A STUDY ON CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME IN A TERTIARY CARE HOSPITAL IN NORTH EAST INDIA

Deepak Chaudhury[1], Jehbi Hasan[2], Subhankar Paul[3], Ilias Ali[4]

[1]Assistant Professor, Department of Emergency Medicine, Gauhati Medical College and Hospital.
[2]Senior Resident, Department of Emergency Medicine, Gauhati Medical College and Hospital.
[3]Postgraduate Student, Department of Emergency Medicine, Gauhati Medical College and Hospital.
[4]Professor and HOD, Department of Emergency Medicine, Gauhati Medical College and Hospital.

ABSTRACT

BACKGROUND

Acute respiratory distress syndrome (ARDS) is a life threatening condition in which respiratory failure occurs due to lung injury caused by various aetiological factors. Acute hypoxemic respiratory failure as occurs in ARDS requires positive pressure ventilation. ARDS is a major cause of morbidity and mortality; and it also leads to major expenditure in intensive care units.

MATERIALS AND METHODS

This is a prospective observational study conducted over a period of one year in Emergency/ICU to study various clinical profiles of ARDS patients. Adult patients who fulfilled the criteria for ARDS according to the Berlin Definition of 2012 were included in the study.

RESULTS

Clinical profiles of 44 ARDS patients were studied. There was predominance of male gender & young age. The mortality in our study was 54.54%. Non-survivors had significantly more incidence of severe ARDS & sepsis as aetiology of ARDS. On discharge from the ICU, there was no major pulmonary or cardiovascular complications.

CONCLUSION

Despite lung protective ventilation, mortality and morbidity in ARDS is quite high worldwide. Therefore, high index of clinical suspicion is required to detect it early.

KEYWORDS

ARDS, Berlin Definition, Lung Protective Ventilation, Sepsis.

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BACKGROUND

Acute respiratory distress syndrome (ARDS) was described for the first time by Ashbaugh and colleagues (1967). They described ARDS as the 'acute onset of tachypnoea, hypoxaemia and loss of compliance after a variety of stimuli'.(1) The term 'adult respiratory distress syndrome' was initially used to describe the condition but it was subsequently renamed as 'Acute Respiratory Distress Syndrome' because it may also occur in children.(2) However, it was not until 1994 that an International American–European Consensus Conference (AECC) laid the foundations for the definition of ARDS(3) which was further modified in Berlin, 2011 which is presently accepted as a universal definition for ARDS.(4)

Acute respiratory distress syndrome (ARDS) is a life threatening respiratory failure due to direct or indirect lung injury caused by many aetiological factors.(5) Clinical features of ARDS are severe dyspnoea, tachypnoea, and hypoxaemia refractory to supplemental oxygen along with the clinical features of the initiating injury.(6) All patients should be assessed for an underlying cause (particularly pneumonia, sepsis, pancreatitis or transfusion related lung injury) and treated promptly. The pulmonary pathology of ALI/ARDS can be divided into acute and fibroproliferative phases(5) which is characterised by diffuse alveolar damage, leakage from alveolar capillaries, and protein rich pulmonary oedema leading to poor lung compliance, severe hypoxaemia, and bilateral infiltrates on chest radiograph.

ARDS is characterised by severe acute hypoxaemic respiratory failure with increased work of breathing and decreased lung compliance, which together usually mandate mechanical ventilation.(4) The role of non-invasive ventilation in ARDS is contentious; there are no large definitive studies, and although some groups report encouraging results these are usually in patients with mild ARDS. NIV failure is common which is associated with more complications and mortality rates, possibly due to delayed intubation, high leaks, abdominal distension, etc.(7) The method and delivery of ventilatory support must consider both the pathophysiology of ARDS and ventilator-induced lung injury (VILI). The ARDS Network randomised 861 ALI patients from 75 ICUs to receive either a tidal volume (VT) of 6 or 12 mL/kg predicted body weight. Mortality was reduced by 22%, from 40% to 31%, in the lower VT group. There was a strict FiO2 & PEEP

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Corresponding Author:
Dr. Deepak Chaudhury,
Panjabari, Lakhimipath,
House No. 3, P. O. Khanapara,
Guwahati-781037, Assam.
E-mail: deepak9891chaudhury@gmail.com
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protocol, and patients were ventilated in assist-control mode to avoid excessive spontaneous VT.[8]

Lung-protective ventilation is still the key of better outcome in ARDS. Though in randomised trials, prone ventilation in severe ARDS, short-term use of neuromuscular blockade at initial stage of mechanical ventilation, and extracorporeal membrane oxygenation in ARDS with influenza pneumonia showed beneficial efficacy.[9-12] However, ARDS mortality still remains high. Therefore, early recognition of ARDS by identifying risk factors and the avoidance of aggravating factors during the patient's hospital stay can help decrease its development and progression. Our study therefore aims at studying the overall clinical profile of ARDS patients starting from ICU admission, undergoing mechanical ventilation to discharge or death, and comparing various parameters among survivors & non-survivors.

MATERIALS AND METHODS

A single-centre prospective observational study was conducted involving the patients admitted in the Emergency/ICU under the Department of Emergency Medicine in Gauhati Medical College & Hospital after obtaining institutional ethical committee clearance. Patients aged 18 years or elder, fulfilling the criteria of ARDS according to the Berlin definition, 2012[4] were included in the study whereas patients of known COPD, bronchial asthma, active pulmonary TB, interstitial lung disease, congestive heart failure, chronic liver disease, chronic kidney disease, and patients with pregnancy were excluded from the study.

Primary outcome variable studied was mortality during ICU stay while time duration on mechanical ventilation, clinical parameters during discharge, etc were the secondary variables studied. Detailed history taking and physical examination were done for every patient at the time of admission to ICU along with relevant investigations viz ABG, Chest X-ray, ECG, haematological and biochemical examinations of blood and appropriate specimen cultures, etc. ABG & Chest X-ray were done routinely every 24 hourly and as and when necessary till weaning from ventilator. Initial ventilator parameters like mode, FiO2, PEEP, peak inspiratory pressure, plateau pressure, tidal volume, respiratory rate were measured after 20 minutes of mechanical ventilation. Lung protective ventilation strategy as laid by ARDS Network protocol was followed for every patient on mechanical ventilation and parameters were noted accordingly. Daily SOFA scoring was done for every patient for signs of organ failure.

Results of numerical variables were reported as mean ± SD and categorical variables were reported in frequency & percentages. Student's t test or Kruskal-Wallis test was applied to test the significance while comparing numerical data & Fisher exact test was applied for categorical data. All statistical analyses were done with SPSS 16.0 software.

RESULTS

After applying inclusion and exclusion criteria, clinical profiles of 44 ARDS patients were studied. There was Male predominance (n = 28, 64%) (Fig-1), with male to female ratio 1.75:1.

The mean age in this study was 40.4 ± 14.12 years (Mean ± SD), with majority of the patients in relatively younger age group (Table 1).

Table 2 shows aetiological factors of ARDS in our study where non-pulmonary sepsis was the commonest cause (n= 13, 29.5%) followed by direct lung injury by aspiration (n=10, 22.7%).

Mean time of onset of ARDS following exposure to a known clinical insult was 3.59 ± 1.56 days. Majority of the patients presented with breathlessness (n = 36, 82%), fever (n = 29, 66%) and altered sensorium (n=28, 63.6%).

Most of the patients fell into the category of Moderate ARDS (100<PaO2/FiO2 <200) as shown in Table 4.

24 patients out of total 44 patients in our study died leading to a mortality rate of 54.5% (Figure 2). Comparison of various parameters between survivors & non-survivors, showed that severe ARDS, sepsis as initial diagnosis were significantly associated with higher mortality.

Most of the survivors who were discharged from ICU had no residual cardiovascular/haematological/hepatic dys-function or any pneumothorax following lung-protective ventilation (Table 6).

AGE Groups (Years)	**18-28**	**28-38**	**38-48**	**48-58**	**58-68**	**68-78**
No. of Patients (%)	11 (25%)	8 (18%)	12 (27.2%)	7 (16%)	4 (9%)	2 (4.5%)

Table 1. Age–wise Distribution of Patients with ARDS

Aetiological Factors		**n, % (n=44)**
Direct lung injury	**Aspiration**	**10 (22.7%)**
	Pneumonia	**6 (13.6%)**
	Fat Embolism	**2 (4.5%)**
Indirect causes	Sepsis	13 (29.5%)
	Shock	9 (20.4%)
	Acute Pancreatitis	5 (11.3%)
	Malaria	4 (9%)
	Major Trauma	3 (7%)
	Anaphylaxis	1 (2.25%)
	Drug overdose	1(2.25%)

Table 2. Direct & Indirect Causes for of ARDS

Signs and Symptoms	**No. of Patients**
Fever	29
Cough	11
Breathlessness	36
Haemoptysis	03
Chest pain	05
Cyanosis	03
Pain abdomen	18
Bilateral Pedal Oedema	10
Ascites	08
Altered sensorium	28
Hypotension	22
Tachypnoea	43
Abnormal respiratory pattern	26
Distended neck veins	0

Table 3. Shows Clinical Features of ARDS Patients on Admission

Category of ARDS	No. of Patients	Percentage
Mild	05	11.3%
Moderate	21	47.7%
Severe	18	10.9%

Table 4. Shows Distribution According to Severity of ARDS

Parameters	Survivors (n=20)	Non-survivors (n=24)	P Value
Age (Mean ± SD)	39.25 ± 17.39	41.3±11.45	0.644
Gender, male (n, %)	12 (27%)	16 (36%)	0.5284
Time of onset (Mean ±SD)	3.45±0.359	3.71±1.55	0.5918
Direct lung injury (n, %)	10 (23%)	7 (16%)	0.2176
Sepsis as Initial diagnosis	3 (15%)	13 (54.1%)	0.0079
Severe ARDS (n, %)	3 (15%)	15 (62.5%)	0.0016
Metabolic Acidosis (n, %)	4 (20%)	9 (37.5%)	0.1753
Duration of MV in DAYS (Mean ±SD)	9.2±2.04	4.79 ± 2.68	<0.0001
ICU Stay Days (Mean ± SD)	12.95 ± 2.85	4.8 ± 2.7	<0.0001

Table 5. Comparison Between Various Parameters among Survivors & Non-survivors

Parameter	No. of Patients
Requirement of supplemental oxygen	06
GCS 14/15	07
Organ dysfunction	
Renal	03
Cardiovascular	0
Biliary	0
Haematological	0
Acid base imbalance	0
Persistent pulmonary infiltrates involving	
4 quadrants	0
3 quadrants	0
2 quadrants	4
1 quadrant	5
Pneumothorax	0
Pneumomediastinum	0
Subcutaneous emphysema	0

Table 6. Clinical Parameters of the Survivors at Discharge from ICU

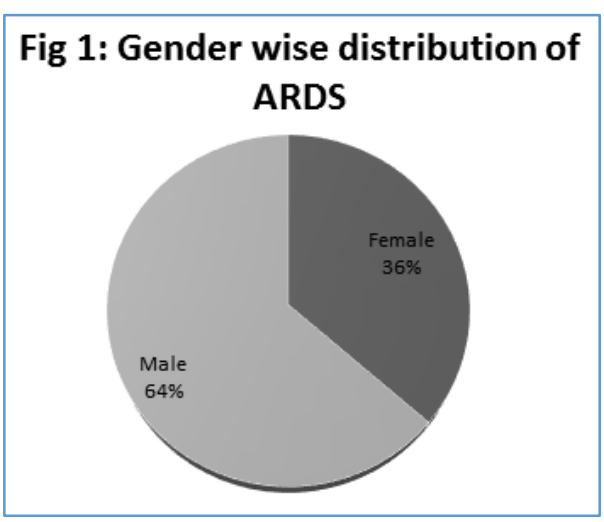

Figure 1. Pie Diagram Showing Gender Distribution of ARDS Patients in our Study

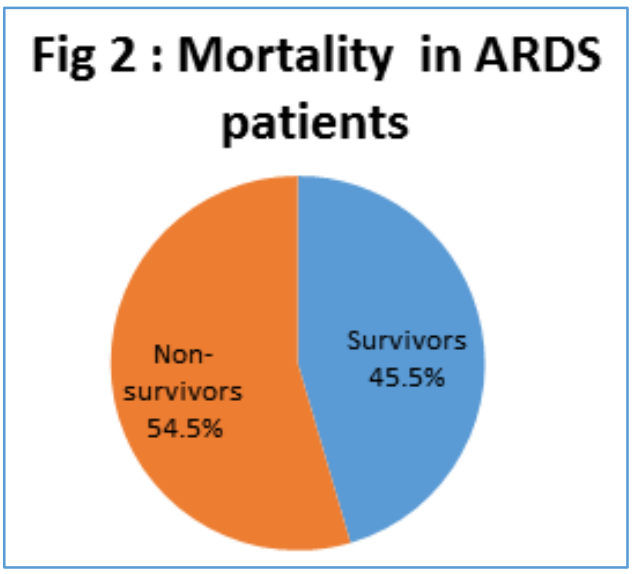

Figure 2. Pie Diagram Showing Mortality in ARDS Patients

DISCUSSION

A prospective study by Heffernan et al[13] showed that females were more likely to develop ARDS (35% versus 25%, p = 0.02) whereas our study exhibited a male predominance. Maximum number of patients belonged to the age group of 38-48 years (27.2%) followed by 25% in the age group of 18 - 28 years. Only about 30% patients were more than 48 years of age. The mean age in this study was 40.4 ± 14.12 years (Mean ± SD). In a study by Bhadade et al,[14] in Maharashtra, the mean age of ARDS patients was 37.9 years. Singh et al[15] found the mean age in ARDS patients in their study to be 44.8 ± 15.5 years. It appears that ARDS is commonly seen in younger age group.

In our study, commonest aetiological factor for developing ARDS was non-pulmonary sepsis (29.5%), followed by aspiration (22.7%) & shock (20.4%) which was similar to the observation by Gajic et al.[6] However, Study by Rubenfeld et al[16] showed most common cause was severe sepsis with pulmonary aetiology (46%) and Agarwal et al[17] also showed pneumonia to be the commonest aetiology for ARDS.

In this study, out of 44 patients, severe ARDS occurred in 18 patients (40.9%), moderate ARDS in 21 patients (47.7%) and mild ARDS in 5 patients (11.3%). In a study by Thille et al,[18] incidence of mild ARDS was 14%, moderate 40% and severe 46%. The ALIVE study group[19] reported the incidence of mild ARDS to be 30% at presentation but half of them later developed moderate or severe ARDS. But mild ARDS being a frequently underdiagnosed condition the incidence of three categories of ARDS only represents an estimate.

The mortality in our study was 54.54%. The study was Esteban et al[20] found the overall mortality rate in the intensive care unit to be 30.7% whereas the mortality was 52% in patients who received ventilation because of ARDS. In studies by Agarwal et al[17] & Rubenfeld et al,[16] the hospital mortality rate for ARDS was 47.8% & 41.1% respectively. Recent studies show a decreasing trend in mortality from ARDS patients which might be attributed to the widespread adoption of lung protective mechanical ventilation strategies in ARDS patients. The ARMA trial of ARDS Net group showed

mortality of 21% in those with lung protective mechanical ventilation vs. 40% in those with conventional ventilation.[8] Erickson et al[21] observed that crude mortality in ARDS was 35% in 1996-1997 and declined during each subsequent time period to a low of 26% in 2004-05. In a recent prospective, multicentre observational study by Villar et al,[22] it was seen that despite the use of lung protective ventilation, the ICU mortality of ARDS patients was still more than 40%.

16 of the 28 male patients (57%) and 8 of the 16 female (50%) did not survive, and this gender difference was not statistically significant (p = 0.756). The study by Luhr et al [23] in 1231 patients with acute respiratory failure and ARDS also demonstrated that gender was not independently associated with mortality. Bhadade et al[14] found mortality in females to be higher than males (73% vs. 51%) but the difference was not statistically significant (p=0.23).

The mean age of the survivors was 39.25 ± 17.39 years (mean ± SD) and that of non-survivors was 41.3 ± 11.45 years (mean ± SD). Although the mean age was more in non-survivors, the difference was not statistically significant (p = 0.644) as also observed by Singh et al.[15] Some studies have shown increased risk of ARDS and increased mortality too in the elderly age group. In a study by Rubenfeld,[16] it was seen that mortality increased with age from 24% for patients 15 through 19 years of age to 60% for patients 85 years of age or older (P<0.001). Suchyta et al found significant increase in mortality in ARDS with age more than 65 years.

In this study, it was also found that severe ARDS patients were more likely to die than mild or moderate ARDS patients (p<0.0002) which was also reflected in studies by Rubenfeld et al.[16] The ARDS task force conducted a meta-analysis of 7 clinical trials and prepared a draft of the Berlin definition in which they observed that the mortality in mild ARDS was 27% (95% CI 24% - 30%), in moderate ARDS 32% (95% CI 29% - 34%) and in severe ARDS 45% (95% CI 42%-48%) and the difference was statistically significant (p <0.001).[4]

In this study, it was seen that 13 patients out of 44 (29.5%) presented with metabolic acidosis on admission to ICU. Though it was statistically not significant (p = 0.1753), Metabolic acidosis has been found to correlate with increased mortality in some studies on ARDS. Bru-Buisson et al[19] observed that pH <7.3 was associated with mortality in ARDS. Bhadade et al[14] found that acidosis is an independent factor associated with mortality.

Mean duration of Mechanical ventilation & ICU stay were significantly high in survivors (9.2 ± 2.04 & 12.95 ± 2.85 days) vs. non-survivors (4.79 ± 2.68 & 4.8 ± 2.7) possibly reflecting the early mortality of the non-survivors. However, Rios et al[24] in 2009 observed that in survivors of ARDS mechanical ventilation was required for an average of 11 days (6-19 days). Bhadade et al[14] found mean duration of survival of ARDS patients was 4.55 days.

The mean duration of survival was 4.8 ± 2.7 days in this study. The mean duration of survival was 4.55 days in the study by Bhadade et al.[14] Incidence of barotraumas viz. pneumothorax, pneumomediastinum, subcutaneous emphysema was zero in this study. At the time of discharge from the ICU, 7 patients (35%) had GCS 14 and 3 patients (15%) had persistent renal dysfunction. 6 (30%) of the 20 survivors were still in need of supplemental oxygen via face mask for maintaining oxygenation at the time of discharge from ICU. None of the survivors had hypotension or acid-base imbalance at the time of discharge. At the time of discharge from ICU, 9 (45%) patients had persistent pulmonary infiltrates involving either one or two quadrants on frontal chest radiograph.

CONCLUSION

ARDS is characterised by progressive and refractory hypoxaemia arising from diverse direct or indirect injuries to lung. Despite the progress in understanding of its pathophysiology, aggressive treatment strategies and lung protective ventilation, mortality and morbidity remain quite high. Therefore, keeping high index of suspicion based on the clinical pictures of the patients and early detection help to halt its progress.

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