

CLINICAL PROFILE OF ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN A TERTIARY CARE CENTRE/ HOSPITAL

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ABSTRACT

BACKGROUND

ARDS is considered as the most severe form of acute lung injury, a form of diffuse alveolar injury and a leading cause of death in critical care settings.

Aims and Objectives-

- To analyse the ARDS cases in admitted patients with special reference to risk factors associated with poor prognosis.
- To study the aetiology of ARDS.
- To study severity and outcome of ARDS cases.

MATERIALS AND METHODS

This study was an observational study. It included 80 patients of ARDS, which are fulfilling diagnostic criteria according to Berlin definitions 2012. The study period was 1 year.

RESULTS

In critically ill patients who were hospitalised in Critical Care Units (CCU), the prevalence of ARDS has been estimated at about 5-15% of patients. In our study period, there were 800 admissions with prevalence of ARDS of 12.50%. Our results are consistent with those of Roupie et al, who reported a twice higher mortality (60%) in patients with ARDS than that recorded in patients with mild ALI (31%). Pulmonary infection (37.5%) followed by Dengue (23.75%) were the most common causes for ARDS in this study. In our study, sepsis was the predominant indirect cause of ARDS with 35 out of 80 patients of Dengue, i.e. 19 (23.75%). There was a significant association between severity of ARDS and various aetiological groups with p-value of 0.0001. Patients with ARDS had lower PO₂, lower PO₂/FiO₂ ratio, severe metabolic acidosis, higher serum creatinine, higher blood urea nitrogen and worsened critical scores including GCS scoring, lower systolic blood pressure and lower mean arterial pressure.

CONCLUSION

1. Prevalence of acute respiratory distress syndrome is quite common in ICU setting.
2. Pulmonary infection was the most common non-tropical direct cause of ARDS, while sepsis was the most common cause of indirect ARDS.
3. Dengue, Malaria and Leptospirosis were most common tropical causes of ARDS.
4. Factors that showed association with mortality-
 - Aetiology had significant association with outcome.
 - Anaemia, tachycardia, raised ESR and high WBC count had significant association with outcome.
 - Deranged serum creatinine and decreased urine output had significant association with outcome.
 - Low systolic blood pressure and low diastolic blood pressure was significantly associated with poor outcome.
 - Duration of ventilator support was associated with mortality significantly.
 - Culture positivity was associated significantly with mortality.

KEY WORDS

ARDS.

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BACKGROUND

Acute Respiratory Distress Syndrome (ARDS) was first described in 1967 in twelve patients presenting with acute respiratory failure that was refractory to oxygen therapy with decreased pulmonary compliance and diffuse infiltrates on chest x-rays.¹ Although, this syndrome was given a name (at that time, "adult respiratory distress syndrome"), there was no well-established criteria for its diagnosis.

In 1988, a lung injury score was created in order to diagnose and evaluate ARDS severity, taking into account four parameters: chest x-ray, hypoxia through the oxygen

tension/ fraction of inspired oxygen ratio, pulmonary compliance and positive end-expiratory pressure (PEEP).²

It was not until 1994 that the American European Consensus Conference on ARDS established diagnostic criteria for ARDS, defining it as a “syndrome of inflammation and increased pulmonary capillary permeability accompanied by a large number of clinical, radiological and physiological abnormalities, which are not caused by pulmonary capillary hypertension but may coexist with it.”³ On that occasion, Acute Lung Injury (ALI) was defined as a clinical profile of acute respiratory failure with bilateral infiltrates on chest x-ray. No left atrial hypertension (pulmonary capillary wedge pressure less than 18 mmHg) and hypoxaemia presenting an arterial oxygen tension/fraction of inspired oxygen ratio less than or equal to 300. If this ratio is less than or equal to 200, the patient is considered ARDS.

Since the 1994 American-European Consensus Conference on ARDS, at which the diagnostic criteria were redefined, the number of epidemiological studies has been steadily growing. In Intensive Care Units (ICUs), ARDS is seen in 2% to 26% of all hospitalised patients and the highest rates are observed among patients on mechanical ventilation.^{4-8,9} In a recent analysis of the ARDS Network Database, Goss et al estimated the incidence of ARDS in the US at 64 per 100,000.¹⁰ In critically ill patients hospitalised in Intensive Care Units (ICUs), the prevalence of ALI/ARDS has been estimated at about 5 - 15% of patients.^(11,9,12,13)

The principal risk factors for development of lung injury that have been identified since the first studies on ARDS carried out were sepsis, pneumonia, aspiration of gastric content, multiple trauma and shock due to multiple transfusions.¹⁴⁻¹⁷ This finding has been confirmed in more recent studies.^{6,7,8,18} In a study of 217 ARDS cases in Argentina,¹⁹ sepsis, pneumonia, shock and trauma were found to be the most frequent risk factors.

The Seattle study included three markers of severe trauma including multiple transfusions for emergency resuscitation (15U within a 24-h period), multiple bone fractures or an unstable pelvic fracture and lung contusion. Of these, the category of multiple transfusions was associated with the highest incidence of ARDS 35%. Of interest, multiple transfusions were also associated with a 35% incidence of ARDS when they occurred in medicine service patients without trauma. Long bone fractures were associated with the lowest incidence of ARDS of these three (11%), whereas the incidence associated with lung contusion was intermediate (22%). Patients with trauma including any or a combination of these three definitions had an overall ARDS incidence of 25.5%.

On ALIVE study, it was found that mortality was independently associated with age and one variable reflecting underlying disease (immunoincompetence) with the severity of acute pulmonary and non-pulmonary organ failures (as reflected by the SAPS II and LOD scores) with acidosis (pH<7.30) and the occurrence of early barotrauma.

Objectives

1. To analyse the ARDS cases admitted patients with special reference to risk factors associated with poor prognosis.
2. To study the aetiology of ARDS.

3. To study severity and outcome of ARDS cases.

MATERIALS AND METHODS

This study was an observational study. 80 patients were included in the ARDS cohort, when meeting for the first time the consensus criteria for ARDS and not having any of the exclusion factors. Patients were classified as having ARDS when the worst PaO₂/ FiO₂ ratio recorded within the first 24 hours of inclusion was 300 or less.

Diagnostic Criteria⁽³⁾

Acute onset of respiratory distress with a relevant clinical setting-

- a. Partial pressure of oxygen in arterial blood (PaO₂ mmHg)/ fractional inspired oxygen (FiO₂) ratio < 300.
- b. Bilateral infiltrates on chest x-ray.
- c. An initial pulmonary artery occlusion pressure less than 18 mmHg or no clinical evidence of left atrial hypertension or congestive cardiac failure at the time of presentation.

Exclusion Criteria

- a. Age < 13 years.
- b. History of ischaemic heart disease or valvular heart disease or cardiomyopathies including diastolic dysfunction.
- c. Patients having signs/ symptoms of cardiac failure like raised jugular venous pressure, raised central venous pressure and radiological features of high pressure oedema (cardiomegaly, dilated upper lobe vessels, Kerley's lines, central lung shadowing with absence of air bronchogram), ECG suggestive of ischaemic heart disease or accelerated hypertension or hypertensive heart disease as documented by 2D echo.
- d. Chronic respiratory failure or patients with moderate-to-severe restrictive or Obstructive Lung Function. (COPD, ILD, lung resection, pulmonary tuberculosis active or old with fibrosis and destruction of lung parenchyma).
- e. Death within 4 hours of admission.

A data collection of 80 patients is done in prospective and randomised manner and from a critical care unit in a tertiary care centre/ hospital. A minimum data set including demographic (age and gender) admission characteristics and discharge information (outcome, cause of death) was collected of all patients. This included demographic characteristics, the patient source (hospital, ward emergency or operating room or transfer), variables used for calculation of acute physiology and chronic health score (APACHE III), underlying diseases including immunoincompetence and its causes and the presence of chronic organ failure and comorbid conditions like diabetes mellitus, alcoholic liver disease etc. This comprised documentation of the diagnostic criteria for the syndrome, the primary cause(s) of ARDS and whether the initial insult was pulmonary (“Direct”) or non-pulmonary (“Indirect”).

Statistical analysis was done using patient related variables as well as process of care variables. Patient related variables included age, gender, diagnosis at the time of hospital admission, immunosuppression associated comorbid conditions and pO₂/ FiO₂ ratio, while process of care variable included ventilatory support and settings, CCU stay,

development of organ failure and outcome from CCU. For statistical analysis, patient having more than one diagnosis were put in one category. Patients developing sepsis irrespective of primary diagnosis like pneumonia were labelled as sepsis.

The data was studied and statistically treated. The univariate analysis was done using chi-square/ Fisher test and simple percentage. The test of significance was set < 0.05. T test was done to test two groups where required.

RESULTS

For the present study, 80 patients were observed in medical CCU of tertiary care hospital and their outcomes for different categories under the requirement of study are as follows:

Out of 80 patients included in study 29 died, while 51 recovered completely.

Age Group	Outcome				Total	Chi-Square	P value
	Recovered		Death				
	N	(%)	N	(%)			
<20 years	1	20	4	80	05	8.76	0.03
20 - 40 years	29	78.38	8	21.62	37		
41 - 60 years	17	54.84	14	45.16	31		
>60 years	4	57.14	3	42.86	07		

Table 1. Age distribution of Patients as per Outcome

The maximum number of patients died from the age group of 40 to 60 years that were 14 (45.16%) and minimum number of patients died from age group > 60 years that were 3 (42.86%), while maximum percentage of patients died from the age group < 20 years that is 80%.

Sex	Outcome				Total	Chi-Square	P value
	Recovered		Death				
	N	(%)	N	(%)			
Female	22	57.90	16	42.10	38	1.07	0.30
Male	29	69.00	13	31.00	42		

Table 2. Sex distribution of Patients

ARDS Severity Distribution

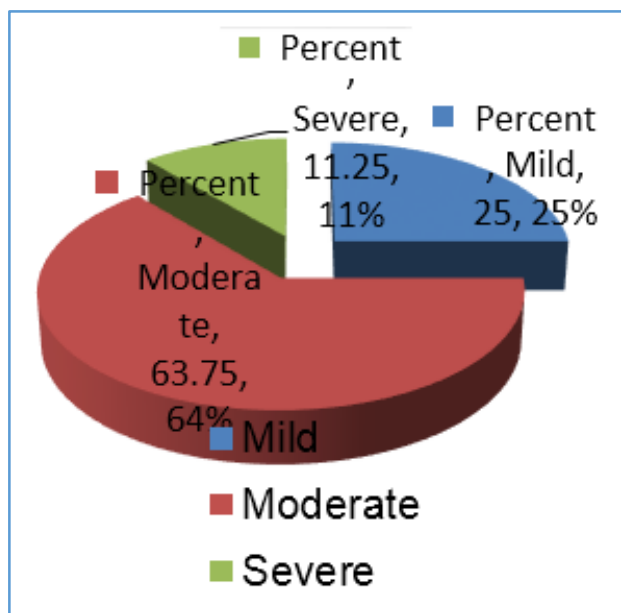


Figure 1. ARDS Severity Distribution

Out of 80 cases 20 were mild, 51 were moderate and 9 cases were severe ARDS.

PO ₂ / FiO ₂ Severity	Recovered	Death	Total	Chi-Square Test	P value
Mild	16 (80.00%)	4 (20.00%)	20	5.92	0.05
Moderate	32 (62.75%)	19 (37.25%)	51		
Severe	3 (33.33%)	6 (66.67%)	9		
Total	51 (63.75%)	29 (36.25%)	80		

Table 3

From the table it is clear that out of 80 patients, maximum mortality were found in severe ARDS 66.67%, while minimum found in mild ARDS 20%.

Sl. No.	Suspected Aetiology	Outcome				Total
		Recovered		Death		
		N	(%)	N	(%)	
1	Aspiration	0	0.00	5	100.00	5
2	Burn	0	0.00	1	100.00	1
3	Dengue	18	94.70	1	5.30	19
4	Leptospirosis	0	0.00	3	100.00	3
5	Malaria	4	66.70	2	33.30	6
6	Malaria + Dengue	2	100.00	0	0.00	2
7	Pancreatitis	1	100.00	0	0.00	1
8	Poisoning	0	0.00	2	100.00	2
9	Pulmonary Infection	25	83.30	5	16.70	30
10	Sepsis	1	10.00	9	90.00	10
11	Transfusion Reaction	0	0.00	1	100.00	1

Table 4. Aetiology Distribution

Pulmonary infection was the most common cause of ARDS in our study with highest number of cases (30) with 16.70% of mortality followed by Dengue (19 cases) with mortality of 5.30%. ARDS secondary to Sepsis associated with 90.00% mortality. Malaria (6 cases) as a cause of ARDS was found with 33.30% mortality. However, the less common causes of ARDS like Aspiration, Burn, Leptospira, Poisoning and Transfusion Reaction was associated with 100% mortality. The highest cases of recovery was found in dengue ARDS.

It was found that the clinical outcome in terms of mortality significantly different among different aetiologies with p-value < 0.0001.

Tracheal/ Sputum Culture	Outcome				Total
	Recovered		Death		
	N	(%)	N	(%)	
Acinetobacter	1	7.10%	13	92.90%	14
H. influenza	0	0.00%	7	100.00%	07
Klebsiella	10	83.30%	2	16.70%	12
MRSA	4	66.70%	2	33.30%	6
Pneumococci	7	87.50%	1	12.50%	08
No Growth	29	87.90%	4	12.10%	33

Table 5. Tracheal/ Sputum Culture versus Outcome

Chi-Square= 44.003; P-value < 0.0001

Tracheal or Sputum culture has been done in 80 patients and found to be positive in 47 (58.75%). 25 (53.19%) culture positive patient have died, while 22 patients (46.80%) have

been recovered. 14 patients (29.78%) were found to be culture positive for Acinetobacter and only 1 patient has been recovered. Statistical analysis of culture positivity and outcome showed significant correlation with p-value <0.0001.

Cases with x-ray suggestive of bilateral infiltrate on admission were 56, while the first x-ray study was normal among 24 cases.

X-Ray on Admission	Recovered	Death	Total
Bilateral Infiltrate	32	24	56
Normal	19	5	24

Table 6. X-ray on admission with Features of ARDS

Variables	Outcome										T-test	P-value
	Recovered					Death						
	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max		
Age	40	14	38	19	72	41	17	46	15	72	0.21	0.84
Resp. Rate	25	6	24	14	36	27	8	28	14	38	1.42	0.16
SBP	118	15	118	90	148	102	19	98	76	142	4.08	0.0001
DBP	68	9	70	50	86	62	9	60	50	80	3.21	0.002
HR	100	15	100	70	130	111	20	112	78	144	2.68	0.009
Temp	99.91	2.11	99.4	96.2	104.6	101.1	4.63	100.4	96	122	1.56	0.12
Hb	11.55	1.41	11.5	7.7	14.4	10.62	2.14	10.6	6.6	16.4	2.34	0.02
WBC	8986	3281	8000	3000	16500	12234	5461	13500	3200	26000	3.33	0.0013
ESR	30	19	24	10	110	40	23	38	10	110	2.05	0.04
Platelets	201824	120681	164000	32000	450000	264655	385557	142000	26000	1700000	1.08	0.28
Creatinine	0.91	0.44	0.9	0.2	2.4	2.06	1.46	1.7	0.2	6.1	5.25	<0.0001
Urea	24	12	21	12	88	44	23	36	14	90	5.01	<0.0001
Na ⁺	134	16	136	33	151	127	20	129	32	144	1.78	0.08
K ⁺	4.22	0.74	4.2	2.2	5.5	4.22	1.19	4.2	2.5	6.5	0.01	0.99
SGOT	86	91	64	18	540	85	103	60	16	540	0.05	0.96
SGPT	121	121	85	16	740	154	154	80	24	540	1.05	0.29
PO ₂ / FiO ₂	171	27	180	80	196	159	41	174	80	196	1.57	0.12
Albumin	4.22	0.74	4.2	2.2	5.5	4.22	1.19	4.2	2.5	6.5	0.01	0.99
Urine Input	2400	599	2400	1200	3600	1959	570	2000	1000	3200	3.22	0.002
Urine Output	1831	600	1900	600	3200	1164	706	1000	100	2800	4.48	<0.0001
GCS	15	0	15	15	15	13	3	15	6	15	4.42	<0.0001
Ventilator Invasive Mode (Days)	3	2	3	0	8	6	2	6	3	11	6.83	<0.0001
Ventilator Non-Invasive Mode (Days)	3	1	3	1	5	1	1	1	0	3	7.05	<0.0001
Ventilator Total (Days)	6	2	6	2	10	7	2	6	4	13	3.34	0.0013
ICU Stay (Days)	9	2	8	5	14	8	2	8	4	13	1.71	0.09

Table 7. Various Parameters and their association with ARDS

DISCUSSION

All the patients included in our study had acute respiratory distress syndrome with pO₂/FiO₂ ratio < 300. Severity of ARDS and its association and correlation with various factors pertaining to patient himself, the illness causing admission to medical intensive care unit and outcome in the form of survival were studied.

Our study was carried in exclusive medical intensive care unit and all surgical patients including trauma patients were not considered.

In critically ill patients hospitalised in critical care units (CCU), the prevalence of ARDS has been estimated at about 5-15% of patients.^{11,9,12,13} In our study period, there were 800 admissions with prevalence of ARDS 12.50%. In our study, overall mortality was 36.25%.

In the recent International survey of mechanically ventilated patients, the ICU mortality rate of the 231 patients with ARDS on ICU admission was 52%.⁹ In other single-centre epidemiological studies of unselected patients, mortality

rates still appear to be greater than 50%.^{12,13,20} Our results were consistent with these studies.

Our results are consistent with those of Roupie et al, who reported a twice higher mortality (60%) in patients with ARDS than that recorded in patients with mild ALI (31%). They differ however from those reported in two recent population-based studies, where the mortality rates of ARDS were similar at about 40% or lower.^{18,11} Exclusion of trauma-related ARDS cases, which usually have better prognosis would be the possible explanation for this result.

ARDS appears to be more common with increasing age in patients with similar underlying risk conditions,^{16,21} (Hudson et al and Artigas et al).

In our study, patients with all age group above 13 had developed acute respiratory distress syndrome. However, there was no significant difference in survival among various age groups. The mean age of the patients enrolled in our study was 40 yrs. There was a statistically significant relation seen in mortality with age group of less than 20 years. A significant association between age and mortality has been

shown in several studies. However, in a study conducted in North India by Agarwal et al²² it was observed that when patients aged more than 50 years were compared to younger patients, the outcome was not significantly different.

In our study, out of 80 patients 42 (52.5%) were male patients and 38 (47.5%) were female patients. As per previous studies, gender appears to have no effect on the likelihood of developing ARDS given similar risk conditions.^{16,23} Our results were consistent with these studies.

The specific infections related to severe sepsis vary considerably by geographic area. For example, leptospirosis is a common cause of ARDS in Brazil²³ and also in Thailand, India and other tropical countries, but not in the United States or Western Europe.

Pulmonary infection (37.5%) followed by Dengue (23.75%) were the most common causes for ARDS in this study. A study conducted by Vigg et al in Hyderabad had made similar observations with primary pulmonary infection being the most common cause of ARDS. In 43.75% of the patients in the study ARDS could be attributed to direct causes, predominantly pulmonary infection. Ninety five percent of the cases of ARDS in this study were secondary to infectious causes. Our results were consistent with this study.

In our study, sepsis was the predominant indirect cause of ARDS with 35 out of 80 patients of Dengue, i.e. 19 (23.75%). Sepsis was the next leading causes of ARDS contributing 12.5%. Other major causes of ARDS were Malaria and Leptospirosis contributing 10.25%.

Direct causes of acute respiratory distress syndrome were pneumonia and aspiration together contributing to 43.75% of patients. Among indirect non-pulmonary non-tropical causes sepsis was the most common, causing acute ARDS in 10 (12.5%) patients.

Other causes which contributed to acute respiratory distress syndrome was poisoning (2), Burn (1) and Transfusion Reaction (1).

A number of factors related to underlying conditions, aetiologies, severity of lung injury, non-pulmonary organ failure and management have been identified in outcome studies of ARDS.^{9,12,13,21,24,25,26} The principal variables influencing outcome appear to be chronic liver disease^{12,20} and immunodepression,^{12,13,21} sepsis (OR= 2.8)^{13,20} and the occurrence of non-pulmonary organ dysfunction.^{13,21,25}

In our study, significant association was seen between mortality and aetiology of ARDS. Mortality was 27.30% in patients with alcoholic liver disease. One study has found that chronic alcoholism carries an increased risk of development of ARDS, given similar risk conditions as observed by Moss M, Bucher B, Moore FA et al (1996).

Patients with ARDS had lower PO₂, lower pO₂/FiO₂ ratio, severe metabolic acidosis, higher serum creatinine, higher blood urea nitrogen and worsened critical scores including GCS scoring, lower systolic blood pressure and lower mean arterial pressure.

A low pH was associated with increased mortality points to the adverse impact of metabolic acidosis on outcome. This finding probably reflects circulatory failure and underlying severity.

This observation supports the previous literature and postulations that ARDS is part of a systemic syndrome, now called multiple organ failure, in which the lung features

heavily but may also include renal failure and injury to liver, gut and skin.²⁶

In patients with ARDS, most of the deaths occurred in six to ten days suggesting rapid course of underlying pathology. The fact that most cases of ARDS occur quickly after the onset of the clinical predisposition underscores the potential need for rapid intervention in these patients.

A study conducted by Michelle Ng Gong had noted that the number of units of blood products transfused were significantly higher in the group of patients that died compared to those that recovered. This apparent increase in mortality amongst patients transfused larger volumes of blood products, may be either because this group has a greater degree of organ dysfunction thus necessitating transfusions or may indicate that the transfusions have contributed to the lung injury. Our study showed that there was significant association between number of blood products transfused and mortality (p-value 0.004).

In this study, there was microbiological growth in trachea or sputum cultures were taken in 100% patients. Where 58.75% patients were having microbial growth, out of which 53.19% patients died. This culture positivity was significantly associated with mortality (p-value 0.0001).

Patients with ARDS were put on ventilator with guidelines from recent ARDS network trial with all patients initially put on assist control volume control pressure support mode with initial tidal volume 6 mg per kg body weight. PEEP was increased whenever possible to increase PaO₂ and decrease requirement of FiO₂, so as to keep FiO₂ at or below 60 and to keep end inspiratory plateau pressure <30 cm H₂O. All patients included in this study required ventilator support.

Limitations

- The relatively small number of ARDS cases that we were able to document.
- It is possible that we missed some patients with our defined clinical risk conditions.
- Left atrial pressure was not directly measured causing exclusion of large number of patients.
- Long-term morbidity and mortality were not studied.
- Study was only observational and non-interventional.
- Because of the overwhelming nature of the lung injury, once it is established, prevention would appear to be the most effective strategy for improving the outlook in this condition.

CONCLUSION

1. Prevalence of acute respiratory distress syndrome is quite common in ICU setting.
2. Pulmonary infection was the most common non-tropical direct cause of ARDS, while sepsis was the most common cause of indirect ARDS.
3. Dengue, Malaria and Leptospirosis were most common tropical causes of ARDS.
4. Factors that showed association with mortality-
 - Aetiology had significant association with outcome.
 - Anaemia, tachycardia, raised ESR and high WBC count had significant association with outcome.

- Deranged serum creatinine and decreased urine output had significant association with outcome.
- Low systolic blood pressure and low diastolic blood pressure were significantly associated with poor outcome.
- Duration of ventilator support was associated with mortality significantly.
- Culture positivity was associated significantly with mortality.

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