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Original Research Article

Etiology, clinical profile, and outcomes of acute respiratory distress syndrome in a tertiary care hospital in Kerala: A cross-sectional study

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Abstract

Background: Acute Respiratory Distress Syndrome (ARDS) is a severe lung condition associated with high morbidity and mortality. There are regional variations in the causes and outcomes of ARDS, which are also influenced by patient demographics and underlying health conditions. This study aimed to identify ARDS etiologies in a tertiary care hospital in Kerala and evaluate clinical factors influencing patient outcomes, focusing on mortality predictors.

Materials and Methods: A cross-sectional study was conducted between September 2019 and June 2021 at a tertiary care hospital in Kerala, including 62 patients diagnosed with ARDS per the Berlin criteria. Data on demographics, clinical history, comorbidities, and outcomes were collected. Investigations included chest X-rays, echocardiograms, and arterial blood gas analysis. Statistical analysis was performed using IBM SPSS, with logistic regression to assess mortality predictors.

Results: Among the 62 patients, 58.1% were male, and the majority (56.5%) were aged 56-75 years. COVID-19 (51.6%) was the most common cause of ARDS, followed by Leptospirosis (22.6%) and H1N1 pneumonia (8.1%). The overall mortality rate was 37.1%. Older age, severe ARDS (PaO_2/FiO_2 ratio <100), high qSOFA scores, and the need for invasive mechanical ventilation were significant predictors of mortality. Patients with mild ARDS had a 93.8% survival rate, while those with severe ARDS had a mortality rate of 76.5%.

Conclusions: ARDS outcomes in this study population reflected the global burden of the disease, with infectious causes, particularly COVID-19, playing a dominant role. Mortality was highest in older patients with comorbidities, severe ARDS, and those requiring invasive ventilation. Early intervention, based on key prognostic markers, is essential for improving outcomes.

Keywords: ARDS, Covid-19, Mortality, PaO_2/FiO_2 ratio, qSOFA score, Mechanical ventilation.

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1. Introduction

Acute Respiratory Distress Syndrome (ARDS) represents a significant and prevalent contributor to respiratory failure in critically ill patients. Characterized by the rapid onset of non-cardiogenic pulmonary edema, ARDS is accompanied by severe hypoxemia and often necessitates mechanical ventilation to support respiratory function.[1] ARDS has become a significant cause of morbidity and mortality among patients admitted to intensive care units (ICUs) globally. Acute respiratory distress syndrome is a rapidly progressive form of respiratory failure, accounting for 10% of ICU admissions, and is associated with a mortality rate of approximately 40% in severe cases. Although ARDS is associated with high mortality and poses a substantial burden on healthcare systems, its management mainly relies on supportive care, with a focus on maintaining oxygenation and organ function.[2]

ARDS is defined by a clear clinical framework by Berlin definition, which categorizes distinct stages to assess mortality risk. However, despite this structured classification, no diagnostic test is available to confirm or exclude ARDS definitively. This lack of a universal diagnostic marker highlights the heterogeneity of ARDS, which is evident in its

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diverse causes, clinical presentations, and varied responses to treatment.[3]

The etiology of acute respiratory distress syndrome (ARDS) is multifactorial, involving both infectious and non-infectious factors. Common triggers include pneumonia (bacterial and viral), nonpulmonary sepsis from sources like the peritoneum and urinary tract, aspiration of gastric contents, and major trauma, including blunt injuries and burns. Less common causes encompass acute pancreatitis, transfusion-related lung injury (TRALI), drug overdoses, near-drowning, hemorrhagic shock, and smoke inhalation.[1] Infectious agents, particularly pneumonia and sepsis, lead to increased permeability of the alveolar-capillary membrane, resulting in pulmonary edema and impaired gas exchange. Non-infectious factors such as aspiration and trauma also contribute to ARDS development. Understanding these diverse etiological factors is crucial, as regional variations can significantly impact clinical outcomes and treatment approaches.[1] The onset of the COVID-19 pandemic has significantly impacted the clinical presentation and outcomes of patients with ARDS. The widespread incidence of COVID-2019 has led to a marked rise in ARDS cases, characterized by a reduced heterogeneity compared to traditional multietiologic ARDS populations; however, substantial variability in physiological responses and clinical outcomes persists.[4] This pandemic has highlighted the formidable challenges associated with ARDS, including its alarmingly high mortality rates and the urgent need for effective pharmacological interventions.[3]

Increased understanding of ARDS in clinical settings is important for early patient identification, enabling the timely application of lung-protective ventilation and conservative fluid management.[1] Targeted research initiatives are key to improving prognostic accuracy and clinical outcomes. Using prognostic and predictive improvement strategies that combine biological markers with clinical variables in randomized trials could help identify specific patient subsets most likely to benefit from tailored interventions, thereby advancing ARDS management.

The etiology, mortality, and factors contributing to mortality are different in different populations and have changed over time. We conducted a cross-sectional study to identify the etiologies of ARDS in patients admitted to a tertiary care hospital in Kerala. Additionally, the study aims to evaluate clinical factors that influence the prediction of outcomes, with the goal of improving early identification of these predictors. Early recognition of such factors may lead to improved management strategies and better clinical outcomes for patients with ARDS in this region.

2. Materials and Methods

2.1. Study design and ethical considerations

This was a cross-sectional study conducted at Lourdes Hospital, a tertiary care hospital in Kochi, Kerala, during the period from September 2019 to June 2021. The study was approved by the Institutional Ethics Committee (IEC) (Approval no. LH/EC/2019; dated Aug 29, 2019). The study was conducted as per the International Council on Harmonization (ICH) guidelines for Good Clinical Practice. Patients and their caretakers were explained the details of the study objectives. Written informed consent was obtained from all participating patients or their caretakers in their vernacular language prior to their inclusion in the study.

2.2. Study population

Adolescents (12-17 years of age) and adults (≥18 to 75 years of age) who were admitted to the hospital, who met the 'Berlin Definition Criteria' of ARDS, and who were willing to participate in the study were included in the study.

Patients with chronic kidney disease and coronary artery disease were excluded from the study. Other exclusion criteria included patients with aspirated gastric contents, severe burns or toxic gas inhalation, near drowning, blunt chest trauma, multiple long bone fractures, fat embolism, obstetric crises, amniotic fluid embolism, or known carcinomatosis. Patients who were under drugs like Heroin, Barbiturates, and Thiazides were also excluded from the study.

According to the sample size analysis, a minimum of 42 patients were planned to be included in the study.

2.3. Data collection

The clinical history, including the duration of symptoms and disease onset, was obtained from either the patient or their caregivers. Additional clinical data relevant to the study were gathered using a structured proforma. The investigator utilized this proforma to document the patient's clinical profile and track their progress throughout the hospital stay.

The study required several key investigations to support the analysis, including Chest X-rays, SpO_2 monitoring, and echocardiograms (ECHO). A Chest X-ray was routinely performed at the time of admission for all patients with ARDS, and SpO_2 monitoring was used to assess oxygen saturation. Echocardiograms were routinely conducted to rule out a cardiogenic cause of pulmonary edema. In addition, arterial blood gas (ABG) analysis was used to obtain the partial pressure of oxygen in arterial blood (PaO_2) value, while the fraction of inspired oxygen (FiO_2) and positive end-expiratory pressure (PEEP) settings were recorded from the ventilator. The diagnostic criteria for ARDS were met using these routine tests without imposing any additional investigative procedures on the patients.

2.4. Study outcomes

The etiology of ARDS in each case was identified and recorded, with special efforts made to document the underlying cause accurately. Data were also collected on the incidence of ARDS across various age groups and between males and females. The most common etiologies leading to ARDS were determined, along with an analysis of the factors that contributed to increased mortality.

The study further explored mortality rates in different age groups and examined additional risk factors associated with poor outcomes. Finally, the results were compared with findings from other national and international studies to contextualize the data and highlight any regional differences in ARDS etiology and outcomes.

2.5. Study analysis

The collected data were analyzed using IBM SPSS Statistics software, version 25. Qualitative variables were summarized using frequencies and percentages. The Chi-Square Test was applied to assess the association between qualitative variables. For quantitative variables, means and standard deviations were used to describe the data. The T-test was used to determine the association between quantitative variables and qualitative outcomes, such as recovery or death. Logistic regression analysis was conducted to evaluate the predictors of mortality. The results were expressed as odds ratios with 95% confidence intervals. A p-value of less than 0.05 was considered statistically significant for all analyses.

3. Results

3.1. Demographic and clinical characteristics of ARDS patients

3.1.1. Sex predilection in the distribution of ARDS

Among the 62 patients included in this study, 58.1% were male, and 41.9% were female (**Table 1**), highlighting a higher prevalence of ARDS among males.

3.1.2. Incidence of ARDS in different age groups

When the patients were stratified according to age (**Table 1**), the first cohort included five patients aged 15-35 years, the second comprised 22 patients aged 36-55 years, and the third consisted of 35 patients aged 56-75 years. More than half of the studied population was grouped in the age group of 56-75 years.

3.1.3. Categorization based on Berlin's criteria

The distribution of ARDS severity at admission revealed that 25.8% of patients fell into the mild category, 46.8% were classified as moderate, and 27.4% were categorized as severe (**Table 1**).

3.1.4. Common etiologies of ARDS

In this study population, the most common etiology of ARDS reported was Covid-19 pneumonia (56.6%), followed by Leptospirosis (28.6%) and H1 N1 viral pneumonia (8.2%). Other associated etiologies were *Escherichia coli* sepsis, *Staphylococcus hemolytic* sepsis, bronchopneumonia of unknown cause, acute pancreatitis, and undiagnosed conditions (**Table 1**).

Analysis of different ARDS etiologies and severity of ARDS at admission, based on the Berlin criteria, revealed varying severity patterns (**Table 2**). Among patients diagnosed with COVID-19, 56.3% had moderate ARDS, 21.9% had severe disease, and the remainder had mild ARDS. In the leptospirosis group, 35.7% presented with mild ARDS, 14.3% with moderate ARDS, and the rest had severe ARDS at admission. For H1N1 viral pneumonia, 60% had severe ARDS, while 20% each fell into the mild and moderate categories.

3.1.5. Comorbidities associated with ARDS

In our study cohort, type 2 diabetes mellitus was the most common comorbidity, affecting 65.2% of patients (**Table 1**). Other major comorbidities included hypertension in 35.5% and dyslipidemia in 12.2% of patients. Some patients also presented with various combinations of these three comorbidities. Interestingly, none of the patients had coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), or chronic liver disease (CLD).

3.1.6. Usage of intravenous steroids and other medications

All patients diagnosed with COVID-19 and H1N1 pneumonia received intravenous corticosteroids, irrespective of their qSOFA scores or lung injury severity. In patients with Leptospirosis and sepsis due to bacterial infections, intravenous steroids were used in case of septic shock. Additional treatment modalities were implemented according to evolving clinical guidelines during the pandemic. These included the use of antiviral agents such as Remdesivir, supplementation with zinc and vitamin C, and administration of monoclonal antibodies targeting SARS-CoV-2 in eligible COVID-19 patients. All patients with H1N1 pneumonia were treated with Oseltamivir as part of the standard antiviral therapy protocol.

3.2. Outcome in ARDS patients and prognostic value of clinical parameters

Outcome analysis revealed a mortality rate of 37.1% in the study population, while 62.9% of patients recovered and were discharged after treatment (**Table 3**).

3.2.1. Gender as a predictor of outcomes in ARDS

In our study, the observed mortality rates were 41.7% in males and 30.8% in females (**Table 3**). Despite the higher mortality in males, statistical analysis using the Chi-square test revealed no significant association between sex and mortality outcomes (p=0.370).

3.2.2. Impact of age on outcomes in ARDS

Age-stratified analysis of clinical outcomes revealed significant variations in mortality and recovery rates across different age groups (**Table 3**). In the 15-35-year cohort, the mortality rate was observed to be 40%, indicating substantial vulnerability within this younger demographic. The 36-55-year group exhibited the most favorable outcomes, with a recovery rate of 72.7% and a corresponding mortality rate of 27.3%. Notably, the 56–75-year group demonstrated the highest mortality rate at 42.9%, while 57.1% of patients in this age range were discharged following successful recovery.

3.2.3. Severity category and PaO_2/FiO_2 ratio at admission as a predictor of outcomes in ARDS

Among patients classified as mild ARDS, 93.8% survived, with a mortality rate of 6.3%. In the moderate category, 31% of patients died, while 69% recovered. The severe group exhibited a 76.5% mortality rate, with only 23.5% of patients recovering (**Table 3**). The mean P/F ratio in patients who survived was 184.08 (±63.53), whereas the mean ratio in those who died was significantly lower at 103.72 (±38.96). Statistical analysis revealed that the difference between these groups was highly significant (p<0.0001).

3.2.4. Impact of etiologies on outcomes in ARDS

The mortality rates across different etiologies in this study showed significant variation (**Table 3**). COVID-19-associated pneumonia exhibited a mortality rate of 25%, with 75% of patients discharged after recovery. H1N1 viral pneumonia had a slightly lower mortality rate of 20%, with 80% of patients recovering. Leptospirosis and bronchopneumonia of unknown etiology presented an equally distributed outcome, with both mortality and recovery rates at 50%. Patients with acute pancreatitis and *Staph hemolyticus* sepsis, each represented by a single case, and all three undiagnosed patients succumbed during hospitalization. In contrast, patients with *E. coli* urosepsis had a favorable outcome, with all three patients achieving complete recovery.

3.2.5. Impact of comorbidities on outcomes in ARDS

Distinct patterns in mortality were observed when the comorbidities were evaluated in relation to ARDS outcomes, although no statistically significant associations were found (**Table 3**). Diabetic patients exhibited a notably higher mortality rate than non-diabetic patients. Despite this apparent increase, the association between diabetes and mortality did not reach statistical significance (p=0.163), indicating that the difference could be due to random variation. Similarly, no significant association was observed (p=0.646) between the mortality rate among ARDS patients with or without systemic hypertension. Interestingly, patients with dyslipidemia had a lower mortality rate compared to those without dyslipidemia; however, this association also did not achieve statistical significance (p = 0.436). These findings suggest that while trends in mortality differences exist based on the presence of these comorbidities, no definitive correlations could be established in this cohort.

3.2.6. qSOFA score at the time of admission as a predictor of outcome of ARDS

In the studied patient population, 8.1% of patients had a qSOFA score of 0, 50% had a score of 1, 24.2% had a score of 2, and 17.7% had a score of 3. When these patients were grouped as per international guidelines, 58.1 % of patients came under the scoring group 0 or 1, and the rest, 41.9 %, came under scoring group 2-3 (**Table 4**).

In the 0-1 score group, 88.1% of patients recovered, with a mortality rate of only 11.9%. In contrast, the 2-3 score group had a starkly higher mortality rate of 73.1%, with just 11.1% of patients achieving recovery. Statistical analysis revealed a significant correlation between qSOFA scores at admission and mortality outcomes. The mean qSOFA score among patients who died was 2.22, compared to 1.10 in those who recovered. The difference in mean scores was highly significant (p<0.0001), highlighting the prognostic value of the qSOFA score in predicting patient outcomes (**Table 4**).

3.2.7. Glasgow coma scale as a contributor to qSOFA score

Upon evaluating the Glasgow Coma Scale (GCS) scores at the time of admission, 62.9% of patients presented with a normal GCS, while 6.5% exhibited mild brain injury (GCS 13-14), 25.8% had moderate brain injury (GCS 9-12), and 4.8% were classified as having severe brain injury (GCS 3-8).

3.2.8. Lung injury score at the time of admission as a predictor of outcome of ARDS

Lung injury score (LIS) at admission and outcome of ARDS are presented in **Table 5**. In our study population, mortality was highest (52.2%) at the most severe lung injury score (3.66), whereas no deaths occurred at the lowest score (2.50), where recovery was most common (38.5%).

The analysis of LIS showed a significant difference between patients who recovered and those who died, with mean LIS values of 2.86 (±0.46) and 3.19 (±0.58), respectively (p = 0.016). A higher LIS at admission strongly correlated with poorer outcomes, with scores above 3.20 predicting mortality and below 2.86 indicating a better prognosis. Notably, an LIS of 3.66 or higher was linked to a significantly increased risk of death. Regression analysis with mortality as the dependent variable showed that both metrics had equal predictive value, with no statistically significant differences ($p > 0.05$).

3.2.9. Respiratory assistance at the time of admission as a predictor of outcome in ARDS

All patients required respiratory support at admission through oxygen masks, non-invasive ventilation (NIV), or invasive mechanical ventilation (IMV). Among those on IMV (10 patients), the mortality rate was 100%. In the NIV group (24 patients), 58.3% survived, while 41.7% died (**Table 6**).

Of the patients on oxygen masks (28 patients), 89.3% survived. A significant correlation ($p<0.05$) was found between the type of respiratory support and outcomes, with invasive ventilation linked to the highest mortality rate (**Table 6**). The requirement of mechanical ventilation in the form of NIV or invasive ventilation during the hospital stay was also studied (**Table 7**).

Patients who only needed oxygen via a mask had 0% mortality. Among the 18 patients who used both NIV and oxygen therapy, mortality was also 0%. However, for patients requiring both NIV and invasive ventilation (n=16), mortality was 68.8%, with 31.2% successfully weaned and discharged. All 12 patients exclusively on invasive ventilation had 100% mortality. In total, 28 patients (45.16%) required invasive mechanical ventilation.

3.2.10. Duration of hospital stay as a predictor of outcome of ARDS

We categorized the patients based on their hospital stay into three groups: 0-10 days, 11-20 days, and 21-30 days (**Table 8**). The first group had a high mortality rate of 51.4%, compared to 15.8% in the second group and 16.7% in the third group, indicating a significant decrease in mortality after ten days ($p=0.014$).

3.2.11. ICU stay as a predictor of outcome in patients with ARDS

A total of 36 patients in our study required ICU admission. In evaluating the duration of ICU stay among patients with ARDS, ICU stay was stratified into two cohorts based on the mode of ventilation used: those receiving invasive mechanical ventilation (n=28) and those managed exclusively with NIV (n=18). Patients in the invasive mechanical ventilation group had an average ICU stay of 7.68 days, while those in the NIV group stayed an average of 6.67 days.

Table 1: Demographic parameters and clinical characteristics of ARDS patients

Demographic Parameters and Clinical Characteristics	Proportion of patients	
	N	**%**
Overall population	62	100.0%
Sex		
Male	36	58.1%
Female	26	41.9%
Age		
15-35 years	5	8.0%
36-55 years	22	35.5%
56-75 years	35	56.5%
Berlin's criteria		
Mild	16	25.8%
Moderate	29	46.8%
Severe	17	27.4%
Common etiologies of ARDS		
Acute Pancreatitis	1	1.6%
Broncho pneumonia, unknown etiology	2	3.2%
Covid-19	32	51.6%
E. Coli Sepsis	3	4.8%
H1 N1 Viral Pneumonia	5	8.1%
Leptospirosis	14	22.6%
Staph hemolytic sepsis	2	3.2%
Undiagnosed	3	4.8%

Table 2: Categorization of different etiologies causing ARDS based on P/F ratio

Diagnosis	Category		
	Mild	**Moderate**	**Severe**
Acute pancreatitis (n=1)	0.0%	0.0%	100.0%

Broncho pneumonia, unknown etiology (n=2)	0.0%	100.0%	0.0%
Covid-19 (n=32)	21.9%	56.3%	21.9%
E. Coli Sepsis (n=3)	33.3%	66.7%	0.0%
H1N1 Viral Pneumonia (n=5)	20.0%	20.0%	60.0%
Leptospirosis (n=14)	50.0%	35.7%	14.3%
Staph hemolytic sepsis (n=2)	0.0%	0.0%	100.0%

Table 3: Outcome in ARDS patients in terms of recovery and death

	Outcomes		**P value**
	Recovery	**Death**	
Overall population (N=62)	62.9%	37.1%	
Sex groups			
Male	58.3%	41.70%	0.370
Female	69.2%	30.8%	
Age groups			
15 to 35 years (n=5)	60.0%	40.0%	0.482
36 to 55 years (n=22)	72.7%	27.3%	
56 to 75 years (n=35)	57.1%	42.9%	
Berlin's criteria			
Mild (n=16)	93.8%	6.3%	<0.0001
Moderate (n=29)	69.0%	31.0%	
Severe (n=17)	23.5%	76.5%	
Etiologies			
Acute pancreatitis (n=1)	0.0%	100.0%	0.010
Broncho pneumonia, unknown etiology (n=2)	50.0%	50.0%	
Covid-19 (n=32)	75.0%	25.0%	
E. Coli Sepsis (n=3)	100.0%	0.0%	
H1N1 Viral Pneumonia (n=5)	80.0%	20.0%	
Leptospirosis (n=14)	50.0%	50.0%	
Staph hemolytic sepsis (n=2)	0.0%	100.0%	
Undiagnosed (n=3)	0.0%	100.0%	
Comorbidity status			
Diabetes mellitus not present (n= 23)	73.9%	26.1%	0.163
Diabetes mellitus present (n= 39)	56.4%	43.6%	
Hypertension not present (n= 40)	65.0%	35.0%	0.646
Hypertension present present (n= 22)	59.1%	40.9%	
Dyslipidemia not present (n= 54)	61.1%	38.9%	0.436
Dyslipidemia present (n= 8)	75.0%	25.0%	

Table 4: qSOFA Score at admission and outcome of ARDS

qSOFA Score	**Proportion of patients**		**Outcome**		**p-value**
	N	**%**	**Recovered**	**Death**	
0 to1	36	58.1%	88.9%	11.1%	<0.0001
2 to 3	26	41.9%	26.9%	73.1%	

Table 5: Lung injury score at admission and outcome of ARDS

Lung injury score	**Outcome**	
	Recovered	**Death**
2.50	38.5%	0.0%
2.66	7.7%	8.7%
3.00	25.6%	17.4%
3.33	15.4%	21.7%

3.50	5.1%	0.0%
3.66	7.7%	52.2%

Table 6: Need of respiratory assistance at the time of admission, need of invasive ventilation and outcomes in ARDS

Mechanical Ventilation	Outcomes		p-value
	Recovery	Death	
Need of respiratory assistance at the time of admission			
Invasive ventilation (n=10)	0.0%	100.0%	<0.001
NIV (n=24)	58.3%	41.7%	
O_2 mask (n=28)	89.3%	10.7%	
Need of invasive ventilation during hospital stay			
Invasive ventilation (n=12)	0.0%	100.0%	<0.001
NIL (n=16)	100.0%	0.0%	
NIV + Invasive ventilation (n=16)	31.3%	68.8%	
NIV (n=18)	100.0%	0.0%	

Abbreviations- NIV: Non-invasive ventilation

Table 7: Duration of hospital stay and outcome of ARDS

Duration of hospital stay	Outcomes		p-value
	Recovery	Death	
0 to10 days	48.6%	51.4%	0.014
11 to 20 days	84.2%	15.8%	
21 to 30 days	83.3%	16.7%	

Table 8: Duration of ICU stay and outcome of ARDS

	Outcome	%	Mean Duration of ICU stay (days)	p-value
Required Invasive ventilation (n=28)	Recovered	17.86%	13.20 ± 3.114	0.007
	Death	82.14%	6.48 ± 4.888	
Did not require invasive ventilation (n=18)	Recovered	100%	6.67 ± 3.395	-
	Death	0	0	

4. Discussion

This study analyzed a cohort of patients diagnosed with ARDS at a tertiary care center in Kerala, with the objective of identifying the underlying causes and key factors affecting their clinical outcomes. A total of 62 patients were included in the analysis. The results revealed a diverse range of etiologies contributing to ARDS. Notably, the analysis demonstrated a significant association between various demographic factors and outcomes, indicating that they play critical roles in the prognosis of ARDS patients.

Distribution of ARDS patients according to sex showed male predominance, which aligns with established trends in the epidemiology of ARDS. In the large-scale LUNG SAFE study, a prospective cohort analysis of 2,377 patients, 62% of the patients were male.[5] Similarly, a nationwide registry-based study from Taiwan, encompassing 40,876 ARDS cases, reported that 67.9% of cases occurred in males, further corroborating the higher incidence of ARDS in this demographic.[6]

To facilitate a more comprehensive analysis, patients in this study were stratified into three distinct age cohorts. A clear age-related trend emerged, with the incidence of ARDS progressively increasing across the cohorts. A similar trend has also been reported earlier by Manzano and coworkers with elevated incidence of ARDS in the elderly, suggesting a potential correlation between advancing age and susceptibility to ARDS.[7] These findings are further substantiated by a large-scale National registry-based study (n= 12,97,190), which documented the lowest incidence of ARDS among pediatric patients and a marked increase in incidence among adults aged 35-64.[8]

The Berlin Definition classifies the severity of hypoxemia in ARDS based on the PaO_2/FiO_2 (P/F) ratio, a key metric derived by dividing PaO_2 obtained through arterial blood gas analysis by FiO_2 delivered to the patient. This classification defines ARDS severity into three categories: mild (P/F ratio ≤300 mmHg), moderate (P/F ratio ≤200 mmHg), and severe (P/F ratio ≤100 mmHg).[9] In the present study, nearly 75% of patients were classified as moderate or severe, highlighting the significant burden of moderate-to-severe ARDS within our cohort.

Earlier published literature has listed various etiologies of ARDS. In the study by Bhadare and coworkers, the primary etiologies identified were malaria, Leptospirosis, and undiagnosed fever, followed by pneumonia and pancreatitis.[10] This trend is further supported by data from an epidemiological study from Manipal, India, which highlighted tropical infections, particularly malaria, as significant contributors to ARDS.[11] These results closely parallel our findings, with the key exception that while malaria was the most prevalent cause in their cohort, in our study, COVID-19 emerged as the leading etiology. In a study from a tertiary care center in North India, pneumonia (68%) and malaria (14%) were identified as the major causes of ARDS.[12] Similarly, a respiratory ICU study from the same region also reported pneumonia as the most frequent cause of ARDS.[13] While a resource-limited urban tropical setting study from Kerala found Leptospirosis to be the leading cause of ARDS.[14] All these studies were conducted in the pre-COVID era and did not consider COVID-19 pneumonia as an etiology of ARDS. In our study, considering that the study was conducted during and after the COVID-19 epidemic, COVID-19 pneumonia was the most common etiology of ARDS in the studied population. Hence, this study adds great value to the current evidence on the etiologies of ARDS.

Emerging evidence consistently demonstrates that patients with preexisting comorbidities exhibit heightened susceptibility to manifestations of ARDS. A recent study identified key comorbid factors associated with ARDS, including diabetes mellitus, arterial hypertension, the combination of diabetes and hypertension, cardiovascular diseases, and obesity.[15] These findings align with our observations, which highlight type 2 diabetes, hypertension, and dyslipidemia-conditions frequently observed in individuals with obesity and cardiovascular diseases as the predominant comorbidities contributing to the exacerbation of ARDS. Our results reinforce the critical role of metabolic and cardiovascular dysfunction in the pathophysiology of ARDS.

The reported mortality rates for ARDS show significant variability across different studies, even among those with similar objectives. For instance, Sharma and coworkers reported a mortality rate of 56.2%,[12] a study comparing pulmonary versus extrapulmonary ARDS recorded a mortality rate of 47.8%,[13] while an old study investigating the accuracy of the ARDS definition found a notable higher mortality rate of 68%.[16] The highest mortality was recorded at 79% by Balakrishnan and coworkers in patients admitted to a medical ICU in South India.[17] In contrast, a study in a rural-urban fringe hospital in South India reported the lowest mortality rate of 36.6%,[18] which was closer to the findings in our study. Similarly, a French Working Group study observed a mortality rate of 41%, which closely aligns with our study.[19] Though these multiple studies demonstrated the wide spectrum of outcomes in ARDS across different regions and clinical settings ranging between 36.60% to 79%, in our study, the mortality rate was comparable to the lower range of the documented values.

We correlated outcomes in ARDS patients with the clinical parameters assessed. In our study, there was no correlation between sex and survival outcomes. This suggests that sex alone does not influence mortality risk in this cohort. These findings align with data from the Lung Safe prospective cohort study evaluating outcomes of ARDS patients, which reported nearly identical mortality rates (40.2%) in both sexes.[5] These results emphasize that factors beyond sex likely contribute to variations in mortality, and sex does not predict the chance of survival among ARDS patients.

A comprehensive analysis of a national registry revealed a U-shaped age distribution in mortality rates associated with ARDS. This analysis demonstrated significantly higher mortality rates at both ends of the age spectrum, while middle-aged individuals exhibited enhanced recovery outcomes.[8] Our findings on the impact of age on outcomes in ARDS are Consistent with the reported literature.

Our study findings highlight a clear relationship between increasing ARDS severity and higher mortality rates. Upon evaluating the severity category based on the P/F ratio at the time of admission, a significant positive correlation emerged between the severity of respiratory impairment and subsequent mortality rates. These results can also be read as, patients with a P/F ratio below 104 had a markedly poor prognosis and a higher likelihood of mortality, while those with ratios exceeding 184 were associated with more favorable outcomes. This indicates a robust association between the initial P/F ratio and patient outcomes, highlighting its utility as a prognostic marker. As seen in our study, multiple other studies have also demonstrated that the P/F ratio-based severity can be used as a prognostic factor for ARDS and can help predict mortality and length of stay in the ICU.[16,20]

When mortality patterns across different etiologies were analyzed in relation to disease severity, no consistent correlation was observed between the ARDS severity and mortality within each etiology. Consistent with our findings, the LUNG SAFE analysis revealed no statistically significant association between the incidence or outcomes of ARDS and the presence of type 2 diabetes mellitus.[21] In patients with COVID-19 pneumonia in our study, mortality was significantly higher among those classified under the severe category, aligning with findings from a global meta-analysis on the incidence of ARDS and clinical outcomes in hospitalized COVID-19 patients. In this meta-analysis, mortality rates were markedly elevated in the moderate and severe ARDS categories.[22] However, in the H1N1 viral pneumonia cohort, despite 60% of patients falling into the severe ARDS category, mortality was not significantly driven by severity, with many patients demonstrating recovery. Also, the Leptospirosis cohort, where 14% of patients were classified as severe ARDS, did not show increased mortality among the severe cases. Notably, the H1N1 group exhibited a lower-than-expected mortality, as several patients in the severe category recovered, whereas the Leptospirosis group had a higher-than-expected mortality, with a substantial number of patients in the mild and moderate ARDS categories succumbing during hospitalization. The observed variation in the impact of ARDS severity on mortality across different etiologies highlighted the complex interplay between disease type, severity, and outcomes, offering significant insights into the etiology-specific patterns of respiratory failure and mortality. Furthermore, there is a notable gap in the current literature regarding the influence of ARDS severity on mortality across various etiologies, with insufficient evidence to draw definitive conclusions. Our study addresses this gap by providing robust data that contributes valuable evidence to the field.

The Sequential Organ Failure Assessment (SOFA) score is widely recognized for its ability to quantify morbidity progression in critically ill patients. The Quick Sequential Organ Failure Assessment (qSOFA) score is a simplified version of the SOFA score, which incorporates key physiological parameters, including respiratory function (respiratory rates), cardiovascular performance (systolic blood pressure), and altered mental status (Glasgow Coma Scale).[23]

In our study, a clear trend emerged when examining the relationship between qSOFA scores at admission and mortality outcomes. Higher qSOFA scores were associated with a significantly worse prognosis. Previous research has consistently demonstrated that the qSOFA score is a reliable predictor of patient outcomes, particularly in relation to mortality risk.(16) Studies have shown that patients with a qSOFA score of 0 or 1 exhibit a markedly reduced risk of mortality, whereas those with scores of 2 or 3 face a significantly higher mortality risk. A pivotal study by de Prost and coworkers showed that mortality rates decline with decreasing qSOFA scores.[24] Another study in a resource-limited urban hospital from Kerala, India, identified a statistically significant correlation between qSOFA scores and disease severity.[14] Additionally, a study from a tertiary care hospital reported that elevated qSOFA scores were more frequently observed in patients who succumbed to their conditions.[11] Findings from our study further validated that lower qSOFA scores (0-1) are associated with favorable outcomes, while scores of 2-3 predict a markedly increased risk of mortality.

Notably, the GCS at admission did not appear to influence overall recovery outcomes significantly. However, patients in the severe brain injury category demonstrated a markedly higher mortality rate. Furthermore, the contribution of GCS to the qSOFA score was significant only in the context of severe brain injury, underscoring its prognostic value in predicting adverse outcomes in this subset of patients.

The Lung Injury Score has become a widely adopted tool for quantifying the severity of acute lung injury (ALI). This composite score considers four key physiologic and radiologic parameters, including chest radiographic findings, the degree of hypoxemia, the level of positive end-expiratory pressure (PEEP) applied, and the static compliance of the respiratory system. These components collectively offer a multidimensional assessment of compromised pulmonary function and structure.(25) Our study indicated a clear trend of worsening outcomes with higher lung injury severity. The findings suggest that early LIS assessment can help predict patient outcomes and guide treatment decisions. When we further compared the LIS and P/F ratios at admission, the results showed that both LIS and P/F ratios are equally reliable for predicting ARDS outcomes at admission. A prospective cohort study found that the predictive capabilities of Berlin's criteria and LIS were comparable in assessing ARDS. Notably, their findings highlighted the significance of the LIS in the prognosis of disease outcomes, even in the context of current diagnostic frameworks that employ the P/F ratio for stratifying severity and predicting mortality risk.[25]

The results of our study depict that the requirement of mechanical ventilation predicts poor outcomes in ARDS patients. There is strong evidence to support our findings. The findings from a working group of the French Society closely align with our results, reporting that 43% of patients required mechanical ventilation.[19] Similarly, in a study conducted in a resource-limited, urban tropical setting, the need for mechanical ventilation was even higher, at 53%.[14] This trend highlights the critical role of respiratory support in patient management across diverse clinical environments. Furthermore, the significance of mechanical ventilation as a predictor of outcomes was also documented by an observational, prospective study, further highlighting its prognostic value in determining patient trajectories.[10]

In our study population, all undiagnosed patients died within ten days, contributing to the high mortality in the group of patients with hospital stays of 0-10 days, while severe cases of Leptospirosis and COVID-19 in this cohort further increased the mortality rate. Patients diagnosed with ARDS primarily succumbed within the first ten days, but those who responded to treatment and extended their stay beyond this period demonstrated a markedly improved chance of recovery. These results highlighted that extended hospital stay beyond ten days predicts better survival outcomes. ICU stay was also an indicator of adverse outcomes among the ARDS patients. There was a difference of 1 day between the average duration of ICU stay between those receiving invasive mechanical ventilation and those managed exclusively with NIV (p=0.474). Analysis of outcomes revealed that recovered patients on invasive mechanical ventilation had a longer average ICU stay of 13.20 days compared to 6.48 days for those who did not survive (p=0.07). These results highlight the significant impact of ventilation type on ICU duration and patient outcomes in ARDS management. In a retrospective analysis investigating the clinical course of Indian patients who succumbed to ARDS, the duration of invasive mechanical ventilation was observed to be less than seven days.(26) This finding aligns with data from a separate study, which reported a median ICU stay of 5 days for ARDS patients, with mortality stratified by pulmonary versus extrapulmonary etiologies.[27] These insights underscore the rapid progression of ARDS in critically ill patients.

Corticosteroids have long been studied for their potential role in the management of ARDS, with several studies suggesting a mortality benefit linked to their anti-inflammatory properties.[28] However, the therapeutic efficacy of corticosteroids in ARDS appears to be influenced by factors such as timing, duration of therapy, and the underlying etiology of lung injury.[29] Evidence supports the use of corticosteroids in severe community-acquired pneumonia (CAP), septic shock, and COVID-19-related respiratory failure, but its role in ARDS overall remains uncertain due to disease heterogeneity. Further trials are required to identify specific subgroups of ARDS patients that may benefit most from steroid therapy.[30] The latest guidelines from the American Thoracic Society provide a conditional recommendation for the use of corticosteroids in ARDS, particularly in patients with a PaO_2/FiO_2 ratio ≤300, while emphasizing the need for additional research to optimize timing and dosage regimens.[31] In our study, all patients with COVID-19 or H1N1 influenza received intravenous corticosteroids, which may have contributed to improved outcomes in these patients with ARDS, irrespective of steroid duration or dosing regimen. However, due to the absence of a comparator group that did not receive corticosteroids, particularly in the cohort receiving corticosteroids, we were unable to evaluate the differential impact of steroid therapy on ARDS outcomes within our population.

5. Limitations

This study has several limitations that must be considered when interpreting the results. First, the cross-sectional design limits the ability to establish causal relationships between identified predictors and outcomes. Second, the study was conducted at a single tertiary care hospital, which may not fully represent the broader population in Kerala or other regions. Third, the relatively small sample size (62 patients) may have constrained the statistical power to detect fewer common predictors of outcomes and limited the generalizability of findings. Additionally, the study period overlapped with the COVID-19 pandemic, which may have disproportionately influenced the etiology and outcomes of ARDS, potentially limiting applicability in non-pandemic settings. Furthermore, the impact of medication use, specifically the use of steroids, on ARDS outcomes could not be assessed, as treatment protocols—particularly during the COVID-19 pandemic—were evolving frequently, making it difficult to isolate the effects of specific interventions. Finally, data collection relied on medical records, which may have introduced information bias or incompleteness in some cases. Future studies with larger multicenter cohorts and longitudinal designs are warranted to validate these findings and explore the long-term outcomes of ARDS.

6. Conclusion

This study provides valuable insights into the etiology, clinical profile, and outcomes of ARDS in a Kerala tertiary care hospital, with COVID-19 being the leading cause, followed by Leptospirosis and H1N1 pneumonia. Older age, comorbidities (especially diabetes and hypertension), and severe ARDS were linked to higher mortality. Key predictors of outcomes included the PaO_2/FiO_2 ratio, qSOFA score, and Lung Injury Score. The need for invasive mechanical ventilation significantly increased mortality risk, while longer hospital stays improved survival.

7. Author Contributions

VV contributed to the investigation, data curation, formal analysis, and methodology and played a significant role in writing and revising the manuscript. JA guided the project, participated in the investigation and project administration, and contributed to the critical review and revision of the manuscript. BU provided nephrology expertise, contributed to the critical review, and assisted in revising the manuscript.

All authors have read and approved the manuscript, have met the journal's authorship criteria, and affirm that the manuscript reflects honest and original work.

8. Data Availability Statement

All data generated has been presented in the manuscript.

9. Source of Funding

No funding was received to conduct the study.

10. Conflicts of Interest

The authors declare no conflicts of interest.

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References

1. Matthay MA, Zemans RL, Zimmerman GA, Arabi YM, Beitler JR, Mercat A, et al. Acute respiratory distress syndrome. *Nat Rev Dis Primers*. 2019;5(1):18.
2. Ramji HF, Hafiz M, Altaq HH, Hussain ST, Chaudry F. Acute Respiratory Distress Syndrome; A Review of Recent Updates and a Glance into the Future. *Diagnostics*. 2023;13(9):1528.
3. Meyer NJ, Gattinoni L, Calfee CS. Acute respiratory distress syndrome. Lancet. 2021;398(10300):622–37.
4. Hendrickson KW, Peltan ID, Brown SM. The Epidemiology of Acute Respiratory Distress Syndrome Before and After Coronavirus Disease 2019. *Crit Care Clin*. 2021;37(4):703–16.
5. McNicholas BA, Madotto F, Pham T, Rezoagli E, Masterson CH, Horie S, et al. Demographics, management and outcome of females and males with acute respiratory distress syndrome in the LUNG SAFE prospective cohort study. *Eur Respir J*. 2019;54(4):1900609.
6. Chen W, Chen YY, Tsai CF, Chen SCC, Lin MS, Ware LB, et al. Incidence and Outcomes of IAcute Respiratory Distress Syndrome. *Medicine*. 2015;94(43):e1849.
7. Manzano F, Yuste E, Colmenero M, Aranda A, García-Horcajadas A, Rivera R, et al. Incidence of acute respiratory distress syndrome and its relation to age. *J Crit Care*. 2005;20(3):274–80.
8. Killien EY, Mills B, Vavilala MS, Watson RS, O'Keefe GE, Rivara FP. Association between Age and Acute Respiratory Distress Syndrome Development and Mortality following Trauma. *J Trauma Acute Care Surg*. 2019;86(5):844–52.
9. Fan E, Brodie D, Slutsky AS. Acute Respiratory Distress Syndrome: Advances in Diagnosis and Treatment. *JAMA*. 2018;319(7):698–710.
10. Bhadade RR, de Souza RA, Harde MJ, Khot A. Clinical characteristics and outcomes of patients with acute lung injury and ARDS. *J Postgrad Med*. 2011;57(4):286-90.
11. Magazine R, Rao S, Chogtu B, Venkateswaran R, Shahul HA, Goneppanavar U. Epidemiological profile of acute respiratory distress syndrome patients: A tertiary care experience. *Lung India*. 2017;34(1):38-42.
12. Sharma SK, Gupta A, Biswas A, Sharma A, Malhotra A, Prasad KT, et al. Aetiology, outcomes & predictors of mortality in acute respiratory distress syndrome from a tertiary care centre in north India. *Indian J Med Res*. 2016;143(6):782-92.
13. Aggarwal A, Agarwal R, Dhooria S, Prasad K, Valliappan Muthu. Etiology and outcomes of ARDS in the elderly population in a respiratory ICU in North India. *Chest*. 2019;156(4):A1004.
14. Kumar SS, Selvarajan Chettiar KP, Nambiar R. Etiology and Outcomes of ARDS in a Resource Limited Urban Tropical Setting. *J Natl Med Assoc*. 2018;110(4):352–7.
15. De Araújo MFM, Monteiro FPM, De Araújo TM, Lira Neto JCG, Santos LFS, Rolim ILTP, et al. Individual and mutual effects of diabetes, hypertension, and obesity on acute respiratory distress syndrome mortality rates in clinical patients: a multicentre study. *Front Public Health*. 2023;11:1219271.
16. Villar J, Pérez-Méndez L, Kacmarek RM. Current definitions of acute lung injury and the acute respiratory distress syndrome do not reflect their true severity and outcome. *Intensive Care Med*. 1999;25(9):930–5.
17. Balakrishnan N, Thabah MM, Dineshbabu S, Sistla S, Kadhiravan T, Venkateswaran R. Aetiology and short-term outcome of acute respiratory distress syndrome: a real-world experience from a medical intensive care unit in southern India. *J R Coll Physicians Edinb*. 2020;50(1):12–8.
18. George T, Viswanathan S, Karnam AHF, Abraham G. Etiology and Outcomes of ARDS in a Rural-Urban Fringe Hospital of South India. *Crit Care Res Pract*. 2014;2014:181593.
19. Roupie E, Lepage E, Wysocki M, Fagon JY, Chastre J, Dreyfuss D, et al. Prevalence, etiologies, and outcome of the acute respiratory distress syndrome among hypoxemic ventilated patients. SRLF Collaborative Group on Mechanical Ventilation. *Intensive Care Med*. 1999;25(9):920–9.
20. Wang Y, Yang H, Qiao L, Tan Z, Jin J, Yang J, et al. The predictive value of PaO2/FIO2 and additional parameters for in-hospital mortality in patients with acute pulmonary embolism: an 8-year prospective observational single-center cohort study. *BMC Pulm Med*. 2019;19:242.
21. Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. *Crit Care*. 2020;24:516.
22. Boyle AJ, Madotto F, Laffey JG, Bellani G, Pham T, Pesenti A, et al. Identifying associations between diabetes and acute respiratory distress syndrome in patients with acute hypoxemic respiratory failure: an analysis of the LUNG SAFE database. *Crit Care*. 2018;22:268.
23. Asmarawati TP, Suryantoro SD, Rosyid AN, Marfiani E, Windradi C, Mahdi BA, et al. Predictive Value of Sequential Organ Failure Assessment, Quick Sequential Organ Failure Assessment, Acute Physiology and Chronic Health Evaluation II, and New Early Warning Signs Scores Estimate Mortality of COVID-19 Patients Requiring Intensive Care Unit. *Indian J Crit Care Med*. 2022;26(4):464-71.
24. de Prost N, Pham T, Carteaux G, Mekontso Dessap A, Brun-Buisson C, Fan E, et al. Etiologies, diagnostic work-up and outcomes of acute respiratory distress syndrome with no common risk factor: a prospective multicenter study. *Ann Intensive Care*. 2017;7(1):69.
25. Kangelaris KN, Calfee CS, May AK, Zhuo H, Matthay MA, Ware LB. Is there still a role for the lung injury score in the era of the Berlin definition ARDS?. *Ann Intensive Care*. 2014;4:4.
26. Vigg A, Mantri S, Vigg A, Vigg A. Clinical profile of ARDS. *J Assoc Physicians India*. 2003;51:855-8.
27. Agarwal R, Aggarwal AN, Gupta D, Behera D, Jindal SK. Etiology and outcomes of pulmonary and extrapulmonary acute lung injury/ARDS in a respiratory ICU in North India. *Chest*. 2006;130(3):724-9.
28. Jayasimhan D, Matthay MA. Corticosteroids in adults with acute respiratory distress syndrome and severe pneumonia. *BJA Educ*. 2023;23(12):456-63.
29. Kuperminc E, Heming N, Carlos M, Annane D. Corticosteroids in ARDS. *J Clin Med*. 2023;12(9):3340.
30. Sinha S, Patnaik R, Behera S. Steroids in acute respiratory distress syndrome: A panacea or still a puzzle?. *World J Crit Care Med*. 2024;13(2):91225.
31. Qadir N, Sahetya S, Munshi L, Summers C, Abrams D, Beitler J, et al. An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome: An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2024;209(1):24-36.

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