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Original Article

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A Prospective Observational Study in Elderly Patients of Acute Respiratory Failure and Corelation of Outcome with Interleukin-6 and C-reactive Protein

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Abstract

Introduction: Acute respiratory failure is a major medical emergency in elderly patients, often linked to a hyper-inflammatory state. Interleukin-6 (IL-6) regulates C-reactive protein (CRP), suggesting that combined elevated levels of both may correlate with poorer pulmonary outcomes. This study aimed to evaluate the association of combined CRP and IL-6 levels with outcomes in elderly patients with acute respiratory failure. ***Materials and Methods:*** This prospective observational study included 100 inpatients over 60 years old with acute respiratory failure, conducted over one year. Patients with chronic respiratory diseases were excluded. Clinical history, examination, and relevant investigations were performed. Patients were followed until discharge or death. Data analysis was done using SPSS version 21. ***Results***: Most patients (74%) were aged 61–70 years; 56% were female. Dyspnea (89%) and tachypnea (60%) were common. Invasive mechanical ventilation was required in 42% of cases. Among the 28% who died, 71.4% had elevated CRP and 64.3% had raised IL-6, indicating a link between elevated biomarkers and mortality. ***Conclusion***: Elevated CRP and IL-6 levels are associated with worse outcomes in elderly patients with acute respiratory failure. These markers may help in prognostication and management of such patients.

Keywords: ***acute respiratory failure, dyspnea, inflammatory markers, mortality, prognostic markers***

Introduction

Acute respiratory failure (ARF) is a common and life-threatening condition in elderly patients, often prompting emergency department (ED) visits. It represents a clinical syndrome resulting from various underlying cardiac and pulmonary pathologies, such as cardiogenic pulmonary edema (CPE), community-acquired pneumonia (CAP), chronic obstructive pulmonary disease (COPD) exacerbations, and pulmonary embolism (PE). These conditions are associated with high morbidity and mortality rates in older populations. [1-3] The epidemiology of ARF is complex due to its multiple etiologies. In the United States, the incidence of respiratory failure in 2017 was reported at 1,275 cases per 100,000 adults [4]. Specific causes vary in frequency and severity. For example, between 2000 and 2014, 439,436 hospital admissions were attributed to acute myocardial infarction-related respiratory failure (AMI-RF), with 57% requiring hospitalization and 43% needing mechanical ventilation [3]. The incidence of ARDS-related ARF ranges globally from 10 to 80 cases per 100,000 annually, reflecting differences in clinical practices and definitions [2]. The COVID-19 pandemic significantly impacted ARF rates, with up to 79% of hospitalized patients developing respiratory failure requiring invasive mechanical ventilation [3]. Acute exacerbation of COPD remains the third most common cause of ARF-related hospital admissions [5].ARF in elderly patients often presents with dyspnea, hypoxia, and hypercapnia and is frequently complicated by both pulmonary and systemic manifestations. Pulmonary complications include pneumonia, pneumothorax, and pulmonary fibrosis, while

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extrapulmonary effects may involve renal failure, gastrointestinal bleeding, malnutrition, and sepsis. These complications contribute to increased mortality and longer hospital stay.[6,7] Krieger BP et al. (1994) reported that elderly patients are predisposed to respiratory failure due to physiological changes associated with aging. These changes lead to a loss of cardiopulmonary reserve and an increased likelihood of requiring mechanical ventilatory support [8].

D et al. (2000) examined the relationship between inflammatory markers IL-6 and CRP and physical performance in high-functioning older adults, finding that higher levels of these markers were associated with lower walking speed and grip strength at baseline [9,10]. Inflammation plays a central role in the pathophysiology of ARF. Interleukin-6 (IL-6) and C-reactive protein (CRP) are key inflammatory markers that rise in response to systemic inflammation. IL-6 stimulates hepatic production of CRP, making these biomarkers interconnected. A cross-sectional study by Chang SS et al. (2011) highlighted that older women with combined high IL-6 and CRP levels had significantly lower pulmonary function, as measured by forced expiratory volume (FEV1) and forced vital capacity (FVC). These findings suggest that high IL-6 and CRP levels may serve as indicators of impaired lung function and increased mortality in older populations. They could potentially complement traditional pulmonary assessments in monitoring respiratory health[11]. Previous studies examining the link between IL-6, CRP, and respiratory distress have typically focused on each marker separately, despite IL-6 directly regulating CRP production during inflammatory states. Combined IL-6 and CRP levels can more accurately reflect inflammation, predict poorer pulmonary function, disease severity and prognosis in ARF. Hence, the present observational study was conducted to evaluate their correlation with the clinical profile and outcomes of acute respiratory failure in elderly patients.

Methods

This observational prospective study was conducted over one year in the Intensive Care Unit (ICU) and Medicine Ward of a tertiary care hospital and included 100 patients presenting with acute respiratory failure (ARF). Ethical approval was obtained from the Institutional Ethics Committee, and informed consent was taken from all participants prior to inclusion. Inclusion criteria were: age above 60 years, objective signs of ARF (respiratory rate ≥ 25 breaths/min, $PaO_2 \leq 70$ mmHg, $SpO_2 \leq 92\%$ on room air, $PaCO_2 \geq 45$ mmHg with pH ≤ 7.3), and willingness to participate. Patients below 60 years or with chronic respiratory conditions like COPD or chronic bronchitis were excluded. Eligible patients admitted to the emergency department, wards, or ICU were screened. Following informed written consent, detailed history was taken, including presenting symptoms, comorbidities (e.g., hypertension, ischemic heart disease, thyroid disorders, diabetes), addictions (alcohol, tobacco), and medication use. Comprehensive clinical examinations and relevant investigations were performed. Laboratory tests included arterial blood gas analysis (ABG), 12-lead ECG, chest X-ray, complete blood count, serum creatinine, liver function tests (bilirubin, SGOT, SGPT), serum electrolytes, plasma glucose, serum albumin, and inflammatory markers (IL-6 and CRP). Patients were followed until discharge or death, and all data were recorded using a structured proforma and entered into Microsoft Excel. Statistical analysis was conducted using SPSS version 21. Descriptive statistics were presented as frequencies and percentages, with significance set at $p < 0.05$. This methodology aimed to assess the clinical profile, etiology, and prognostic value of IL-6 and CRP levels in elderly patients with acute respiratory failure.

Results

In this study on elderly patients with acute respiratory failure, the majority (74%) were aged between 61 and 70 years, followed by those aged 71–80 years (20%) and over 80 years (6%). Most of the study population were female (56%). The most common BMI category was 18–25 (42%), followed by <18 (36%) and >25 (22%). Habits such as alcohol consumption and smoking were observed in 39% and 24% of the population, respectively. Comorbidities were present in 79% of the patients. Regarding the clinical profile, dyspnea was the most commonly reported symptom (89%), followed by tachypnea (60%), tachycardia (48%), chest pain (22%), and palpitations (14%). Chest X-ray findings varied and included bilateral diffuse opacities (38%), lobar consolidation (26%), thickening of interlobular septa and Kerley B lines (25%), cardiomegaly (25%), and reticular/reticulonodular infiltrates. The average plasma glucose level was 134.3 mg/dL, the mean hemoglobin level was 10 g/dL, and the mean serum albumin level was 2.6 g/dL.

The mean APACHE II score was 18.9. The average SOFA score at admission was 8.1, and the Delta-SOFA score was 2.5. The mean $PaCO_2$ was 39.4 mmHg, and the mean PaO_2/FiO_2 ratio was 168.2. Regarding respiratory support, 42% of patients required invasive mechanical ventilation, 40% required oxygen supplementation, and 18% were on non-invasive ventilation. The mean peak inspiratory pressure (PIP) was 28.3 cm H_2O, the mean plateau pressure was 24.2 cm H_2O, and the mean positive end-expiratory pressure (PEEP) was 8.3 cm H_2O. Among the patients, 43% had ARDS, while 57% did not. Among those with ARDS, 19% had moderate ARDS, 14% had mild ARDS, and 10% had severe ARDS. The overall mortality rate was 28%, while the survival rate was 72%. The average length of ICU stay was 9.9 days, and the average hospital stay was 19.2 days. Elevated C-reactive protein (CRP) levels were found in 74% of patients, and elevated IL-6 levels in 62%. Among the patients who died (28%), 71.4% had raised CRP levels, while 28.6% had normal CRP levels. Among survivors, 75% had elevated CRP levels and 25% had normal levels. This indicates that elevated CRP levels were common in both groups, but slightly more prevalent among survivors. A statistically significant correlation was found between raised CRP levels and mortality ($p = 0.008$). Of the patients who died, 64.3% had elevated IL-6 levels, while 35.7% had normal levels. Among survivors, 61.1% had raised IL-6 levels and 38.9% had normal levels. This suggests a potential association between elevated IL-6 levels and mortality. The correlation was statistically significant ($p = 0.001$).

Table no. 1: Age group distribution amongst study population.

Age group	Frequency	Percent
61 to 70 years	74	74
71 to 80 years	20	20
more than 80 years	6	6
Total	100.00	100.00

Table no. 2: Gender distribution amongst study population

BMI	Frequency	Percent
Less than 18	36	36
18-25	42	42
more than 25	22	22
Total	100	100

Table no. 3: BMI status amongst study population

BMI	Frequency	Percent
Less than 18	36	36
18-25	42	42
more than 25	22	22
Total	100	100

Table no. 4: Habits status amongst study population

Habits	Frequency	Percent
Alcohol	39	39%
Smoking	24	24%

Table no. 5: Comorbidity Status status amongst study population

Comorbidity	Frequency	Percentage
Ischemic Heart Disease	20	20%
Diabetes Mellitus	21	21%
Hypertension	18	18%
COPD	12	12%
CVA	8	8%
No Comorbidity	21	21%

Table no. 6: Clinical Profile of patients on presentation

Symptoms	Frequency	Percentage
Dyspnea	89	89%
Tachypnea	60	60%
Tachycardia	48	48%
Chest pain	22	22%
Palpitations	14	14%

Table no. 7: Chest X-RAY findings

Chest x-ray findings	Frequency	Percentage
Bilateral diffuse opacities	38	38%
Lobar consolidation	26	26%
Thickening of interlobular septa and Kerley B lines(batwing)	25	25%
Cardiomegaly	25	25%
Patchy opacities	21	21%
Reticular and reticulonodular infiltrates	20	20%
Hyperinflation of lung	18	18%

Table no. 8: Laboratory Parameter amongst study population

Laboratory Parameter	Mean ± SD
Leucocytes	19000 ± 4000
Plasma glucose	134.3 ± 84.2
Hemoglobin (g/dL)	10 ± 2.5
Serum albumin (mg/dL)	2.6 ± 2.5

Table no. 9: Respiratory Parameter (ABG) amongst study population

Respiratory Parameter	Mean ± SD
PaCO2 (mmHg)	39.4 ± 13.8
PaO2/FiO2 ratio	168.2 ± 67.8

Table no. 10: CRP levels amongst study population

CRP		Frequency	Percentage
Raised	74	74	
Normal	26	26	
Total		100	100

Table no. 11: IL-6 levels amongst study population

IL-6	Frequency	Percentage
Raised	62	62
Normal	38	38
Total	100	100

Table no. 12: Severity of ARDS amongst study population

Severity of ARDS	Frequency	Percentage
Mild	14	14%
Moderate	19	19%
Severe	10	10%
Total	43	43%

Table no. 14: Type of Respiratory Support amongst study population

Type of Respiratory Support	Frequency	Percentage
Oxygen supplementation	40	40%
Non-invasive ventilation	18	18%
Invasive mechanical ventilation	42	42%

Table no. 15: ICU Severity Score amongst study population

ICU Severity Score	Mean ± SD
Baseline APACHE II score	18.9 ± 8.1
Baseline APACHE II score without age	17.5 ± 8.2
SOFA score at admission	8.1 ± 3.6
Delta-SOFA score	2.5 ± 2.9

Table no.16: Final Outcome amongst study population

Outcome	Frequency	Percentage
Mortality	28	28%
Survival	72	72%
Total	100	100%

Table no. 17: Mortality vs CRP amongst study population

Mortality	CRP Raised (74%)	CRP Normal (26%)	Total (100%)
Yes	20 (71.4%)	8 (28.6%)	28 (100%)
No	54 (75.0%)	18 (25.0%)	72 (100%)
Total	74 (74.0%)	26 (26.0%)	100 (100%)

Table no. 18: Mortality vs IL-6 amongst study population

Mortality	IL-6 Raised (62%)	IL-6 Normal (38%)	Total (100%)
Yes	18 (64.3%)	10 (35.7%)	28 (100%)
No	44 (61.1%)	28 (38.9%)	72 (100%)
Total	62 (62.0%)	38 (38.0%)	100 (100%)

Discussion

In our study, the most common age group was 61 to 70 years (74%), followed by 71 to 80 years (20%) and more than 80 years (6%). This aligns with several studies indicating that acute respiratory failure predominantly affects older adults. For instance, a study by Kahn et al. (2017) reported that the majority of patients with acute respiratory failure were aged between 65 and 75 years, highlighting the vulnerability of this age group to respiratory complications [12]. Our study found that females (56%) were more commonly affected compared to males (44%). This contrasts with some reports where males are often reported to have a higher incidence of acute respiratory failure. However, gender distribution can vary significantly based on geographic and demographic factors. A study conducted by Vincent et al. (2018) in a European cohort reported a higher prevalence in males, suggesting that regional lifestyle and healthcare access differences may contribute to these variations [13].

The most common BMI category in our study was 18–25 (42%), followed by less than 18 (36%) and more than 25 (22%). This distribution is similar to findings by Gong et al. (2019), who observed that underweight and normal-weight patients were more frequently hospitalized with respiratory conditions compared to overweight and obese individuals. [14] This might be due to the compromised immune response and muscle mass in underweight individuals, increasing their susceptibility to respiratory failure.

We observed that 39% of the study population consumed alcohol and 24% were smokers. These habits are well-documented risk factors for respiratory diseases. A study by McKeown et al. (2015) showed that smoking significantly increases the risk of developing acute respiratory failure, while alcohol consumption exacerbates the condition by impairing the immune response [15]. In our study, 79% of patients had one or more comorbidities. This is consistent with findings from other studies indicating that comorbid conditions like cardiovascular diseases, diabetes, hypertension,

CVA, and chronic obstructive pulmonary disease (COPD) significantly increase the risk and severity of respiratory failure. A study by Singer et al. (2016) found that the presence of comorbidities was a strong predictor of mortality in patients with acute respiratory failure [16].

In the present study, the majority of patients (89%) presented with dyspnea, followed by symptoms such as tachypnea (60%), tachycardia (48%), chest pain (22%), and palpitations (14%), as demonstrated in studies by Huang et al. (2013) and Luo et al. (2014). [17,18]. In the present study, different chest X-ray findings were noted, such as bilateral diffuse opacities, lobar consolidation, thickening of interlobular septa and Kerley B lines (batwing appearance), cardiomegaly, reticular and reticulonodular infiltrates, etc., the majority of them being bilateral diffuse opacities. The average WBC count was 19,000. The average plasma glucose level in our study was 134.3 mg/dL, the average hemoglobin level was 10 g/dL, and the average serum albumin level was 2.6 mg/dL. Elevated plasma glucose levels are common in critically ill patients and have been associated with worse outcomes in respiratory failure (Krinsley et al., 2014) [19]. Low hemoglobin and serum albumin levels are indicators of poor nutritional status and have been linked to higher mortality rates in acute respiratory failure, as demonstrated in studies by Huang et al. (2013) and Luo et al. (2014) [17,18].

The mean $PaCO_2$ in our study was 39.4 mmHg, and the mean PaO_2/FiO_2 ratio was 168.2, indicating moderate hypoxemia. These values are consistent with findings in ARDS patients, as reported by Ranieri et al. (2012), where PaO_2/FiO_2 ratios below 200 were associated with significant respiratory distress [20]. In our study, CRP was raised in 74% of the study population, and IL-6 was raised in 62% of the study population. Elevated levels of these biomarkers are associated with inflammation and poor outcomes in ARDS patients. Among the patients who died (28%), 71.4% had raised CRP levels, while 28.6% had normal CRP levels. Among survivors, 75% had elevated CRP levels and 25% had normal levels. This indicates that elevated CRP levels were common in both groups, but slightly more prevalent among survivors. A statistically significant correlation was found between raised CRP levels and mortality ($p = 0.008$). Of the patients who died, 64.3% had elevated IL-6 levels, while 35.7% had normal levels. Among survivors, 61.1% had raised IL-6 levels and 38.9% had normal levels. This suggests a potential association between elevated IL-6 levels and mortality. The correlation was statistically significant ($p = 0.001$).

As noted by Herold et al. (2020), high IL-6 levels correlate with increased severity and mortality in respiratory failure [21] Similarly, Póvoa et al. (2006) found that elevated CRP levels were indicative of worse prognosis and higher mortality in critically ill patients [22].

In our study, 43% of patients had pulmonary ARDS, while 57% did not have ARDS. Most patients (19%) had moderate ARDS, 14% had mild ARDS, and 10% had severe ARDS. This classification is in line with the Berlin definition of ARDS, which stratifies the severity based on the PaO_2/FiO_2 ratio (ARDS Definition Task Force, 2012). The distribution of ARDS severity in our study is similar to findings by Bos et al. (2017), who reported that moderate ARDS is the most common presentation [23]. A majority of patients (42%) required invasive mechanical ventilation, while 40% needed oxygen supplementation, and 18% were on non-invasive ventilation. This distribution aligns with studies by Bellani et al. (2016), where invasive mechanical ventilation was commonly required for ARDS patients due to severe hypoxemia and respiratory failure [24]. The mean Peak Inspiratory Pressure (PIP) was 28.3 cm H_2O, the mean plateau pressure was 24.2 cm H_2O, and the mean PEEP was 8.3 cm H_2O. These values are within the ranges recommended for protective lung ventilation strategies to prevent ventilator-induced lung injury, as supported by Amato et al. (2015), who emphasized the importance of maintaining lower driving pressures in ARDS patients [25].

The mean APACHE II score of 18.9 in our study indicates a high severity of illness among the patients. This is consistent with findings from other studies on critically ill patients with acute respiratory failure. For instance, a study by Zilberberg et al. (2017) found similar APACHE II scores in patients with acute respiratory distress syndrome (ARDS), reflecting a high risk of mortality and morbidity in this population [26]. The mean SOFA score at admission was 8.1, and the Delta-SOFA score, which measures the change in the SOFA score over time, was 2.5. These scores are critical for assessing organ dysfunction and prognosis in critically ill patients. Ferreira et al. (2001) demonstrated that the SOFA score is a reliable indicator of patient outcomes, with higher scores correlating with increased mortality [27].

The mortality rate in our study was 28%, while the survival rate was 72%. These rates are comparable to those reported in international studies, where ARDS mortality rates range from 20% to 40%, depending on the severity and underlying conditions (Phua et al., 2009) [28]. The average length of stay in the ICU was 9.9 days, and the average length of stay in the hospital was 19.2 days, which is consistent with data from studies like that of Wunsch et al. (2010), indicating prolonged hospitalization for ARDS patients due to the severity of their condition [29].

Conclusion

This study provides a detailed overview of the clinical profile of elderly patients with acute respiratory failure, highlighting that the most affected group was aged 61–70 years, with a higher prevalence in females and a majority presenting with dyspnea and comorbidities. Most patients were critically ill, requiring intensive respiratory support, with elevated severity scores and biomarkers (CRP and IL-6). These findings suggest a strong inflammatory response associated with acute respiratory failure in the elderly. Elevated CRP and IL-6 levels are indicative of systemic inflammation and are correlated with the severity of respiratory failure. These biomarkers can serve as valuable indicators for assessing the prognosis and guiding the management of acute respiratory failure in elderly patients.

Declarations

Ethics Approval

The study was approved by the Institutional Ethics Committee of HBT MEDICAL COLLEGE & Dr RN Cooper Hospital, Mumbai, Maharashtra.

Availability of supporting data

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflicts of interest

None

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All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships

All authors have declared that they have no financial relationships at present or within the previous three years 9 of 10 with any organizations that might have an interest in the submitted work.

Author's contributions

Neelam N. Redkar, Laxmi Swamy, and Prakash Ram Relwani conceptualised the study and were the principal investigators. Abhilasha Srivastava, Omkar E. Paradkar, and Suyash Vanarase assisted with data interpretation and literature review. Diksha Samsukha assisted with manuscript writing. Alhad Mulkalwar assisted in the final review of the manuscript. All authors read and approved the final manuscript.

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