ventilator and / or hemodynamic support [54]. PSI, WBC, PCO_2, HCO_3 , ABGs and diastolic blood pressure have positive relationship alongside the clinical finding [52, 58-60]. Among outpatients with pneumonia, oxygen saturations <90% were associated with increased morbidity and mortality [61]. This agree with our model result.

Our aims of this study to make rapid evaluation about patient condition at the admission time; by looking for the results obtained (zinc, vitamin C supplements, Enoxapirin, Neutrophils count, platelet count, ALT, MCV, ABGs, PCO_2, HGB, pH, WBC, HCO_3 and O_2 saturation) are main predictors for mortality and these results can be obtained rapidly at the admission time [62]. There are some predictors have opposite clinical findings results such as CVDs and COVID-19 these findings indicate that we must do further investigation and choosing for models and features selection.

Predicting the etiology of CAP

A heatmap was generated to assess the correlation between clinical variables and the target outcome (infection with bacteria). Enoxaparin, and other anti-coagulant treatments exhibited the strongest positive correlations with bacterial infection, this correlation has negative clinical findings result ; Severe bacterial pneumonia and sepsis trigger coagulation activation both locally in the lungs and systemically, leading to tissue injury and reduced survival. This has prompted extensive investigation into therapies that modulate inflammation caused by coagulation activation. Various anticoagulant strategies have been explored for bacterial pneumonia, sepsis, and acute respiratory distress [63].

Notably, Vitamin C supplementation showed also high correlation with Zinc with bacterial CAP. These results have opposite clinical results. In recent study published showed that higher doses of vitamin C and zinc resulted in greater inhibition of *Klebsiella pneumoniae* biofilm formation, demonstrating their potential as alternative agents to combat biofilm-associated antibiotic resistance [64].

Using Logistic regression analysis to evaluate feature importance showed that Lymphocytes was the most influential predictor, and this result has opposite clinical research [65, 66].

HCO_3 serum level also the same result for clinical research; elevated serum bicarbonate levels have been observed in patients with bacterial pneumonia [67]. Severe bacterial lung infections (like pneumonia) can cause respiratory acidosis due to poor gas exchange and carbon dioxide retention. Regarding WBCs, typical bacterial CAP was associated WBC ≥15,000/mL [65]. This agree with our result.

Regarding BUN ,one study conducted for bacterial unirany tract infection showed decrease in BUN level [68]. This agree with our model result. The most clinical predictor for bacterial infection is neutrophils count as it increase in bacterial infection , the model showed opposite result [65, 66].

SHAP (SHapley Additive exPlanations) values were employed to interpret model predictions, Antibiotics, Basophils, and initial finding fever emerged as key variables influencing the model's output.

Bacterial CAP needs antibiotic treatment [69] and obtaining result opposite for this (antibiotics intake increases bacterial infection) has no clinical meaning.

About basophils. A study performed on mice found that basophils can enhance the innate immune response against bacterial infection and help prevent sepsis [70].

While fever is a key feature of both bacterial and viral CAP, its presence and characteristics alone are not sufficient to differentiate the two. A combination of clinical, laboratory, and imaging findings is necessary for accurate diagnosis. The symptoms of bacterial pneumonia can develop gradually or suddenly. Fever may rise as high as a dangerous 105 degrees F, with profuse sweating and rapidly increased breathing and pulse rate [71].

Lastly, The correlation coefficients between selected features and the target variable. The most clinical predictors are initial fever and Basophils that are alongside with clinical finding. [70, 71]

In summary, models showed (HCO_3, BUN, WBC, and initial fever) are main predictors for bacterial CAP. Also showed opposite clinical results with lymphocyte count. This indicates we need further models and features selection.

The small sample size (n=251) may limit the generalizability and robustness of our findings. As part of future work, we aim to scale up the study by collaborating with additional clinical sites to collect a larger, multi-center dataset with consistent data quality standards. This expansion will enable more rigorous model training, external validation, and improved confidence in the predictive performance of the ML models.

The observational nature of the dataset introduces potential confounding variables that may not have been fully accounted for in the models. Certain predictors, such as medication usage (e.g., enoxaparin or insulin bolus), may reflect treatment decisions based on illness severity rather than causal relationships. Additionally, imbalances in the distribution of bacterial versus non-bacterial CAP, or survivor versus non-survivor groups, could introduce class bias into model training, influencing performance and feature interpretation.

Different ML models have inherent assumptions and biases that can affect variable selection and interpretation. For instance, LASSO regression is effective for feature reduction but limited in capturing non-linear interactions. Random forest models handle non-linearity but may overemphasize variables with high cardinality or variance. SHAP values, while providing detailed interpretability, may diverge from classical regression coefficients and can be misinterpreted without sufficient contextual knowledge. Inconsistencies between SHAP results and established clinical findings (e.g., regarding antibiotics or lymphocyte counts) further underscore the need for domain-aware interpretation.

Although the study focuses on early admission features, not all patients had complete laboratory or radiological data available at standardized time points. Missing values may have necessitated imputation or led to the exclusion of potentially informative features. Furthermore, variables like medication use (e.g., antibiotics or vitamins) may have been recorded without precise timing relative to symptom onset or diagnosis, complicating causal inference.

CONCLUSION

This study explored key predictors for mortality and bacterial etiology in CAP, using machine learning models to analyze various clinical features. Key findings include the association of zinc and vitamin C supplements and enoxaparin with increased survival rate. Neutrophil count, ALT, MCV, HGB and platelet count with increased mortality. Insulin bolus therapy also reduced mortality, emphasizing the importance of glycemic control in CAP patients.

However, some variables like lymphocyte count, COVID-19, and cardiovascular disease presented conflicting results, requiring further investigation. Regarding bacterial etiology, features like HCO_3, BUN, WBC, and initial fever were significant predictors, though some discrepancies in lymphocyte count suggest model refinement is needed.

Overall, rapid evaluation of clinical variables at admission is crucial for predicting mortality and bacterial infections in CAP, but further validation and model adjustments are necessary for more accurate outcomes.

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TABLES AND FIGURES WITH LEGENDS

Table 1. The list of features used in the machine learning algorithm

Demographic	Age
	Gender

Clinical finding	Number of hospitalizations	Number of pneumonia	Temperature
	Pulse	Respiratory rate	Systolic Blood pressure
	Diastolic Blood pressure	Length of stay	PSI class
	Oxygen saturation	Oxygen therapy	PSI
	CURB-65	Initial finding fever	Initial finding Shortness of breath
	Location	ICU length of stay	
laboratory results	Glucose serum	Hemoglobin A1C (HbA1c)	Random blood glucose
	Partial pressure of oxygen (PaO_2)	Partial pressure of carbon dioxide (PCO_2)	Bicarbonate (HCO_3)
	Base Excess of arterial blood gas (ABGs BE)	Albumin serum	Creatine phosphokinase (CPK)
	Blood urea nitrogen (BUN)	Alkaline phosphatase	Alanine aminotransferase (ALT)
	Aspartate aminotransferase (AST)	Total Bilirubin	Direct Bilirubin
	Amylase serum	pH	Hemoglobin
	Hematocrit (HCT)	Mean corpuscular hemoglobin (MCH)	Mean corpuscular volume (MCV)
	Mean corpuscular hemoglobin concentration (MCHC)	Platelet distribution width (PDW)	Platelet count
	White blood cell (WBC)	Red blood cell distribution width (RDW)	Mean platelet volume (MPV)

	Red blood cell (RBC)	Erythrocyte sedimentation rate (ESR)	Lymphocytes count
	Monocytes count	Eosinophils count	Basophils count
	Neutrophils count	Magnesium serum	Potassium serum
	Calcium serum	Sodium serum	Total protein
	Serum glutamic-oxaloacetic transaminase (SGOT)	Serum glutamic-pyruvic transaminase (SGPT)	Creatinine serum
	Urine PH	C reactive protien	Procalcitonin (PCT)
	Uric acid	High-density lipoprotein (HDL) cholesterol	Low -density lipoprotein (LDL)_cholesterol
	Prothrombin time	D dimer	The international normalized ratio (INR)
	Lactate dehydrogenase (LDH)	Troponin	Activated partial thromboplastin time (aPTT)
	Culture	Sputum culture	Urine character hazy
	PCR		
medical history	Diabetes mellitus	Hypertension	Cardiovascular disease
	Alzheimer	COVID_19	Hypotension
	Septic shock	Cough	Dry cough
	Chest pain		
medication	Imipenem	Cefepime	Vancomycin
	Meropenem	Ceftriaxone	Levofloxacin

	Susceptibility Imipenem	Susceptibility Pipracillin tazobactam	Imipenem cilastatin
	Susceptibility Meropenem	Susceptibility Cefepime	Susceptibility Levofloxacin
	Susceptibility Ceftazidime	Susceptibility Aztreonam	Susceptibility Ciprofloxacin
	Susceptibility Amikacin	Amlodipine	Aspirin
	Bisoprolol	Vitamin C	Atorvastatin
	Cilastatin	Furosemide	Lansoprazole
	Enoxaparin	Insulin basal	Lactulose
	Enalapril	Insulin bolus	Omeprazole
	Prednisolone	Tocilizumab	Anti-platelet
	Zinc	Antibiotics	Anti-coagulant
	B complex	Antiviral	Number of PRN medications
	mAb tocilizumab	Number of medications	
	Number of regular medications	Guideline concordant antibiotics	

PRN: Per registered nurse (as needed).

Table 2. Demographic and clinical data for the participants (N= 251)

Feature	**Frequency**	**Valid percentage %**	**Median (IQR)**
Gender			
Age (years)			60 (IQR=25)
Location			
Ward	30	12.0	

ICU	221	88.0	
LOS			10 days (IQR=13)
ICU_LOS			4.77 days (IQR=1.77)
Current COVID_19	18	7.2	
Previous COVID_19	9	3.6	
Diseases			
Diabetes Mellitus	76	30.3	
Septic shock	64	25.5	
HTN	33	13.1	
Cardiac disease	22	8.8	
Alzheimer	17	6.8	
Another lung disease	14	5.6	
CKD	12	4.8	
Anemia	7	2.8	
Asthma	6	2.4	
COPD	5	2.0	
Hypotension	5	2.0	
GERD	5	2.0	
Dyslipidemia	4	1.6	
History			
Number of previous pneumonias			0.77 (IQR=0)
Number of previous hospitalizations			2.4 (IQR=3.7)
Kidney transplantation	4	1.6	

Table 3. Treatment related descriptive data

Feature	Frequency	Valid percentage
Chronic treatment		
Vitamin C	73	29.1
Zinc	69	27.5
Insulin bolus	62	24.7
Omeprazole	48	19.1
Bisoprolol	45	17.9
B complex	41	16.3
Insulin basal	40	15.9
Antiplatelet	39	15.6
Aspirin	38	15.1
Amlodipine	31	12.4
Furosemide	31	12.4
Atorvastatin	27	10.8
Lactulose	24	9.6
Lansoprazole	21	8.4
Enalapril	17	6.8
Prednisolone	16	6.4
MAb_tocilizumab	16	6.4
Tocilizumab	16	6.4
Ipratropium inhaler	13	5.2
Clopidogrel	12	4.8
Hydrochlorothiazide	12	4.8
Azithromycin	11	4.4
Piperacillin - Tazobactam	11	4.4

Budesonide inhaler	10	4.0
Vitamin D	10	4.0
Metformin	9	3.6
Colchicine	9	3.6
Ca carbonate	7	2.8
Candesartan	7	2.8
Metronidazole	7	2.8
Valsartan	7	2.8
Bromazepam	6	2.4
Carvedilol	4	1.6
Short term treatment		
Antibiotics	201	80.1
Anticoagulant	196	78.1
Enoxaparin	195	77.7
Antiviral agent	20	8.0
Albumin	12	4.8
Favipiravir	12	4.8
Norepinephrine Injection	12	4.8
Paracetamol	11	4.4
Guaifenesin	11	4.4
Dextrose Injection	11	4.4
Morphine	8	3.2
Remdesivir Injection	8	3.2

Table 4. Pneumonia specific descriptive data

Feature	**Frequency**	**Valid percentage**
PSI class		

1	48	19.1
2	102	40.6
3	58	23.1
4	33	13.2
5	10	4.0
CURB 65		
0	47	18.7
1	132	41.8
2	62	24.7
3	10	4.0
Bacterial infection		
Yes	215	85.7
No	36	14.3
Outcome		
Survivor	169	67.3
Non survivor	82	32.7
Initial findings		
SOB	97	38.6
Fever	41	16.3
Productive cough	17	6.8
Dry cough	16	6.4
Pleuritic chest pain	16	6.4
Headache	11	4.4
Vomiting	11	4.4
Abdominal pain	10	4.0
Intubation / mechanical	10	4.0

ventilation		
Diarrhea	10	4.0
Fatigue	8	3.2
Nausea	6	2.4
Constipation	5	2.0
Muscular or joint pain	4	1.6
Loss of taste and smell	4	1.6

Table 5. Performance Metrics of Logistic Regression Models for Predicting Mortality and Bacterial Infection

Metric	Mortality Outcome (Training Set)	Mortality Outcome (Test Set)	Bacterial Infection Outcome (Training Set)	Bacterial Infection Outcome (Test Set)
Accuracy	0.88	0.86	0.98	0.95
AUROC	0.90 (95% CI: 0.85-0.95)	0.88 (95% CI: 0.83-0.93)	0.99 (95% CI: 0.97-1.00)	0.96 (95% CI: 0.92-0.98)
Sensitivity	0.95	0.94	1	1
Specificity	0.85	0.8	0.95	0.9
PPV	0.9	0.88	0.97	0.95
NPV	0.92	0.91	0.98	0.96

Table 6: Comparative Variable Importance

Feature	Mutual Information	LASSO Coefficient	Logistic Regression Odds Ratio	Mean SHAP Value
Zinc	✓	–	–	✓
Vitamin C	✓	–	–	✓

Enoxaparin	✓	–	✓	✓
Neutrophils	✓	✓	–	✓
Meropenem	–	✓	–	✓
ICU Stay	–	–	✓	✓
pH	–	✓	✓	✓
WBC	✓	✓	✓	✓
Platelets	✓	✓	✓	✓

Table 7. Forest Plot Data

Variable	Odds Ratio	95% CI	P-value
Forest Plot Data for Mortality Outcome			
ICU Stay	2.5	1.5-4.1	0.001
pH	0.6	0.4-0.9	0.025
WBC	1.8	1.2-2.7	0.005
Platelets	1.7	1.1-2.6	0.010
Meropenem	2.0	1.3-3.1	0.003
Forest Plot Data for Bacterial Infection Outcome			
Lymphocytes	1.4	1.0-2.0	0.045
WBC	2.1	1.5-3.0	0.002
MCV	1.3	0.9-1.9	0.060*
Neutrophils	2.5	1.8-3.4	0.001
Basophils	1.6	1.1-2.4	0.010

*Despite being statistically insignificant, it is kept in the table due to its close to the significant limit.

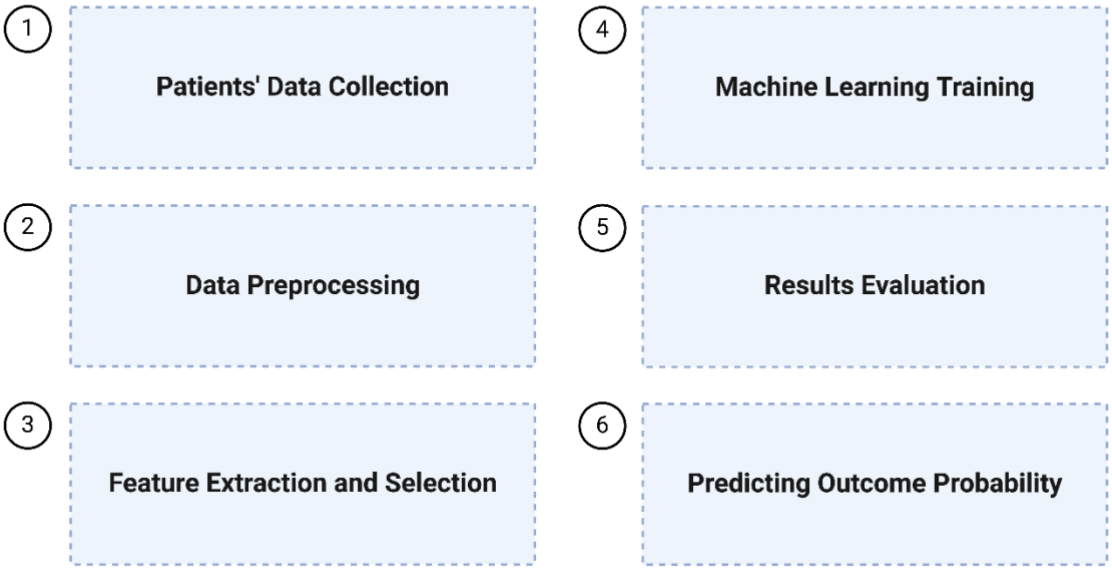


Figure 1. Overview of the Six-Steps Machine Learning Workflow for Predicting Outcome Probabilities

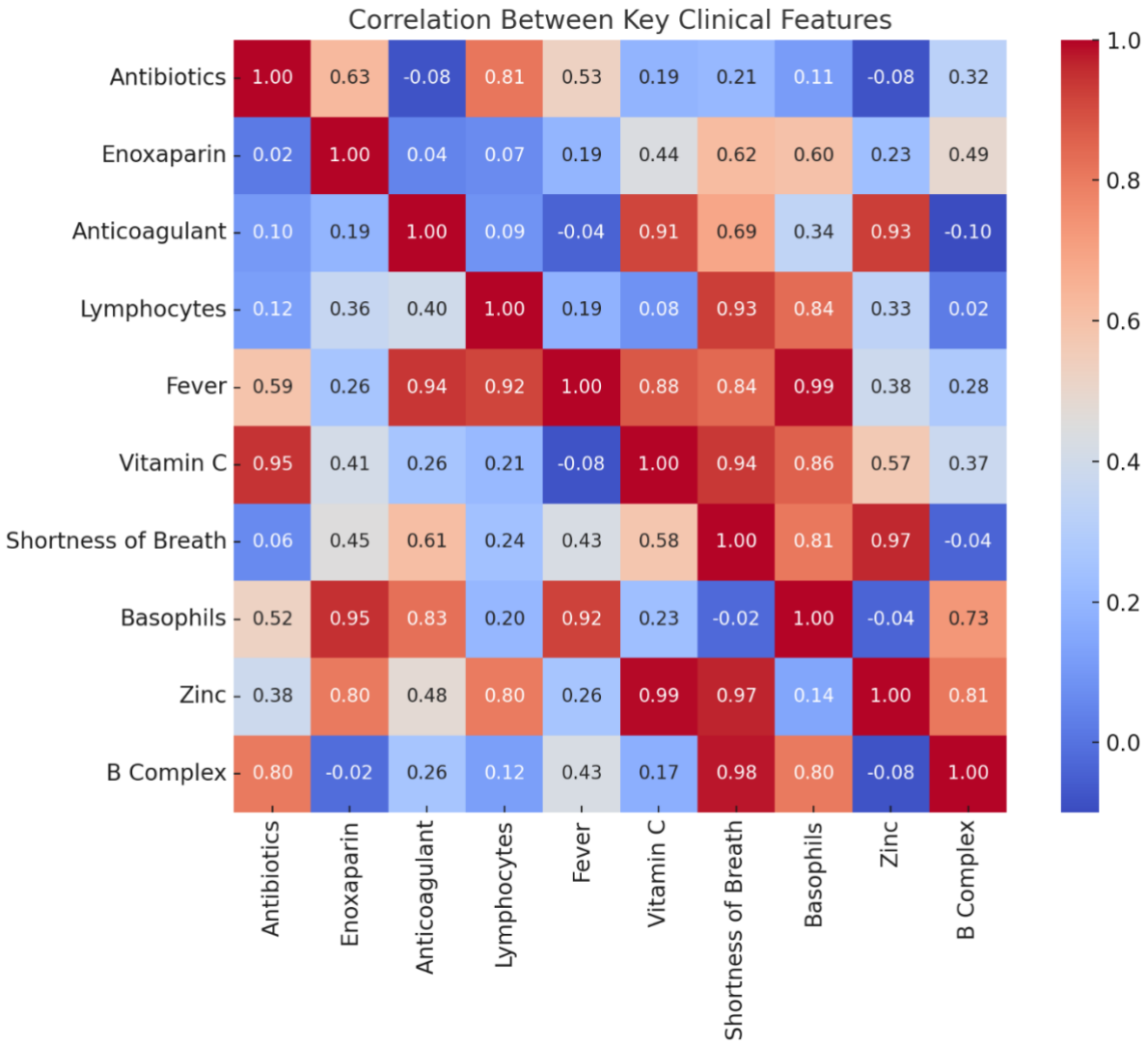


Figure 2. Heatmap of Highly Correlated Features

1. Pearson Correlation Coefficients — Heatmap of higly correlated features. Warm colors show higher correlations, whereas cool colors are indicative of negative correlations.

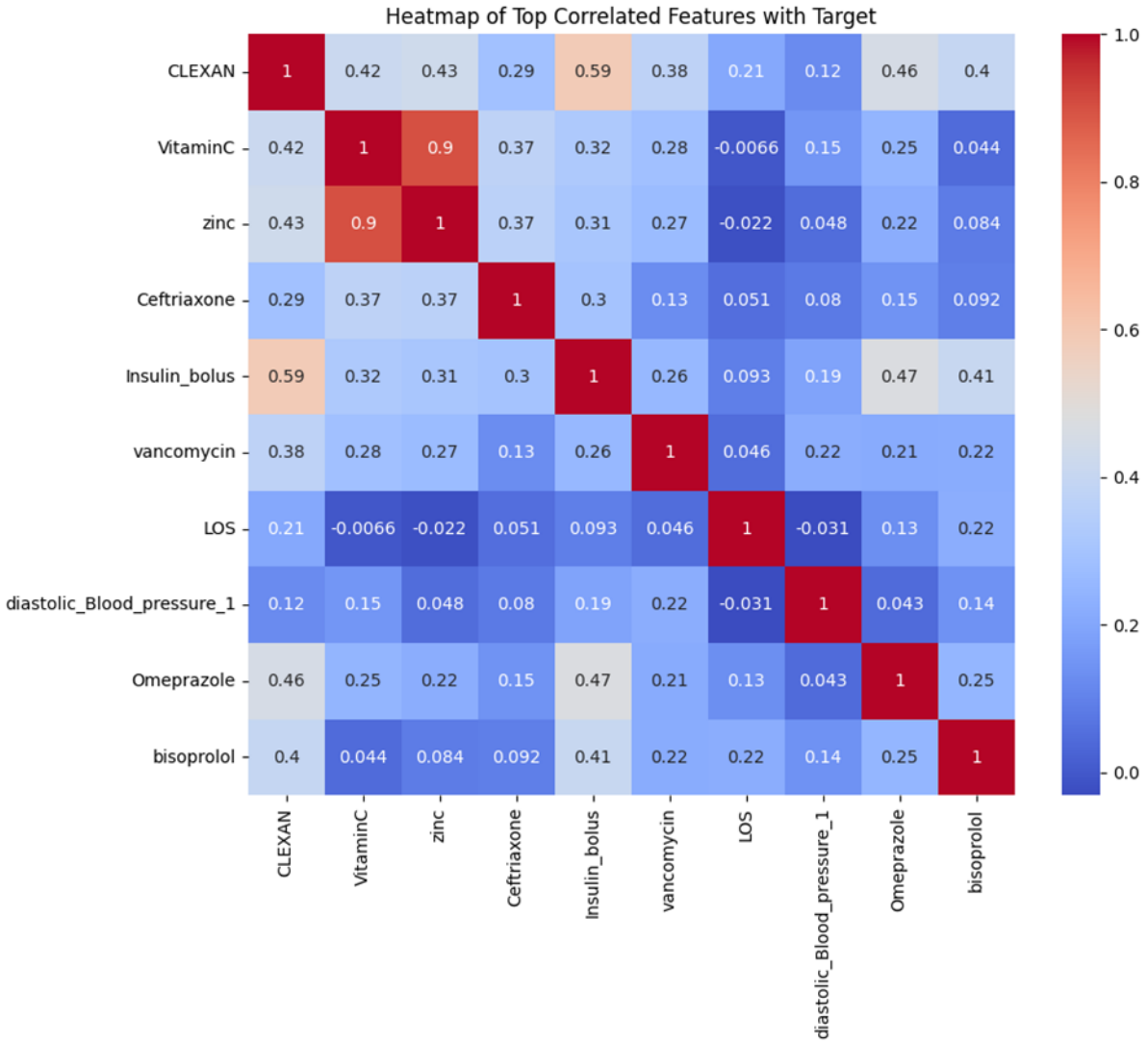


Figure 3. Heatmap of Top Correlated Features with Mortality Target

Pearson Correlation Coefficients — Heatmap of Features and Target Outcome. Warm colors show higher correlations, whereas cool colors are indicative of negative correlations

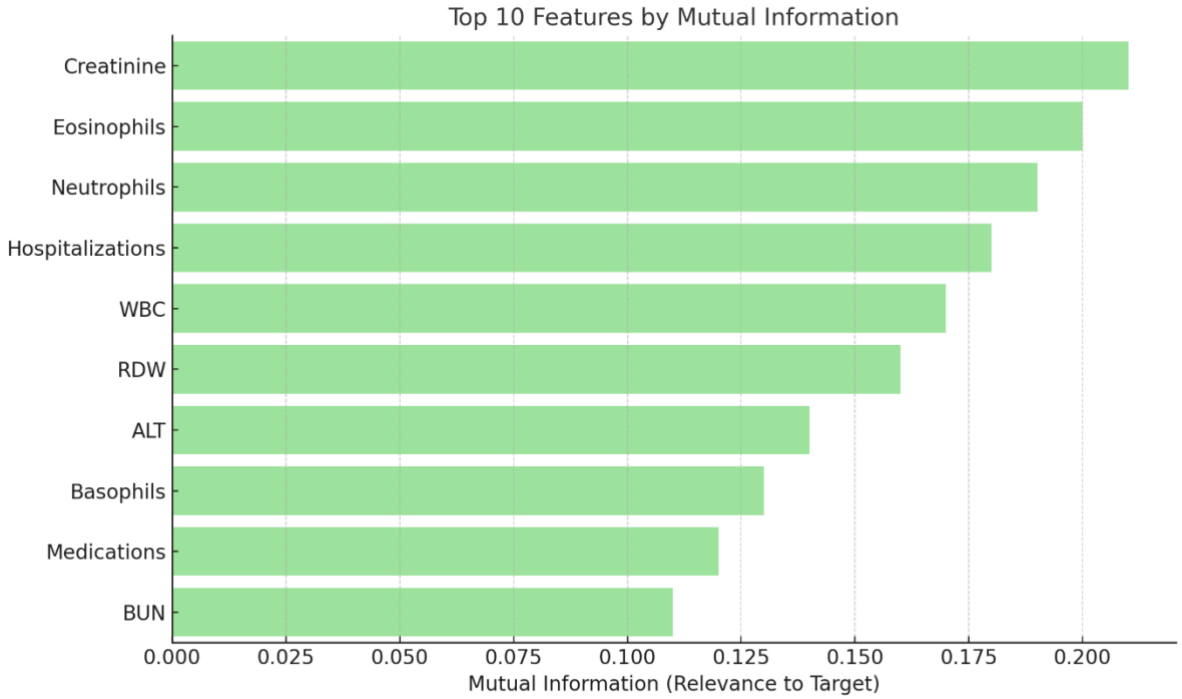


Figure 4. Mutual Information of Features Regarding Mortality Outcome

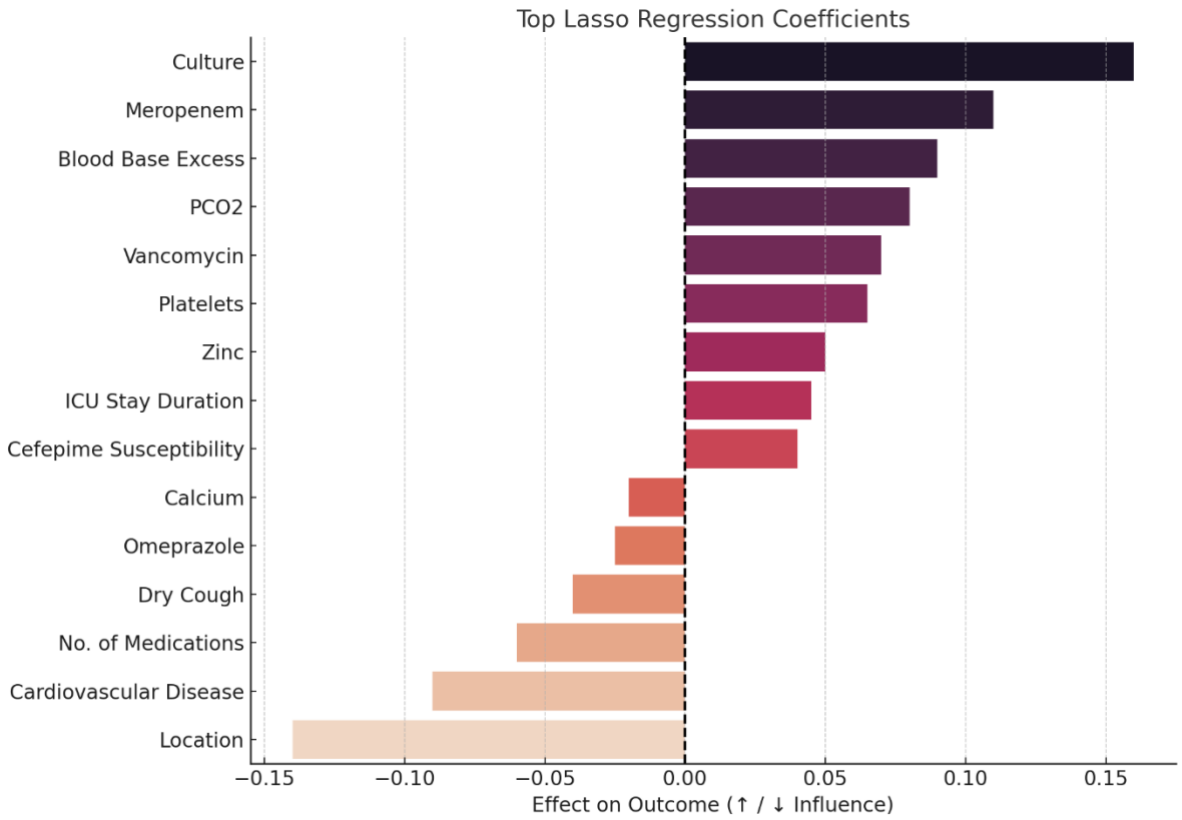


Figure 5. Top Feature Coefficients from Lasso Regression

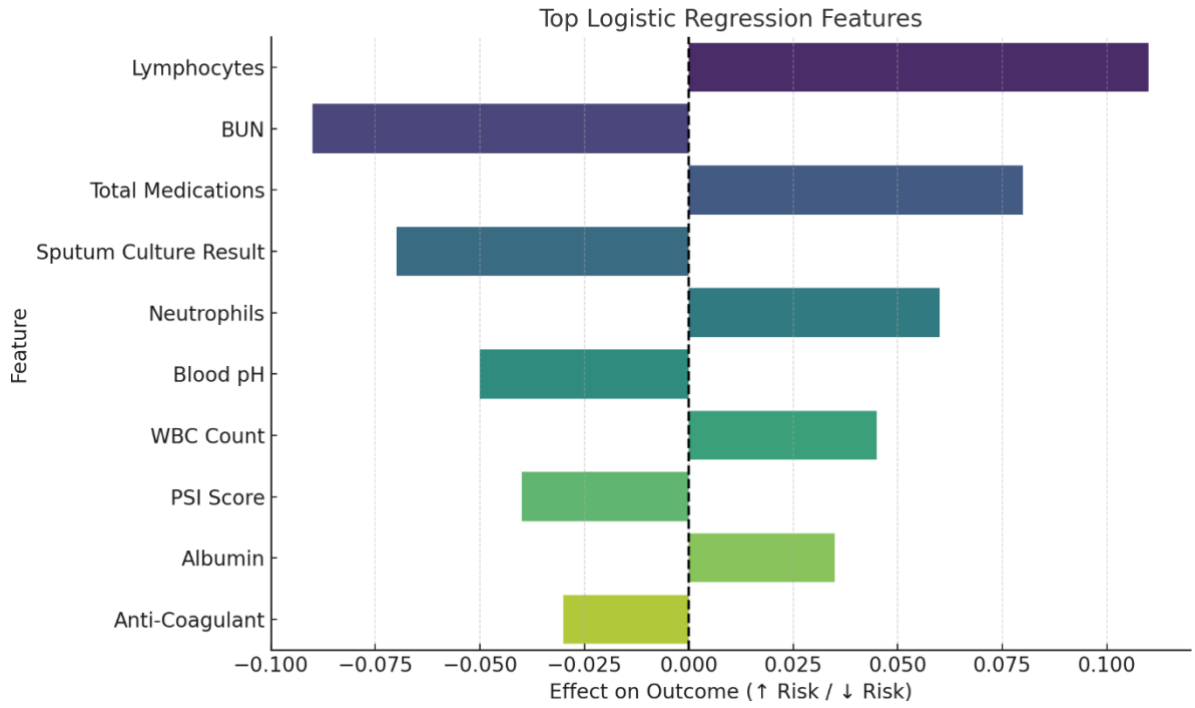


Figure 6. Feature Importance from Logistic Regression

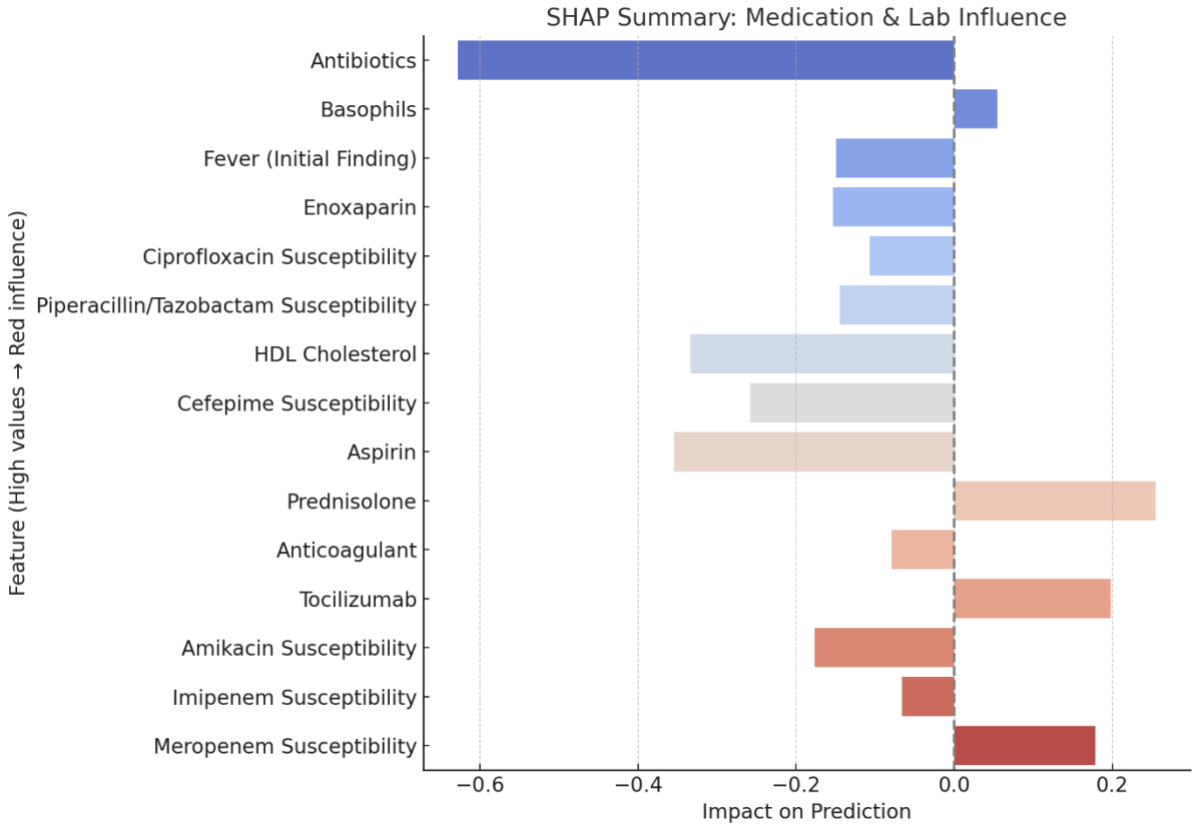


Figure 7. SHAP Summary Plot Showing the Impact of Medications and Laboratory Findings on Model Predictions

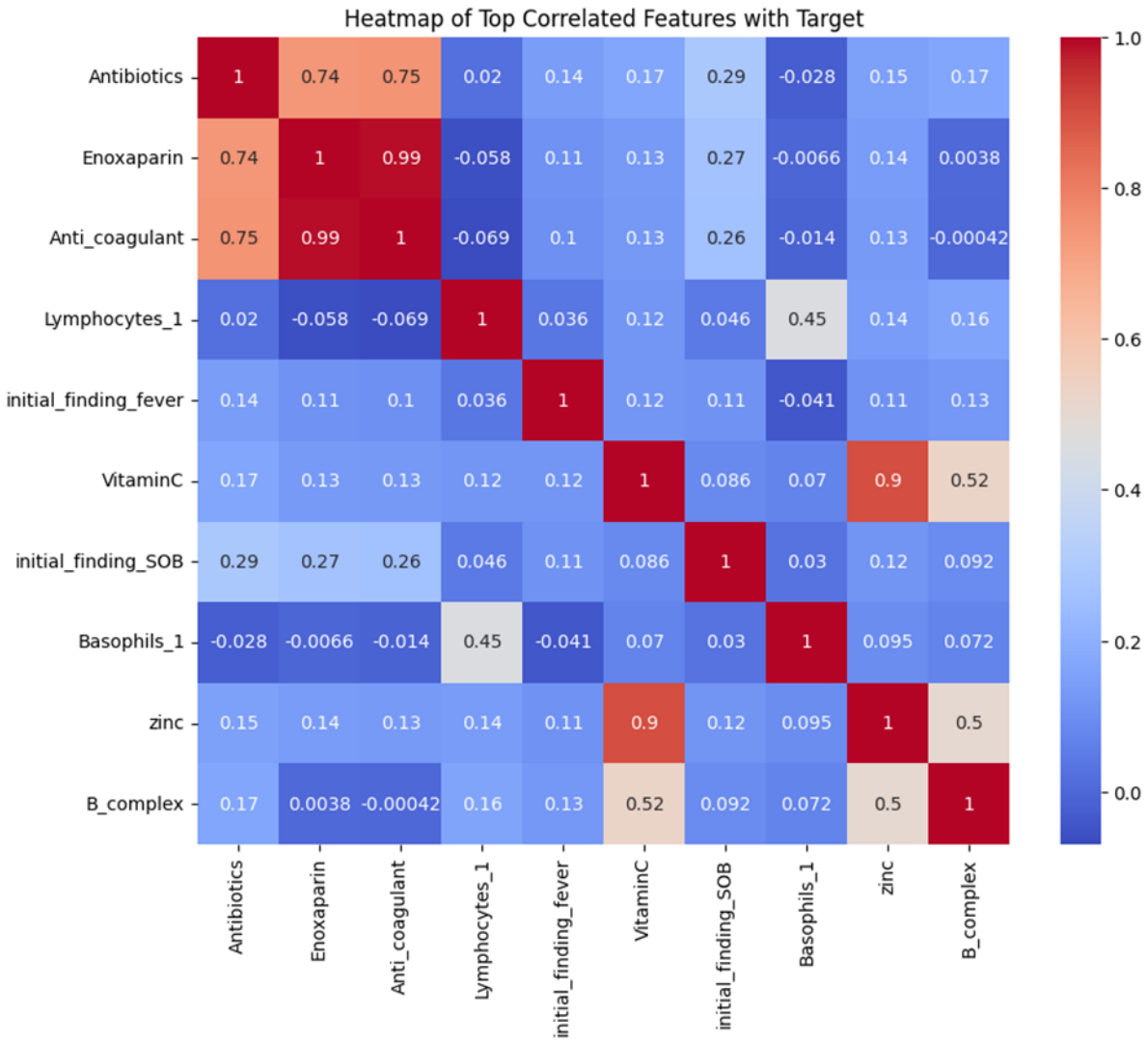


Figure 2. Heatmap of Correlations Between Clinical Variables and Bacterial Infection. Pearson Correlation Coefficients — Heatmap of Features and Target Outcome. Warm colors show higher correlations, whereas cool colors are indicative of negative correlations.

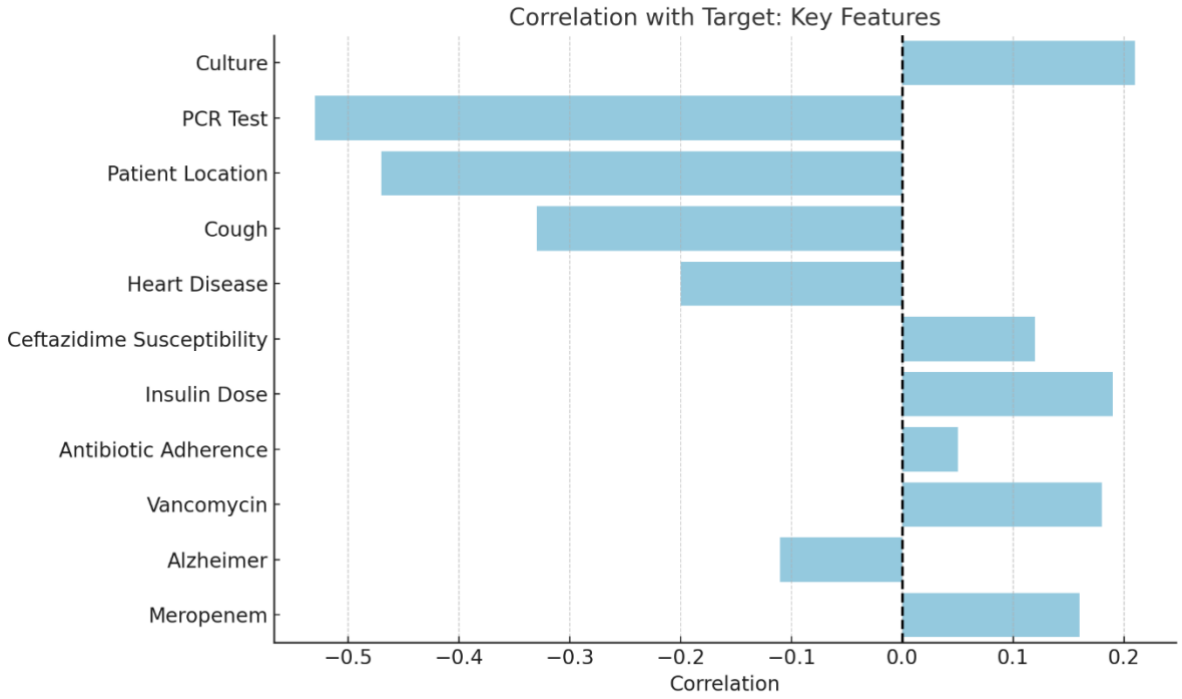


Figure 3. Feature Importance from Logistic Regression Model

The horizontal bar plot shows each feature's coefficient, which mirrors the actual contribution of the feature to the predictions of the model. A positive coefficient means positively associated with the target, and a negative coefficient means negatively associated with the target.

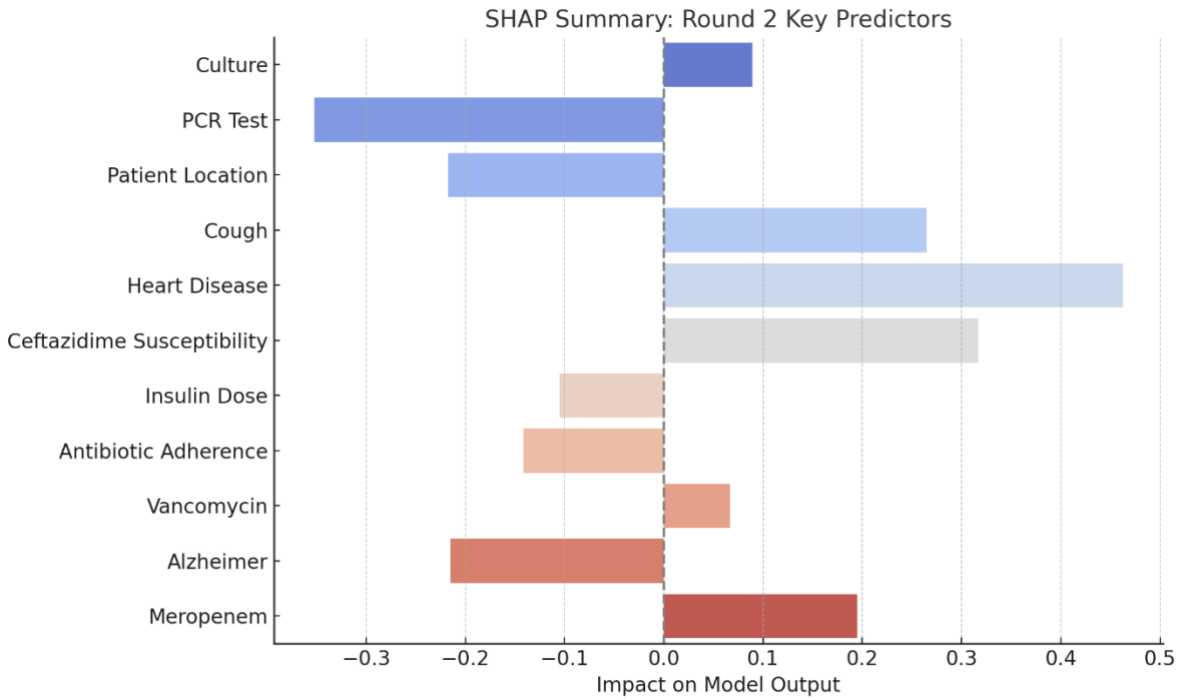


Figure 4. SHAP Summary Plot of Feature Impact on Model Output

This figure illustrates the SHAP values representing the impact of various features on the model's predictions. Positive SHAP values indicate a positive contribution to the outcome, while negative values signify a negative impact. The color gradient from blue (low feature value) to red (high feature value) highlights how feature magnitude influences the model output. Key influential features include Antibiotics, Basophils, and initial finding fever, with varying effects based on their respective values.

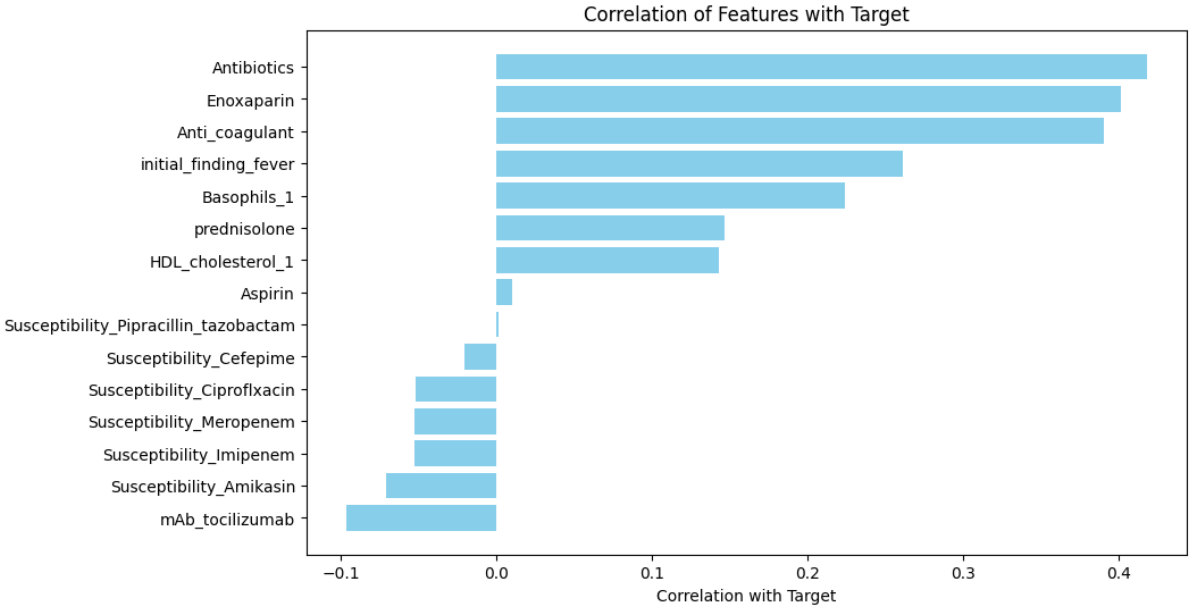
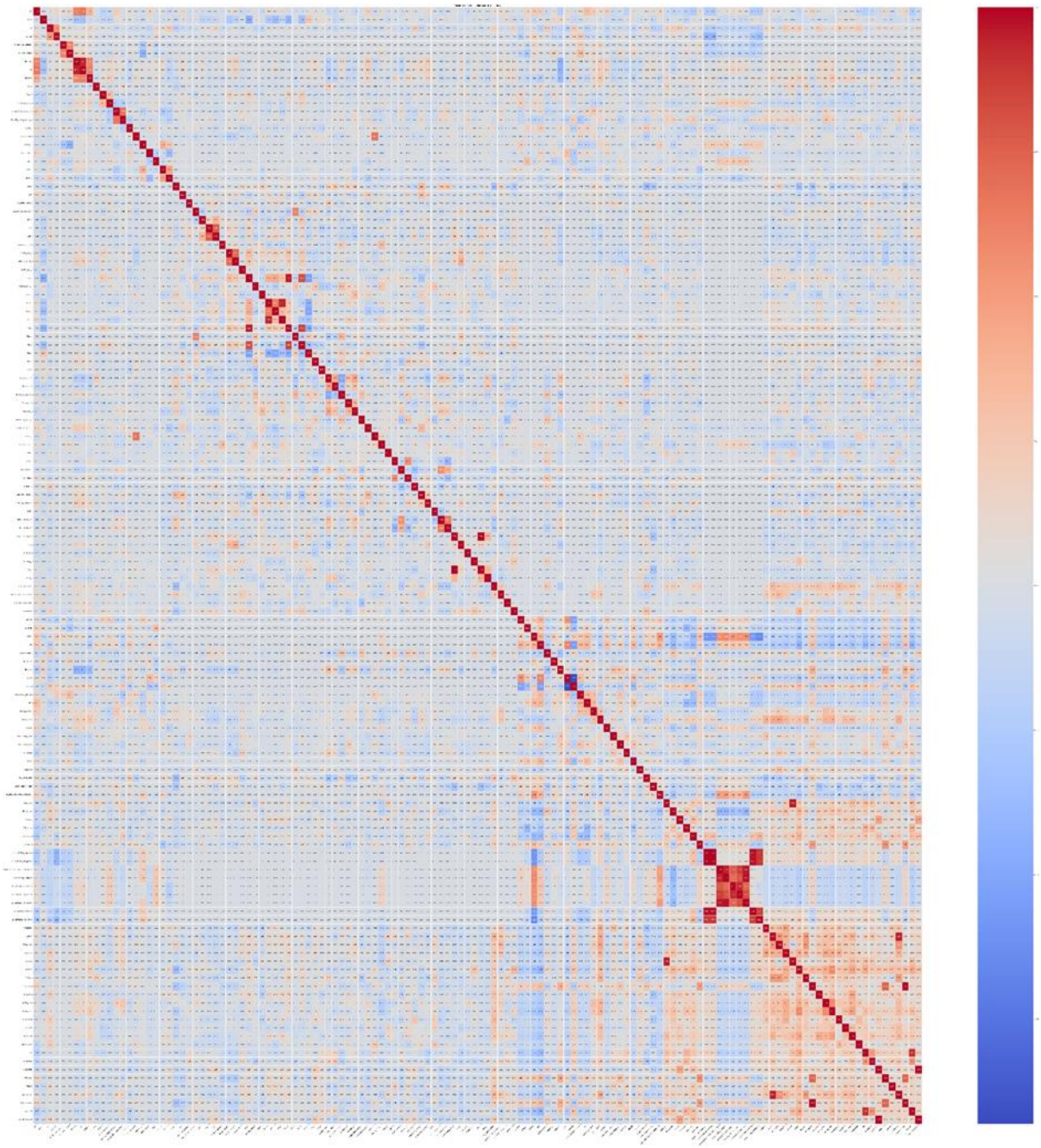


Figure 5. Correlation of Clinical and Treatment Features with Bacterial Infection as a Target Outcome

SUPPLEMENTAL DATA



Appendix 1. Complete Heatmap of All Features.