Epidemiological profile of acute respiratory distress syndrome patients: A tertiary care experience

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ABSTRACT

Background: Acute respiratory distress syndrome (ARDS) is seen in critically ill patients. Its etiological spectrum in India is expected to be different from that seen in western countries due to the high prevalence of tropical infections. Aim: To study the epidemiological profile of ARDS patients. Setting: A tertiary care hospital in Karnataka, India. Materials and Methods: Retrospective analysis of 150 out of the 169 ARDS patients diagnosed during 2010–2012. Data collected included the clinical features and severity scoring parameters. Results: The mean age of the study population was 42.92 ± 13.91 years. The causes of ARDS included pneumonia (n = 35, 23.3%), scrub typhus (n = 33, 22%), leptospirosis (n = 11, 7.3%), malaria (n = 6, 4%), influenza (H1N1) (n = 10, 6.7%), pulmonary tuberculosis (n = 2, 1.3%), dengue (n = 1, 0.7%), abdominal sepsis (n = 16, 10.7%), skin infection (n = 3, 2%), unknown cause of sepsis (n = 18, 12%), and nonseptic causes (n = 15, 10%). A total of 77 (51.3%) patients survived, 66 (44%) expired, and 7 (4.7%) were discharged against medical advice (AMA). Preexisting comorbidities (46) were present in 13 survivors, 19 nonsurvivors, and four discharged AMA. History of surgery prior to the onset of ARDS was present in one survivor, 13 nonsurvivors, and one discharge AMA. Mean Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE III, and Sequential Organ Failure Assessment scores in survivors were 9.06 ± 4.3, 49.22 ± 14, and 6.43 ± 2.5 and in nonsurvivors 21.11 ± 7, 86.45 ± 23.5, and 10.6 ± 10, respectively. Conclusion: The most common cause of ARDS in our study was pneumonia, but a large percentage of cases were due to the tropical infections. Preexisting comorbidity, surgery prior to the onset of ARDS, higher severity scores, and organ failure scores were more frequently observed among nonsurvivors than survivors.

KEY WORDS: Acute respiratory distress syndrome, pneumonia, tropical infectious diseases

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a term which refers to a specific form of lung injury seen in critically ill patients. Various conditions which cause lung injury, either directly (pneumonia, toxic gas inhalation) or indirectly (sepsis, trauma) are implicated in the causation of ARDS.^[1] Understanding of the pathogenesis of ARDS has

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grown substantially over the last few decades. However, ARDS continues to be a major cause of morbidity and mortality in the critically ill. Plenty of work has been done on ARDS in western countries. Its incidence, clinical course, morbidity pattern, and outcome have been studied.^[2-4] The etiology of ARDS can be expected to be different in India due to the higher incidence of tropical

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infectious diseases.^[5] However, not many studies have been done in India on ARDS. With this study, we plan to evaluate the epidemiological profile of patients with ARDS in a tertiary care hospital in India.

Aims and objective

To study the epidemiological profile of patients with ARDS in a tertiary care teaching hospital.

MATERIALS AND METHODS

This was a retrospective study done at a tertiary care teaching hospital in south India. Data of 150 out of the 169 ARDS patients admitted in the Intensive Care Unit (ICU) were collected over a period of 3 years from January 2010 to December 2012, after obtaining the Institutional Ethical Committee approval.

Inclusion criteria

This study included patients aged >18 years, who were diagnosed to have ARDS during the study period. Diagnosis of ARDS was based on American/European Consensus Conference (AECC) criteria for ARDS which included the following:

- PaO_2/FiO_2 ratio ≤ 200
- Bilateral infiltrates on chest radiograph
- Absence of clinical signs of left heart failure.

Exclusion criteria

- Patients with clinical signs of left heart failure
- Patients aged ≤ 18 years.

Patients with ARDS, meeting the above mentioned criteria, were included in the study. Nineteen cases were excluded based on the exclusion criteria or due to the lack of complete data availability. The study group included moderate to severe ARDS cases as per the latest Berlin definition for ARDS proposed in 2011.^[6] Data were collected as per a predesigned proforma and included patients age, gender, past major illness, clinical disorders precipitating ARDS, presence of organ failure, Glasgow Coma Scale, clinical severity of ARDS within 24 h of diagnosis, and length of hospital stay. Blood biochemistry, arterial blood gases. hematocrit, total leukocyte count, platelet count, chest radiograph, and other variables were noted. The clinical and biochemical variables collected were noted within the first 24 h of the diagnosis of ARDS, and the severity scores were calculated from the above data. The data of the subjects were collected till discharge from hospital or death. The final diagnosis and outcome were recorded.

Severity scores

The data collected was used to calculate the severity scores. The severity scores used in our study were as follows:

- 1. Acute Physiology and Chronic Health Evaluation (APACHE) II
- 2. APACHE III.
- 3. Sequential Organ Failure Assessment score (SOFA).
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- APACHE II: APACHE II is a point score system based on the initial values of 12 routine physiologic measurements along with age and chronic health points. It provides a general measure of severity of disease and is used in the assessment of critically ill
- APACHE III: APACHE III scoring system uses 17 physiological and biochemical parameters along with age and comorbidities to assess the severity of the disease. The score can be used for predicting the risk of hospital mortality in critically ill patients
- SOFA score: The SOFA score is a simple and effective method to describe organ failure in critically ill patients. Regular scoring enables the clinician to assess patient condition and response to treatment.

Statistical analysis

The data were entered on SPSS Version 16.0 (SPSS Inc., Chicago, USA) and were analyzed using descriptive statistics, frequencies, and cross tabulations.

RESULTS

The study population consisted of 150 patients meeting the AECC criteria for ARDS. The baseline characteristics of the patients are shown in Table 1. The mean age of the study population was 42.92 ± 13.916 years. A considerable number of the patients (48%, n = 72) were <40 years of age. The mean age (mean \pm standard deviation) was 40.14 ± 11.7 years among survivors and 45.12 ± 15.5 years among nonsurvivors. There were 90 (60%) males and 60 (40%) females. Three (5%) of the women were pregnant. The males comprised 54.5% (n = 42) of survivors and 63.6% (42) nonsurvivors. The study population included 23 (15.3%) smokers, 21 (14%) patients with history of alcohol use, and 14 (9.3%) with history of both smoking and alcohol consumption. Smokers comprised 12.9% (n = 10) of survivors and 12.1% (n = 8) of nonsurvivors. The alcohol users comprised 12.9% (n = 10) and 12.1% (n = 8) of survivors and nonsurvivors, respectively.

Only 15 patients had surgery done (eight emergency surgeries and seven elective surgeries) prior to the onset of ARDS. History of surgery prior to the onset of ARDS was present in one survivor, 13 nonsurvivors, and one discharge against medical advice (AMA) case.

Preexisting comorbidities (46) were present in 13 survivors, 19 nonsurvivors, and four among those discharged AMA. Among the 36 patients who had comorbidities, ten cases had dual comorbidities (diabetes mellitus and hypertension).

Etiology of ARDS in the study population is shown in Table 2.

Body fluid sample for culture was collected in 136 cases. Microbiological cultures were positive in 43 cases (28.6%) of the study population. These 43 cases produced 53

Table 1: Baseline characteristics of the study population (*n*=150)

Baseline characteristics	n (%)
Age (year)	
<40	72 (48)
40-60	60 (40)
>60	18 (12)
Gender	
Male	90 (60)
Female	60 (40)
Smoker	
Yes	23 (15.3)
No	127 (84.7)
Alcohol consumption	
Yes	21 (14)
No	129 (86)
Preexisting comorbidities	
Pulmonary disease	10 (6.7)*
Diabetes	18 (12)*
Hypertension	14 (9.3)*
HIV	2 (1.3)
Hepatic disease	2 (1.3)
None	114 (76)
Etiology of ARDS	
Infective	135 (90)
Noninfective	15 (10)
Surgery prior to ARDS onset	
Yes	15 (10)
No	135 (90)
APACHE II score	
0-9	49 (32.7)
10-19	59 (39.3)
20-29	35 (23.3)
>30	7 (4.7)
APACHE III score	
0-49	44 (29.3)
50-99	84 (56)
>100	22 (14.7)
SOFA score	
0-5	42 (28)
6-9	64 (42.7)
10-14	41 (27.3)
>15	3 (2)
Outcome	
Survivors	77 (51.3)
Nonsurvivors	66 (44)
Discharge against medical advice	7 (4.7)

*Some of the patients had more than one comorbidities. ARDS: Acute respiratory distress syndrome, SOFA: Sequential Organ Failure Assessment, APACHE: Acute Physiology and Chronic Health Evaluation

positive body fluid culture samples, and a total of 59 organisms were isolated from these samples. Among the culture positive cases, 23.3% (n = 10) had cultures positive from more than one body fluid. More than one organisms were isolated in 27.9% (n = 12) of the 43 cases which were culture positive. Out of the 53 positive body fluid cultures, blood (34%, n = 18) was the most common source of positive culture followed by endotracheal aspirate (30.1%, n = 16), sputum (20.7%, n = 11), and others (15.2%, n = 8). Yield from various body fluid cultures is shown in Table 3.

The distribution of organisms isolated from various body cultures is shown in Table 4. Out of the total 150 cases, the duration of hospitalization in majority of patients

Table 2: Etiology of acute respiratory distress syndrome in the study population

Etiology	n (%)
Sepsis	
Pneumonia	35 (23.3)
Scrub typhus	33 (22)
Leptospirosis	11 (7.3)
Malaria	6 (4)
Influenza (H1N1)	10 (6.7)
Pulmonary tuberculosis	2 (1.3)
Dengue	1 (0.7)
Abdominal sepsis	16 (10.7)
Skin infection	3 (2)
Unknown cause	18 (12)
Nonsepsis	
Pancreatitis	8 (5.3)
Burns	3 (2)
Head injury	2 (1.3)
Snake bite	1 (0.7)
Poisoning	1 (0.7)
Total	150 (100)

Table 3: Yield from various body fluid culture

Body fluid	Total number of samples sent	Number of positive cultures	Percentage yield from body fluids
Blood	130	18	13.9
Endotracheal aspirate	46	16	34.7
Sputum	24	11	41.7
Others			
Wound swab	8	6	75
Peritoneal fluid	5	1	20
Pus	2	1	50
Urine	15	0	0
Total	230	53	23.04

(61.33%, n = 92) was more than 7 days. The mean duration of hospital stay was 9.7 ± 5.5 days. The means of various severity scores observed in survivors and nonsurvivors are shown in Table 5.

DISCUSSION

Majority of the subjects in our study were males with mean age of the patients at 42.9 ± 13.9 years. This is similar to the results reported by other investigators from India; Bhadade *et al.* from Mumbai and Vigg *et al.* from Hyderabad reported figures of 37.9 years and 39.2 ± 2.5 years, respectively, for the mean age of the patients.^[5,7] However, the mean age reported in many of the western studies is higher. Studies done in Boston and Washington found the mean age to be 60 years and 60.6 years, respectively.^[8,9] The lower mean age of ARDS patients in our study, when compared to western studies, may be explained by the higher percentage of tropical infectious diseases as a cause of ARDS. The environmental exposure to these vector-borne tropical diseases is more among young working population.^[5]

In our study, 24% (n = 36) of the cases had preexisting comorbid illness [Table 1]. A retrospective study done in the medical ICU at a medical center in Japan found that 89.4% of patients with a diagnosis of acute lung

Table 4: Distribution of organisms isolated from various body cultures

Organism	n (%)
Acinetobacter spp.	16 (27.1)
Klebsiella spp.	15 (25.4)
Escherichia coli	11 (18.7)
Pseudomonas spp.	5 (8.5)
Enterococcus	5 (8.5)
Candida	2 (3.4)
Cryptococcus neoformans	2 (3.4)
Staphylococcus aureus	2 (3.4)
Streptococcus	1 (1.6)
Total	59 (100)

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Severity score	Mean score among survivors	Mean score among nonsurvivors	Overall mean score
APACHE II	9.06±4.3	21.11±7	14.67±8.2
APACHE III	49.22±14	86.45±23.5	66.53±26.3
SOFA	6.43±2.5	10.6±10	8.27±7.3

SOFA: Sequential Organ Failure Assessment, APACHE: Acute Physiology and Chronic Health Evaluation

injury or ARDS had preexisting comorbid illnesses. This difference in percentage of preexisting comorbid illnesses could be due to the higher mean age (71.0 \pm 12.4 years) of the study population in the latter study.^[10] In our study, 28.8% of nonsurvivors and only 16.9% of the survivors had a preexisting comorbid illness. Similar results were noted in the study from Boston, where the occurrence of comorbidities was more frequent in nonsurvivors.^[8]

In the present study, 19.7% of the nonsurvivors and only 1.2% of survivors had history of prior surgery. Various studies have found that patients undergoing elective and nonelective surgeries were at increased risk of developing lung injury. This could be due to several factors such as the use of fluids during surgery, preexisting comorbid conditions, and type of surgery being performed which may predispose to the development of lung injury because of ischemia and reperfusion, type of anesthesia, and duration of postoperative ventilation.^[11,12]

In the present study, most of the patients had an infectious cause for ARDS (90%, n = 135). Most common cause was pneumonia followed by scrub typhus, leptospirosis, malaria, and dengue. Most common noninfectious cause for ARDS was pancreatitis (5.3%, n = 8). Pneumonia has been found to be the most common cause for ARDS in many other studies. A study done in Canada found 58% of the cases having pneumonia.^[13] Similar finding was noted in a study done in the United States where the pulmonary source of sepsis was found in 43% cases.^[14] Vigg et al. in India reported that 30% of cases of ARDS were due to pneumonia whereas other causes included gastrointestinal disease (25%) and polytrauma (12%).^[7] The study done by Bhadade et al. in India found significant percentage of cases of ARDS secondary to tropical infections. In their study, they have reported 27.6% cases of malaria, 20.7% cases of leptospirosis, and 5.2% cases of malaria with dengue.^[5] In our study as well, a significant number of patients had such tropical infections [Table 2]. However, the distribution of various tropical infections was different, and this could be due to the regional differences in the occurrence of these infections.

In the present study, microbiological diagnosis could be obtained only in 28.6% (n = 43) of the cases. Out of the 53 positive body fluid cultures in our study, the highest number of microbiological diagnosis was obtained from blood culture (34%, n = 18) followed by endotracheal aspirate (30.1%, n = 16). The most common organism isolated was *Acinetobacter* spp. (27.1%, n = 16) followed by *Klebsiella* spp. (25.4%, n = 15). Vigg *et al.* found a higher percentage of positive cultures with 49% of the cases having microbiological diagnosis. In their study, most common positive culture was also from blood (21.5%) followed by endotracheal aspirate (14%) but the most common organism isolated was *Pseudomonas* spp.^[7] Another study analyzed the respiratory microbiological pattern within 24 h of ARDS. The specimen collected included tracheobronchial aspirate and bronchoscopy-guided specimens. A potentially pathogenic organism was isolated in 44% cases and the most common organism isolated was Pseudomonas spp.^[15] The low yield (23%) of microbiological culture in our study may be due to the higher percentage of pathogens such as scrub typhus, leptospira, and malaria, which are not isolated in routine body fluid cultures. Though in the abovementioned studies, Pseudomonas spp. was the most common isolated organism but Acinetobacter spp., the most common organism isolated in our study, was also frequently isolated from clinical specimens in the ICUs. In this regard, our results are similar with the finding of studies from Thailand and China.^[16,17]

The severity scores that were used in our study were APACHE II, APACHE III, and SOFA score. The mean APACHE II score in our study among nonsurvivors was 21.1 ± 7 while that among survivors was 9.06 ± 4.3 . Various studies have shown that the APACHE II score among nonsurvivors is higher than among nonsurvivors.^[13,18,19] In the present study, the mean APACHE III score among nonsurvivors was 86.45 ± 23.5 while that among survivors was 49.2 ± 14 . Studies from various university hospital ICUs across the United States of America have reported varying findings, with some showing a similar difference in scores while others observing no such difference.^[8,20,21] In our study, the mean SOFA score among nonsurvivors was 10.6 ± 10 while that among survivors was 6.43 ± 2.5 . A similar difference was observed in a study from the Postgraduate Institute of Medical Education and Research, Chandigarh, and investigators reported the mean SOFA score among nonsurvivors to be ten while that among survivors it was seven.^[22]

Studies from Australia and India have reported a mean hospital stay of 10.5 ± 2 days and 9.4 days, respectively, which is similar to the value observed in our study.^[22,23]

However, the mean duration of ICU stay and hence hospital stay in a study done by Navarrete-Navarro *et al.* was higher, i.e., 28.5 ± 24.5 days. This study included only trauma patients with ARDS.^[24] The shorter mean duration of hospital stay in the present study may be due to lower percentage of trauma cases which usually have a prolonged ICU and hospital stay as reported in a study from surgical ICU of an academic trauma center in the United States of America.^[25]

Past studies had observed that the mortality rate for ARDS was high but over time there has been a decreasing trend. A study done at university-affiliated Rhode Island Hospital, which was a 9-year, retrospective review of 980 patients with ARDS (1990–1998), found a significant decrease in death rates during this time period from 70% to 51.5%.^[21] A study done by ARDS network in 2005 noted a mortality rate of 26%.^[26] In developed countries, the decrease in mortality rates of ARDS is due to the improvement in the management strategies of these patients. The mortality rate in the present study was 44% (n = 66). This is lower than what was reported from India between 2008 and 2009, where the investigators had found 57% mortality in their study.^[5]

The limitation of this study is that being a descriptive study, the significance of the observed differences between various clinical variables among survivors and nonsurvivors could not be assessed.

CONCLUSION

Pneumonia is the most common etiology followed by tropical infections in the causation of ARDS in our hospital. Presence of preexisting comorbidity, surgery prior to ARDS, higher severity scores at admission, and organ failure scores are frequently associated with poor survival.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- 1. Dushianthan A, Grocott MP, Postle AD, Cusack R. Acute respiratory distress syndrome and acute lung injury. Postgrad Med J 2011;87:612-22.
- Sigurdsson MI, Sigvaldason K, Gunnarsson TS, Moller A, Sigurdsson GH. Acute respiratory distress syndrome: Nationwide changes in incidence, treatment and mortality over 23 years. Acta Anaesthesiol Scand 2013;57:37-45.
- 3. Zambon M, Vincent JL. Mortality rates for patients with acute lung injury/ARDS have decreased over time. Chest 2008;133:1120-7.
- Kallet RH, Jasmer RM, Pittet JF, Tang JF, Campbell AR, Dicker R, et al. Clinical implementation of the ARDS network protocol is associated with reduced hospital mortality compared with historical controls. Crit Care Med 2005;33:925-9.
- 5. 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;57:286-90.

- 6. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, *et al*. Acute respiratory distress syndrome: The Berlin definition. JAMA 2012;307:2526-33.
- Vigg A, Mantri S, Vigg A, Vigg A. Clinical profile of ARDS. J Assoc Physicians India 2003;51:855-8.
- Sheu CC, Gong MN, Zhai R, Chen F, Bajwa EK, Clardy PF, et al. Clinical characteristics and outcomes of sepsis-related vs non-sepsis-related ARDS. Chest 2010;138:559-67.
- Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, et al. Incidence and outcomes of acute lung injury. N Engl J Med 2005;353:1685-93.
- Ando K, Doi T, Moody SY, Ohkuni Y, Sato S, Kaneko N. The effect of comorbidity on the prognosis of acute lung injury and acute respiratory distress syndrome. Intern Med 2012;51:1835-40.
- 11. Matthay MA, Jayr C. Acute respiratory distress syndrome after surgery: Can the risk be decreased? Anesth Analg 2010;111:268-9.
- Hughes CG, Weavind L, Banerjee A, Mercaldo ND, Schildcrout JS, Pandharipande PP. Intraoperative risk factors for acute respiratory distress syndrome in critically ill patients. Anesth Analg 2010;111:464-7.
- Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med 2003;348:683-93.
- Gong MN, Thompson BT, Williams P, Pothier L, Boyce PD, Christiani DC. Clinical predictors of and mortality in acute respiratory distress syndrome: Potential role of red cell transfusion. Crit Care Med 2005;33:1191-8.
- Bauer TT, Valencia M, Badia JR, Ewig S, González J, Ferrer M, et al. Respiratory microbiology patterns within the first 24 h of ARDS diagnosis: Influence on outcome. Chest 2005;128:273-9.
- Reechaipichitkul W, Phondongnok S, Bourpoern J, Chaimanee P. Causative agents and resistance among hospital-acquired and ventilator-associated pneumonia patients at Srinagarind Hospital, Northeastern Thailand. Southeast Asian J Trop Med Public Health 2013;44:490-502.
- Liu YN, Cao B, Wang H, Chen LA, She DY, Zhao TM, et al. Adult hospital acquired pneumonia: A multicenter study on microbiology and clinical characteristics of patients from 9 Chinese cities. Zhonghua Jie He He Hu Xi Za Zhi 2012;35:739-46.
- Estenssoro E, Dubin A, Laffaire E, Canales H, Sáenz G, Moseinco M, et al. Incidence, clinical course, and outcome in 217 patients with acute respiratory distress syndrome. Crit Care Med 2002;30:2450-6.
- Kamal M, Khan AN, Ali G. A comparison of APACHE II and APACHE IV scoring systems in predicting outcome in patients with acute lung injury (ALI) and the adult respiratory distress syndrome (ARDS) in intensive care unit (ICU). Rawal Med J 2013;38:234-8.
- Eachempati SR, Hydo LJ, Shou J, Barie PS. Outcomes of acute respiratory distress syndrome (ARDS) in elderly patients. J Trauma 2007;63:344-50.
- Rocco TR Jr., Reinert SE, Cioffi W, Harrington D, Buczko G, Simms HH. A 9-year, single-institution, retrospective review of death rate and prognostic factors in adult respiratory distress syndrome. Ann Surg 2001;233:414-22.
- 22. 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;130:724-9.
- Bersten AD, Edibam C, Hunt T, Moran J; Australian and New Zealand Intensive Care Society Clinical Trials Group. Incidence and mortality of acute lung injury and the acute respiratory distress syndrome in three Australian States. Am J Respir Crit Care Med 2002;165:443-8.
- Navarrete-Navarro P, Ruiz-Bailén M, Rivera-Fernández R, Guerrero-López F, Pola-Gallego-de-Guzmán MD, Vázquez-Mata G. Acute respiratory distress syndrome in trauma patients: ICU mortality and prediction factors. Intensive Care Med 2000;26:1624-9.
- 25. Salim A, Martin M, Constantinou C, Sangthong B, Brown C, Kasotakis G, et al. Acute respiratory distress syndrome in the trauma intensive care unit: Morbid but not mortal. Arch Surg 2006;141:655-8.
- National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, et al. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006;354:2564-75.