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Pulmonary and Extrapulmonary Causes of Acute Respiratory Distress Syndrome (ARDS) with Thrombocytopenia in Adults Admitted in Intensive Care Areas in A Tertiary Care Hospital

Medical Science

KEYWORDS : Acute Respiratory Distress Syndrome (ARDS), Pulmonary and extrapulmonary causes, Prognostic factors of ARDS.

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ABSTRACT

Background:*Acute Respiratory Distress Syndrome (ARDS) is caused by pulmonary injuries to the lung like community acquired pneumonia (CAP), aspiration, trauma, tuberculosis, etc. and extrapulmonary injuries like sepsis, malaria, leptospirosis, etc. Patients with ARDS may develop thrombocytopenia. There are very few documented studies on comparison of pulmonary and extrapulmonary causes of ARDS patients with thrombocytopenia.*

Objectives: *This study aimed to find out the pulmonary and extrapulmonary causes of ARDS, to correlate the biochemical parameters in these two groups and to assess the prognostic factors of ARDS patients.*

Materials and Method: *This prospective observational study enrolled 100 consecutive cases of ARDS with thrombocytopenia admitted to Medical and Respiratory Intensive Care Units of a tertiary care hospital, over a period of one year.*

Results: *Incidence of ARDS with thrombocytopenia was 10.26 %. ARDS due to extrapulmonary causes were in 79% cases, commonest being acute febrile illness (AFI) in 28%, followed by malaria in 16%. ARDS due to pulmonary causes were 21%, commonest being CAP in 17%. Overall mortality was 49% which was more in pulmonary causes (66.6%). Percentage of cases as well as mortality was more in age group > 60 years. Expired patients had significantly lower hemoglobin and PaO2/FiO2 as compared to survived patients.*

Conclusion: *Acute febrile illness, community acquired pneumonia and malaria were the predominant causes of ARDS. Percentage of ARDS cases due to tropical illnesses were quite high, which can be prevented by early diagnosis and proper treatment of these diseases. Low hemoglobin, low PaO2/FiO2 and old age were significant predictors of mortality in adult ARDS patients with thrombocytopenia admitted in ICUs.*

Introduction

Acute Respiratory Distress Syndrome (ARDS) is caused by pulmonary injuries to the lung like community acquired pneumonia (CAP), aspiration, trauma, tuberculosis, etc. and extrapulmonary injuries like sepsis, malaria, leptospirosis, etc.[1] Patients with ARDS may develop thrombocytopenia secondary to deposition of platelets in pulmonary capillary bed.[2]

The American-European Consensus Conference (AECC) has published the diagnostic criteria for Acute Respiratory Distress Syndrome (ARDS): [3, 4]

Acute onset

Ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (PaO_2 /FiO_2) of ≤ 200, regardless of positive end-expiratory pressure

Bilateral infiltrates seen on frontal chest radiograph and pulmonary artery wedge pressure of 18 mm Hg or less when measured, or no clinical evidence of left atrial hypertension.

ARDS is a major cause of morbidity and mortality worldwide.[3, 4]

The present study was conducted with the following aims and objectives:

To find out the pulmonary and extrapulmonary causes of ARDS

To correlate the biochemical parameters in pulmonary and extrapulmonary groups

To assess the prognostic factors of ARDS patients.

Materials &Method

This prospective observational study enrolled 100 consecutive cases of ARDS with thrombocytopenia admitted to Medical Intensive Care Unit (MICU) and Intensive Respiratory Care Unit (IRCU) of a tertiary care hospital over a period of one year, i.e. from June 2012 to May 2013. Institutional Ethical Committee approval was obtained for this study. Patients with ARDS were identified through a prospective daily ICU surveillance, based on the American-European Consensus Conference criteria (AECC). All adult patients with ARDS with thrombocytopenia admitted in ICUs were included in this study and patients with chronic obstructive pulmonary disease, HIV seropositive, cardiac failure and age below 12 years were excluded. After the valid written consent from the patients,name, age, sex, address, diagnosis, general and clinical examination,biochemical investigations (complete blood count, arterial blood gasanalyses), chest radiographand duration of stay in the ICU were documented in an Excel sheet.

ARDS cases were divided into two groups according to pulmonary and extrapulmonary causes.

Causes of ARDS were diagnosed clinically, by chest X- rayand by biochemical tests. Malaria was diagnosed by antigen detection test (Accucare, Lab-care Diagnostics Pvt. Ltd., Mumbai) and peripheral smear; dengue by rapid antigen detection test (Dengue NS1 card, Melrose Healthcare Pvt. Ltd., Chennai) and rapid antibody detection test (Dengue IgG / IgM WB, SD Bioline, Haryana, India); and leptospira by rapid antibody detection test (Rapid test for IgM Antibodies to Leptospira, Leptocheck, Goa). All patients with febrile illness, who were not diagnosed by the above tests, were put in the group of Acute Febrile Illness (AFI).

Statistical analysis was performed using computer based program SPSS version 15. Student©-test was performed for

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continuous variables. ◎ value <0.05 was considered to be statistically significant.

Results

During the study period, 974 patients were admitted in MICU and IRCU, out of which 100 patients were diagnosed as ARDS. Therefore, incidence of ARDS in this study was 10.26%. Maximum cases were males (60%) and Male: Female ratio was 3:2. Maximum number of cases was in the age group of >60 years (32%) (Figure1). Characteristics of ARDS patients are shown in Table 1.

Causes of ARDS and mortality are shown in Table 2. ARDS due to extrapulmonary cause was seen in 79% cases, commonest being Acute Febrile Illness (AFI) in 28%, followed by malaria in 16% cases.ARDS due to pulmonary cause was 21%, commonest being Community Acquired Pneumonia (CAP) in 17%, followed by aspiration in 2% cases. Mortality due to leptospirosis was 75%, followed by CAP in 70.58% and cases of sepsis (60%).

Pulmonary and extrapulmonary causes were compared in Table 3. All patients included in this study had platelet count <1,00,000/cu.mm. Maximum ARDS patients had platelet count between 80,000 to 1,00,000 / cu.mm (Figure 2). Mortality was maximum in patients with platelet count between 80,000 to 1,00,000/cu.mm and minimum in patients with platelet count between 10,000 to 20,000/cu.mm. PaO_2/FiO_2 of all patients was< 200 and 69% patients showed ground glass opacity in Chest X-ray, which is characteristic of ARDS.[5](Figure3).

Overall mortality was 49% in this study. Mortality was maximum in age group of > 60 years of age (46.93%). Mortality was 66.7% in extrapulmonary causes and 44.3% in pulmonary causes (Figure 4). On comparison expired and survived patients of ARDS, mean age was significantly higher and mean hemoglobin was significantly lower in expired patients. PCO_2 was significantly higher, where as PaO_2 and PaO_2/FiO_2 was significantly lower in expired patients (Table 4).

Discussion

Acute respiratory distress syndrome (ARDS) manifests as rapidly progressive dyspnoea, tachypnea and hypoxemia. Diagnostic criteria include acute onset, profound hypoxemia, bilateral pulmonary infiltrates and the absence of left atrial hypertension.[2]

Total 100 patients of ARDS were enrolled in this study. The incidence of ARDS with thrombocytopenia in ICUs during the study period of one year was 10.26% (100/974). A study from India showed incidence of ARDS in ICUs as 10%, which is almost similar to the present study,[6] whereas studies from western countries like Spain[7] and Belgium[8] showed much lesser incidence in ICUs(2.2% and 2.4% respectively) possibly due to early interventions and better care taken in western countries.

Maximum number of cases of ARDS was seen in the age group of > 60 years (32%) (Figure 1). Both Gordan *et al* and Elosie *et al* have stressed that incidence of ARDS increases with age.[3,9] Study by Eachempati *et al* showed higher incidence of ARDS in old age (61% patients in age group > 65 years).[10] In this study, mean age was 46.47years (SD ±17.18) (Table1). A study from South India showed mean age as 41.9 years (SD ±15.35)[11], whereas a study from North India showed mean age as 43 years.[12] A study in Switzerland reported mean age of 46 years.[13]

In this study, the commonest etiology in ARDS patients was acute febrile illness (28%), followed by community acquired pneumonia (17%), malaria (16%) and sepsis (10%) (Table 2). A previous study from Mumbai, India showed commonest etiology to be AFI (27.6%) and malaria (27.6%).[14] Study from Iceland showed incidence of ARDS more in pneumonia and sepsis (29% in both).[15] Study from South Australia showed sepsis (32%) to be the most common cause, followed by pneumonia (30%).[16]

In the present study, ARDS due to malaria was seen in 16%, dengue in 10% and leptospirosis in 8% cases. Thus ARDS due to tropical diseases was seen in total 34% of patients. A study from South India showed that tropical infections contributed to 26% of total ARDS cases.[11]A previous study from Mumbai showed malaria (27.6%), followed by leptospirosis (20.7%) and dengue (5.2%).[14]This can be attributed to the increased prevalence of these tropical diseases in India owing to favourable climatic conditions for both the agent and the vector.

ARDS has different underlying pathologies resulting from two different pathogenic pathways: "pulmonary" and "extrapulmonary" insult to the lung parenchyma. In the present study, mean age (43.95 years) and mean platelet count (53.06 /cu.mm in thousands)of extrapulmonary causes was significantly lower than mean age (55.95 years) and mean platelet count (84.43/cu.mm in thousands) of pulmonary causes (Table 3). Possible explanation for this is thattropical illnesses are included in extrapulmonary causes, which were mostly seen in lower age group and platelet count was also very low in these cases as compared to that in pulmonary causes.

Mean of PaO_2 and PaO_2/FiO_2 was significantly lower in pulmonary causes (72.48 mmHg and 123.71 respectively) as compared to extrapulmonary causes (87.95 mmHg and 159.01 respectively) (Table 3). A similar study from North India compared pulmonary and extrapulmonary causes of ARDS, where mean age was lower in extrapulmonary (36 years) than pulmonary causes (46 years) and mean PaO_2/FiO_2 ratio was also lower in pulmonary (147.7) than in extrapulmonary causes (157.9).[12]Another study from Switzerland also reported mean PaO_2 and PaO_2/FiO_2 lower in pulmonary causes (91.7 mmHg and 123.8) and higher in extrapulmonary causes (105.9 mmHg and 149.4), similar to the present study.[13]

The mortality rate of ARDS is estimated to be between 37% to 57%.[12, 14, 17-19] In the present study, overall mortality was 49%. A study from North India showed mortality in ARDS to be 47.8%, which is almost similar to this study.[12]A study from Mumbai showed mortality in ARDS patients to be 56.8%.[14] A recent study from Tamilnadu showed 41.8% mortality.[17] A study from Spain[18] and another study by Valta *et al* [19] showed 42.7% and 37% mortality respectively, in ARDS patients.

In the present study, mortality increased with age in ARDS patients. Mortality was maximum in age group of > 60 years of age (46.93%). A study by Gordan *et al* also showed that mortality increases with age which was 60% in > 85 years of age.[9] A study from North India also showed that mean age in expired (45 years) was more than in survivors (41 years).[12]

In this study, mortality was maximum in patients with platelet count between 80,000 to 1,00,000/cu.mm. Possible explanation is that maximum patients in this group were of community acquired pneumonia (CAP), which was seen

in older age group. Mortality was low in patients suffering from tropical illnesses as most of them were from younger age group and were diagnosed by rapid tests and treatment started immediately (Table 2).

Mortality due to leptospirosis was 75% (6/8) in this study, followed by cases of sepsis (60%).A study from Brazil showed mortality in Leptospirosis as 51%.[20] A study from Belgium showed that ARDS patients with sepsis was associated with highest mortality (49%).[8] In the present study, out of 16 malaria cases, 6 died (37.5%) (Table 2). Study by Sahoo *et al* had a much higher mortality (75%) in ARDS patients with malaria.[21]

Both the survivors and expired were compared in this study (Table 4). Mean age in expired (52.80 years) was significantly higher than survivors (40.39 years). Study from Belgium also showed mean age in expired (58 years) higher than survivors (47 years).[8]

In the present study, mean PCO_2 was significantly higher in expired (59.37 mmHg) than survivors (43.08 mmHg). Mean haemoglobin, PaO_2 and PaO_2/FiO_2 were significantly lower in expired (7.25 gm/dl, 80.90 mmHg and 126.80), as compared to survivors (8.41 gm/dl, 88.35 mmHg and 175.43) (Table 4). Rubenfeld *et al* in his study demonstrated significantly more mortality (p< 0.001) in patients with PaO_2/FiO_2 <200 (41.1%), as compared to those with >200 (28.6%)[9] though in our study all patients had PaO2/FiO2 was < 200 (Table 4).

Conclusion

febrile illness, community acquired pneumonia and malaria were the primary causes of ARDS, followed by dengue, sepsis and leptospirosis. Percentage of ARDS cases due to tropical illness is quite high (34%), which can be prevented by early diagnosis and treatment of these diseases. Low hemoglobin, low PaO_2/FiO_2 and old age were significant predictors of mortality in adult ARDS patients with thrombocytopenia.

Table 1: Characteristics of ARDS patients

Parameters	Mean	Standard deviation (±)
Age (years)	46.47	17.18
Platelet (/cu.mm in thousands)	59.65	27.12
PaO_2/FiO_2	148.83	33.39
Hospital stay (days)	15.53	5.01

Table 2: Pulmonary and extrapulmonary causes of ARDS with outcome

Causes	No. of cases	Expired No. (%)
Pulmonary cause		
Community acquired pneumonia (CAP)	17	12 (70.58)
Aspiration	02	02 (100.00)
Tuberculosis	02	00 (00.00)
Total	21	14
Extrapulmonary causes		
Acute fibrile illness (AFI)	28	10 (35.71)
Malaria	16	06 (37.50)
Sepsis	10	06 (60.00)
Dengue	10	03 (30.00)
Leptospirosis	08	06 (75.00)
Others*	07	04 (57.14)
Total	79	35

*Pancreatitis (3), Ventilator associated pneumonia (2), Snake bite (1), Urinary tract infection (1).

Table 3: Comparison of pulmonary and extrapulmonary causes of ARDS

Parameters	Pulmonary cause (21) Mean (± SD)	Extrapulmonary cause (79) Mean (± SD)	P value	Significance
Age (years)	55.95(± 14.28)	43.95(± 17.094)	0.004	Significant
Hb (gm/dl)	7.61(± 1.173)	7.90(± 1.175)	0.312	Not significant
Platelet (/cu.mm in thousands)	84.43(± 7.941)	53.06(± 26.615)	0.000	Significant
PCO_2 (mmHg)	51.95(± 13.113)	50.82(± 12.469)	0.716	Not significant
PaO_2 (mmHg)	72.48(± 17.270)	87.95(± 11.203)	0.000	Significant
PaO_2/FiO_2	123.71(±21.875)	159.01(±34.399)	0.000	Significant
Duration of hospital stay (days)	15.52(± 05.828)	15.28(± 5.618)	0.860	Not significant

Table 4: Comparison of survived and expired in ARDS patients

Parameters	Survived (51) Mean (± SD)	Expired (49) Mean (± SD)	P value	Significance
Age (years)	40.39(±16.387)	52.80(±15.781)	0.000	Significant
Hb (gm/dl)	8.41(± 0.960)	7.25(± 1.086)	0.000	Significant
Platelet (/cu.mm in thousands)	59.92(± 27.868)	59.37(± 26.613)	0.919	Not significant
PCO_2 (mmHg)	43.08(± 7.378)	59.37(± 11.398)	0.000	Significant
PaO_2 (mmHg)	88.35(± 10.600)	80.90(± 16.277)	0.008	Significant
PaO_2/FiO_2	175.43(±23.856)	126.80(±26.992)	0.000	Significant
Duration of hospital stay (days)	15.00(±4.783)	15.67(±6.434)	0.553	Not significant

Fig. 1: Age distribution in 100 ARDS cases

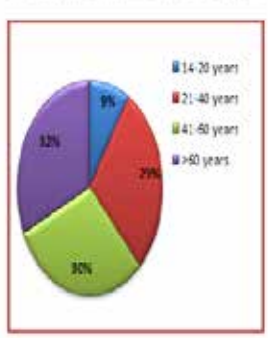

Fig. 2: Platelet count in 100 ARDS cases

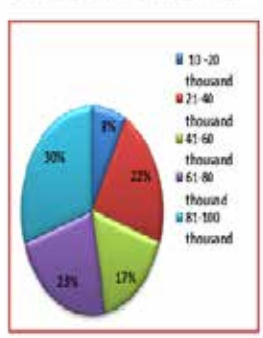

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Fig. 3: X ray findings in 100 ARDS cases

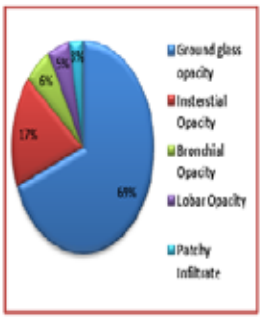
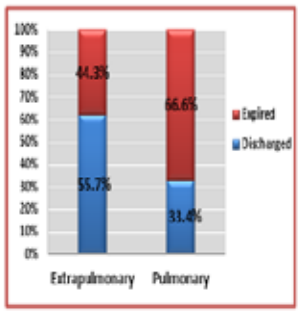


Fig. 4: Mortality due to pulmonary and extrapulmonary causes



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