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Predictors of In-Hospital Mortality in COVID-19-Associated Hospital-Acquired Pneumonia: Experience from a Tertiary Care Hospital

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ABSTRACT

Background: COVID-19 has significantly increased the risk of hospital-acquired pneumonia (HAP), especially in critically ill patients. The overlap of viral and secondary bacterial infections contributes to increased morbidity and mortality. Identifying key predictors of in-hospital mortality in such patients is essential for improving clinical outcomes and guiding targeted interventions.

Objective: To identify and evaluate the clinical, laboratory, and microbiological factors associated with in-hospital mortality among patients diagnosed with COVID-19-associated hospital-acquired pneumonia (HAP) in a tertiary care setting.

Methodology: A retrospective observational analysis was performed on 110 adult COVID-19 patients who had HAP ≥48 hours after hospitalization during the period from January 2023 to December 2023. Demographic, clinical, laboratory, and microbiological information were compared between non-survivors and survivors. Statistical significance was evaluated by using appropriate univariate tests.

Results: Mortality was strongly correlated with advanced age ($p = 0.01$), chronic kidney disease ($p = 0.01$), ICU stay ($p < 0.001$), and mechanical ventilation ($p < 0.001$). Non-survivors had highly raised inflammatory and renal markers: ferritin >1000 µg/mL ($p < 0.001$), D-dimer >1.3 mg/L ($p = 0.01$), procalcitonin >2.0 ng/mL ($p < 0.001$), and creatinine >1.3 mg/dL ($p = 0.001$). Aspergillus species were much more frequent among non-survivors (31.8% vs. 12.1%, $p = 0.05$), indicating an association with higher mortality from invasive fungal infections.

Conclusion: Advanced age, renal impairment, ICU-level treatment, mechanical ventilation, high inflammatory markers, and Aspergillus coinfection are major mortality predictors in COVID-19 patients with hospital-acquired pneumonia. These results underscore the need for earlier risk stratification, fungal diagnostics, and early intervention to minimize mortality in resource-constrained environments.

Keywords: COVID-19; Hospital-Acquired Pneumonia; Mortality; Inflammatory Markers

Introduction

The COVID-19 pandemic has resulted in severe health issues worldwide since it first appeared in late 2019.[1] The disease, produced by the SARS-CoV-2 virus, primarily targets the lungs and respiratory system.[2] Although most individuals infected with the virus recover on their own at home with relatively mild signs such as fever, cough, or fatigue, some individuals particularly older persons or those with underlying medical conditions become severely ill. These patients usually have to be hospitalized, and some of them need treatment in the intensive care unit (ICU), where they can be put on a ventilator to assist them with breathing. Unfortunately, staying in the hospital for extended periods raises the risk of acquiring new infections, like hospital-acquired pneumonia (HAP), which can significantly worsen the patient's condition.[3]

Hospital-acquired pneumonia (HAP) is an infection of the lung that occurs 48 hours or more following admission to the hospital and was not present or incubating during the time of admission.[4, 5] It is usually caused by bacteria and tends to happen in critically ill patients, those on ventilators, or those with compromised immune systems. In contrast to community-acquired pneumonia, HAP commonly includes drug-resistant bacteria, for which it is more difficult to treat. HAP can result in severe complications, such as respiratory failure, longer hospitalization stays, and higher rates of death, particularly in high-risk patients.

In already weakened patients of COVID-19, this form of pneumonia can be particularly threatening. Such patients have already infected lungs due to the virus, and their immune systems are weakened by either the virus or the intake of medicines such as steroids, immunomodulators, or other drugs that are anti-inflammatory but also suppress normal defense systems of the body. Extended lengths of stay in the hospital, ventilation, and invasive therapy also raise the risk for hospital-acquired pneumonia. Additionally, since COVID-19 impacts the lung in an overlapping manner with the typical bacterial infection, it may be challenging for physicians to determine if the worsening of symptoms in a patient is a result of the viral infection by itself or as a consequence of a new bacterial infection. This delay in diagnosis will result in delayed treatment, leading to worse outcomes and more risk of complications.

There are a lot of risk factors for death among COVID-19 patients developing hospital-acquired pneumonia. These include advanced age, male gender, and other diseases such as diabetes, hypertension, kidney disease, cancer, or heart disease.[6,7] Long-term use of ventilators is another risk factor for infection. If the infection is caused by bacteria that are resistant to usual antibiotics, or if the patient gets improper treatment initially, the likelihood of a negative outcome is greater. In addition, delays in diagnosis or initiation of appropriate treatment, particularly in busy or resource-poor hospitals, can result in worse outcomes. In others, the patient can get sepsis, a potentially fatal response to infection that can lead to the failure of several organs.

In hospitals, particularly in the case of a pandemic, it may be challenging to treat all the patients properly. Physicians have to make a choice regarding which patients require more attention, more powerful medications, or the ICU. Therefore, it is extremely crucial to identify the principal reasons for increased patient mortality due to COVID-19 and hospital-acquired pneumonia. If physicians can discover high-risk individuals in advance, they can give quicker and improved treatment, and even save lives. It also aids in the efficient use of limited hospital resources, particularly in developing nations where healthcare systems tend to come under immense pressure.

There is some data already published in the developed world on how hospital-acquired pneumonia impacts COVID-19 patients. Still, little to no data has been published from low- and middle-income country hospitals, where conditions, resources, and patient populations can be extremely different. All of these factors, including the availability of ICU beds, delayed laboratory reporting, and availability of antibiotics, can affect patient outcomes.

This research was carried out in a tertiary care hospital to determine what factors are associated with an increased risk of mortality in patients who have both COVID-19 and hospital-acquired pneumonia. The goal is to gather and compare data on patient age, gender, medical history, infection type, and treatment administered, and then determine how these are correlated with survival. Such a study can make patient care in the future better by instructing physicians on how to rapidly identify and treat the most critical cases. It can assist hospital administrators and health policymakers in better planning infection control, antibiotic prescription, and patient management practices, not just during this ongoing pandemic but also in other future health crises.

Objective

To identify and evaluate the clinical, laboratory, and microbiological factors associated with in-hospital mortality among patients diagnosed with COVID-19-associated hospital-acquired pneumonia (HAP) in a tertiary care setting.

Methodology

This retrospective observational study was done among 110 patients at a Lady Reading Hospital, Peshawar, that was actively treating COVID-19 cases since the pandemic started. The hospital has a specialized COVID-19 ward and ICU, where a vast variety of critically ill patients are

treated. Data were gathered from January 2023 to December 2023 among patients admitted. The investigation aimed to determine the factors related to mortality in patients who had hospital-acquired pneumonia (HAP) while hospitalized with COVID-19.

The population of the study included adult patients aged 18 years and above who had a confirmed diagnosis of COVID-19 using reverse transcriptase-polymerase chain reaction (RT-PCR) and later developed HAP during hospitalization. Hospital-acquired pneumonia was operationally defined as a new or progressive infiltrate on chest imaging that occurred in association with at least two of the following: fever, purulent respiratory secretions, leukocytosis or leukopenia, and hypoxia, developing 48 hours or more after admission to hospital. Exclusion criteria from the study included those patients who had evidence of pneumonia at the time of admission or who developed pneumonia within the first 48 hours.

We used retrospective data from electronic hospital records, patient paper records, and laboratory reports. Data gathered were demographic information (age and gender), clinical background (comorbidities like diabetes mellitus, hypertension, chronic kidney disease, cardiovascular disease, malignancy, and chronic lung disease), and admission severity of COVID-19. Other variables used were length of hospital stay, length of ICU stay, mechanical ventilation duration, and need for vasopressor therapy. Laboratory results like white blood cell counts, C-reactive protein (CRP), serum creatinine, liver function tests, and inflammatory markers like ferritin, D-dimer, and procalcitonin (where available) were noted upon diagnosis of HAP. Microbiological information was examined to determine the causative organism.

In this study, patients were categorized into two groups: non-survivors (died in hospital) and survivors (discharged alive). The two groups were compared in terms of the clinical and laboratory parameters that contributed to higher risk of death.

The information was entered and processed with the help of software SPSS version 27. Continuous variables were presented as means and standard deviations or medians and interquartile ranges, based on data distribution. Categorical variables were reported as frequencies and percentages. Statistical tests were employed to compare continuous variables, whereas the Chi-square test was utilized for categorical variables. Statistical significance was assumed at a p-value of less than 0.05. Consent was taken and patient confidentiality was maintained throughout the study.

Results

Non-survivors were older than survivors and more had chronic kidney disease (27.2% vs 9%) with a p-value of 0.01. Admission to the ICU and ventilation were also much more prevalent in non-survivors, both with extremely significant p-values (<0.001), indicating their strong relationship with death. Male gender and diabetes were more common in non-survivors but were not statistically significant. Median length of stay in the hospital was longer in non-survivors but not significantly different (Table 1).

Table 1. Baseline characteristics of survivors and non-survivors

Variable	Total (n=110)	Survivors (n=66)	Non-survivors (n=44)	p-value
Mean age (years)	57.7 ± 14.2	53.2 ± 13.7	60.7 ± 14.1	0.01
Male gender (%)	68 (61.8%)	35 (53.0%)	29 (65.9%)	0.08
Diabetes mellitus (%)	66 (60.0%)	33 (50.0%)	31 (70.4%)	0.07
Chronic kidney disease (%)	17 (15.4%)	6 (9.0%)	12 (27.2%)	0.01
ICU admission (%)	55 (50.0%)	18 (27.2%)	35 (79.5%)	<0.001
Mechanical ventilation (%)	54 (49.0%)	13 (19.6%)	34 (77.2%)	<0.001
Median hospital stay (days)	13 (7–21)	12 (6–18)	15 (9–25)	0.08

Non-survivors had profoundly higher values of ferritin, D-dimer, procalcitonin, and creatinine than survivors, all with p-values showing high statistical significance. To illustrate, 75% of non-survivors presented with ferritin values >1000 µg/mL compared with 34.8% of survivors ($p < 0.001$). Lymphopenia was very marginally more frequent among non-survivors (93.1%) than survivors (81.8%), however, and the difference was not statistically significant. These findings imply that increased markers of inflammation and renal function are correlated with worse outcomes (Table 2).

Klebsiella pneumoniae and Pseudomonas aeruginosa

Table 2. Laboratory findings associated with mortality

Parameter	Survivors (n=66)	Non-survivors (n=44)	p-value
Ferritin >1000 µg/mL (%)	23 (34.8%)	33 (75.0%)	<0.001
D-dimer >1.3 mg/L (%)	41 (62.1%)	38 (86.3%)	0.01
Procalcitonin >2.0 ng/mL (%)	13 (19.6%)	25 (56.8%)	<0.001
Creatinine >1.3 mg/dL (%)	21 (31.8%)	29 (65.9%)	0.001
Lymphopenia (<17.5%) (%)	54 (81.8%)	41 (93.1%)	0.12

were the predominant pathogens, present in roughly equivalent proportions among survivors and non-survivors. Aspergillus species were significantly more common among non-survivors (31.8%) than among survivors (12.1%), p-value = 0.05, implying a potential link with high mortality. There were no statistically significant differences in other organisms such as Acinetobacter baumannii and MRSA between the two groups (Table 3).
Results showed that Klebsiella pneumoniae was the most frequently recovered organism in 34 patients, followed by Pseudomonas aeruginosa in 30 patients. Aspergillus species, a fungal agent commonly seen with immuno-suppression, was cultured in 22 patients, Acinetobacter baumannii in 16 patients, and MRSA in 8 patients. The graph highlights the prevalence of gram-negative bacteria and draws attention to the significant frequency of fungal infections, which are especially problematic among critically ill and immunocompromised patients (Figure 1).

Discussion

Hospital-acquired pneumonia (HAP) has been known to be a severe complication among hospitalized patients, especially critically ill or immunocompromised patients.[8] With the outbreak of the COVID-19 pandemic, the risk and severity of HAP have become more significant. COVID-19 is known to involve the respiratory system predominantly and commonly results in prolonged hospitalization, intensive care unit (ICU) treatment, and the use of mechanical ventilation; all of which are known risk factors for acquiring HAP.[9] The combination of viral lung injury, immune dysregulation and the use of immunosuppressive agents such as corticosteroids enhances the susceptibility to secondary bacterial or fungal infections. These superinfections not only make the clinical course more complicated but also considerably increase the risk of morbidity and mortality. It is important to identify the predictors of poor outcomes in patients with COVID-19-associated HAP in order to improve early diagnosis, direct appropriate antimicrobial treatment, optimize resource utilization, and finally decrease mortality in this high-risk population.
The current study from a tertiary care facility provides valuable insights into predictors of mortality among patients with COVID-19-associated hospital-acquired pneumonia (HAP). It indicates that both older age and chronic kidney disease (CKD) were more common among non-survivors, suggesting that both age-related immune decline and intrinsic renal impairment play a role in adverse outcomes for such patients. The average age of non-survivors was 60.7 years vs 53.2 in survivors, with a

Table 3. Organisms isolated from respiratory cultures

Organism	Total (n=110)	Survivors (n=66)	Non-survivors (n=44)	p-value
Klebsiella pneumoniae	34 (30.9%)	21 (31.8%)	13 (29.5%)	0.63
Pseudomonas aeruginosa	30 (27.2%)	17 (25.7%)	13 (29.5%)	0.81
Aspergillus species	22 (20.0%)	8 (12.1%)	14 (31.8%)	0.05
Acinetobacter baumannii	16 (14.5%)	7 (10.6%)	9 (20.4%)	0.34
MRSA	8 (7.2%)	5 (7.5%)	3 (6.8%)	0.71

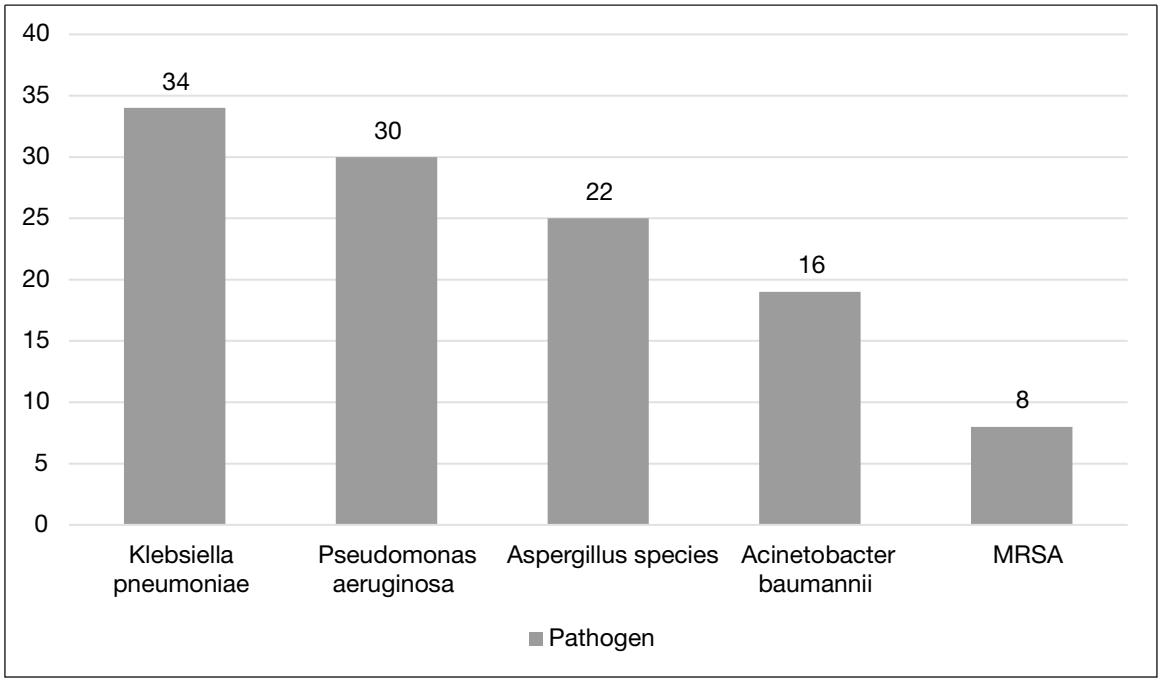

Figure 1. Frequency of different microorganisms isolated from cases

statistically significant p-value of 0.01. Likewise, CKD was present in 27.2% of non-survivors vs just 9% of survivors, also statistically significant (p = 0.01). Male gender and diabetes mellitus were also more common in non-survivors, though these failed to reach statistical significance here.

The necessity of ICU admission and mechanical ventilation were significantly more pronounced in the nonsurvivors, and both these variables had very high statistical significance (p < 0.001). All these results reflect the worldwide trend observed in other researches. For example, another study by Alonazi published at Saudi Healthcare in 2023 also mentioned ICU admission and respiratory failure to be the most reliable independent predictors of death in patients with COVID-19 pneumonia who had secondary infection, such as HAP.[10] Likewise, a study by Daniel et al. (2022) also noted that admission severity and requirement for mechanical ventilation significantly increased mortality risk, particularly when compounded by bacterial or fungal superinfection.[11]

In terms of laboratory results, increased markers of inflammation and kidney damage were significantly linked with mortality. Ferritin above 1000 µg/mL was present in 75% of non-survivors versus 34.8% of survivors (p < 0.001), and D-dimer above 1.3 mg/L was observed in 86.3% of non-survivors versus 62.1% of survivors (p = 0.01). Likewise, procalcitonin and creatinine were highly elevated in non-survivors, reflecting both organ dysfunction and systemic infection. These findings are supported the results of a study published by Zayed et al. (2022) in The Egyptian Journal of Bronchology, in which elevated ferritin, procalcitonin, and creatinine levels were among the strongest predictors of mortality in COVID-19 patients admitted to hospital.[12] Likewise, research by Assal et al. (2022) also reported that COVID-19 was more serious and was associated with higher mortality in those with increased TLC, D-dimer, CRP, renal impairment, respiratory co-infections, and mechanical ventilation.[13] Whereas lymphopenia was prevalent in both groups, the mild increase amongst non-survivors was not statistically significant within the current study; nonetheless, a study by Cilloniz et al. (2021) has established lymphopenia to be a credible prognostic indicator that reflects immunosuppression caused by viral or secondary bacterial/fungal infections as having a critical effect on outcomes.[14]

Microbiologically, the most common isolates were Klebsiella pneumoniae and Pseudomonas aeruginosa, which are in line with other reports from around the world that find gram-negative bacteria to be foremost causes of hospital-acquired pneumonia among COVID-19 patients. Nevertheless, this study's most characteristic result was the significantly increased frequency of Aspergillus species among non-survivors (31.8% compared to 12.1%, p = 0.05). Fungal infections, especially invasive pulmonary aspergillosis, have been increasingly seen in critically immunocompromised COVID-19 patients, particularly those on corticosteroids or immunomodulators. One meta-analysis of COVID-19 patients by Chong et al. (2022) revealed that 17.5% developed COVID-19-associated pulmonary aspergillosis (CAPA),

with higher mortality (OR 2.63 significantly).[15] In the same manner, a study by Kluge et al. (2022) also indicated that invasive aspergillosis (IA) is becoming more frequently reported among ICU patients with severe COVID-19, sepsis, COPD, or liver failure.[16] This serves to emphasize the need for early fungal diagnostics and antifungal treatment in COVID-19 ICU management, particularly in resource-poor settings where diagnostic delays may prove to be deadly.

Given the high burden on healthcare systems, the results indicate an urgent requirement for more effective risk stratification, early antifungal and antimicrobial treatment, and enhanced resource distribution to critically ill COVID-19 patients with hospital-acquired infection. The information collected here can potentially contribute to the creation of tailored clinical protocols, enhance triage judgments, and inform antibiotic stewardship and infection control regulations in order to minimize mortality in subsequent pandemics or outbreaks caused by serious respiratory viruses.

Conclusion

This analysis emphasizes that patients with COVID-19 who develop hospital-acquired pneumonia are significantly more likely to die when they are older, have chronic kidney disease, need ICU treatment or mechanical ventilation, and exhibit high levels of inflammatory and renal biomarkers. It was observed that Aspergillus species was significantly more common among non-survivors, highlighting the critical role of fungal coinfections in deteriorating outcomes. These results highlight the importance of early detection of high-risk patients, early use of proper antimicrobial and antifungal therapy, and enhanced infection control measures to limit mortality, particularly in resource-limited healthcare facilities.

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