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Original Research Article

A comparative analysis of the clinical course, ICU stays and final outcome in different etiological situations in patients of ARDS at a tertiary centre located in rural area

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Abstract: Acute respiratory distress syndrome (ARDS) is a devastating clinical disorder that is seen in critically ill patients with a broad range of clinical disorders and is characterized by widespread inflammatory response. During the last two decades the incidence of ARDS has been reported to be as low as 1.5 to 3.5 cases or as high as 75 cases per 100,000 populations per year by various study groups. ARDS is a huge burden on medical facilities the world over as on an average the patients spend 20 days on the ventilator , 22 days in the intensive care unit (ICU), and 32 days in the hospital and there are heavy charges incurred during hospitalization. An overall complication rate of 43% is seen in patients with ARDS. Complications include pneumonia, deep venous thrombosis (DVT), pulmonary embolism (PE), acute renal failure (ARF), and disseminated intravascular coagulopathy (DIC), therefore ARDS patients have longer hospital stays than similarly matched controls, longer ICU stays, and higher hospital charges. The method in this study was an observational study to identify the major etiological factors associated with ARDS, clinical course and final outcome in patient admitted at Sri Aurobindo medical college and PG institute located in rural area near Indore (m.p.). The study was done during 1.5 years duration. A total of 40 patients were included in results the study show that the most common etiology responsible for ARDS is sepsis 42.5%, pulmonary infection 22.5%, Patients had H1N1 infection 20%. No association could be established between survival statuses with etiology. No association could be established between survival statuses with hospital stay. No association could be established between survival statuses with infective organism. Survival status is independent of the organism seen on culture. The mean PEEP value and mean PaO2/FiO2 value for patients who survived were statistically not significant.
Keywords: ARDS, Chest infections, Sepsis.

INTRODUCTION:

Text - The name acute respiratory distress syndrome for such clinical scenarios was established for the first time in the year 1967 but it had been documented and possibly to some extent described prior to the 20th century. Over the last century the nomenclature for ARDS has passed through various changes which include: shock lung, wet lung, DaNang lung, fat embolism, congestive atelectasis, oxygen toxicity, stiff lung syndrome, white lung syndrome, and pump lung, to mention a few [1-3].

During the last two decades the incidence of ARDS has been reported to be as low as 1.5 to 3.5 cases or as high as 75 cases per 100,000 populations per year by various study groups [4-5]. This is partly due to differing diagnostic criteria as well as the lack of consistent definitions. To bring uniformities and consistency in the research work, the American-European Consensus Conference (AECC) on ARDS convened in 1994 to establish a uniform definition and criteria for diagnosis of acute lung injury (ALI) and ARDS and concluded that the condition should be referred to as acute, not adult, respiratory distress syndrome, due to its occurrence in children as well [6]. ARDS is a huge burden on medical facilities the world over as on an average the patients spend 20 days on the ventilator , 22 days in the intensive care unit (ICU), and 32 days in the hospital and there are heavy charges incurred during hospitalization [7]. There are very few studies on the pattern of ARDS seen in our country. Though there are anecdotal reports of ARDS in Indian literature associated with different tropical diseases [8-11] and certain rare metabolic disorders [12]. the exact association of these life threatening disorders with ARDS is not clearly described .The incidence of ARDS in the at-risk populations is not certain, but prospective global estimates range from 1.5 to 12.9 cases per

100000 people per year depending on the diagnostic criteria [13].

Etiology and risk factor

The major categories of ARDS risk / etiology discussed by the AECC [14] (American European consensus conference) subcommittee were as follows:

I. Direct injury:

A. Aspiration
B. Diffuse pulmonary infection (e.g., bacterial, viral, Pneumocystis infection,)
C. Near-drowning
D. Toxic inhalation
E. Lung contusion

II: Indirect injury

A. Sepsis syndrome,
B. Severe non-thoracic trauma
C. Hyper transfusion for emergency resuscitation.
D. Cardiopulmonary bypass (rare)

AIMS AND OBJECTIVE

To evaluate clinical course, ICU stay and final outcome in different etiological situations in patients of ARDS

METHOD OF COLLECTION OF DATA

- 1.5 years prospective, cross-sectional observational study.
- A detailed history was noted and a physical examination performed on all patients.
- Standard baseline Investigations done. At sri aurvindo medical college and post graduate institute bhanwarasla central laboratory

Inclusion Criteria

- Patients that were diagnosed with ARDS in the Intensive care unit ofsri Aurobindo Medical College & Post Graduate Institute Indore included in the study.
- Patients fulfilling the Berlin modification AECC criteria for ARDS.
- Acute onset of respiratory distress(within 1 week of known a clinical insult)
- Bilateral opacities on CXR not explained by effusions, collapse, or nodules.
- Respiratory failure not fully explained by heart failure or fluid overload

Exclusion Criteria

- known congenital heart disease or pre existing valvular heart disease

Baseline Investigations

- A Complete blood count
- Blood sugar
- Renal function test
- Liver function test,
- Serum electrolyte,
- Arterial blood gases ,
- Relevant body fluid cultures and
- Serology for suspected infective agent.
- Data will be recorded on the day of diagnosis of ALI/ARDS and every twenty four hours thereafter.
- Chest radiographs on the day of diagnosis and at periodic intervals

OBSERVATIONS AND RESULTS

Table 1: Distribution of patients according to age (N=40)

Age	Number	Percentage
14-20 years	5	12.5
21-40 years	16	40.0
41-60 years	15	37.5
>60 years	4	10.0
Total	40	100.0

The above table shows the distribution of patients according to age.

There were 5 (12.5%) patients in age group 14-20 years, 16 (40%) in the age group 21-40 years, 15 (37.5%) in the age group 41-60years and 4 (10%) in the age group >60 years.

Table 2: Distribution of death and survived patients according to age(N=40)

Age Group	Death (n=17)		Survived (n=23)	
	No.	%	No.	%
14-20 years	3	17.65	2	8.70
21-40 years	5	29.41	11	47.83
41-60 years	7	41.18	8	34.78
>60 years	2	11.76	2	8.70
Total	17	100.0	23	100.0

The above table shows the distribution of patients according to death and survived in relation to age group.

In the death group (n=17), 3 (17.65%) were in the age group 14-20 years, 5 (29.41%) were in the age group 21-40 years, 7 (41.18%) were in the age group 41-60 years and 2 (11.76%) were in the age group > 60 years. In the survived group (n=23), 2 (8.70%) were in the age group 14-20 years, 11 (47.83%) were in the age group 21-40 years, 8 (34.78%) were in the age group 41-60 years and 2 (8.70%) were in the age group > 60 years. The distribution of death cases was nearly comparable in all the age groups.

Table 3: Distribution of patients according to gender (N=40)

Gender	Number	Percentage
Female	23	57.5
Male	17	42.5
Total	40	100.0

The above table shows the distribution of patients according to gender.

There were 23 (57.5%) females and 17 (42.5%) males in the present study. There was female preponderance in the study.

Table 4: Distribution of patients according to etiology (N=40)

Etiology	Number	Percentage
Sepsis	17	42.5
Pulmonary infection	9	22.5
H1N1 infection	8	20.0
Complicated malaria	2	5.0
Trauma	2	5.0
Transfusion related ALI	1	2.5
Acute pancreatitis	1	2.5
Total	40	100.0

The above table shows the distribution of patients according to etiology. There were 17 (42.5%) patients who had sepsis, 9 (22.5%) had pulmonary infection, 8 (20%) patients had H1N1 infection, 2 (5%) had complicated malaria, 2 (5%) had trauma, 1 (2.5%) each had Transfusion related ALI and acute pancreatitis.

Majority of the patients had etiology of sepsis, pulmonary infection or H1N1 infection.

Table 5: Distribution of patients according to co-morbidities (N=40)

Co-morbidities	Number	Percentage
Cardiac	8	20.0
Hypertension	8	20.0
Respiratory	5	12.5
Smoking	5	12.5
Diabetes Mellitus	3	7.5

The above table shows the distribution of patients according to co-morbidities. 8 (20%) each patients had cardiac and hypertensive co-morbidities respectively, 5 (12.5%) each patients had respiratory and smoking co-morbidities respectively and 3 (7.5%) patients had diabetes mellitus.

Table 6: **Distribution of patients according to blood transfusion (N=40)**

Blood transfusion	Number	Percentage
Required	16	40.0
Not required	24	60.0
Total	40	100.0

The above table shows the distribution of patients according to requirement of blood transfusion. Blood transfusion was required in 16 (40%) of the patients and rest 24 (60%) patients did not require any blood transfusion.

Table 7: **Distribution of patients according to organism (N=40)**

Age	Number	Percentage
Not done	16	40.0
No growth	13	32.5
Candida	5	12.5
Gram negative bacilli	5	12.5
Pseudomonas aeruginosa	2	5.0
Klebsiella pneumoniae	1	2.5
Micrococcus luteus	1	2.5
Enterococcus faecium	1	2.5
Staphylococcus hominis	1	2.5
E. coli	1	2.5
Staphylococcus aureus	1	2.5

The above table shows the distribution of patients according to organism. Culture was not done in 16 (40%) of the patients. No growth was seen in 13 (32.5%) of the patients, 5 (12.5%) each had candida and gram negative bacilli, 2 (5%) had pseudomonas aeruginosa, while the rest 1 (2.5%) each had Klebsiella pneumonia, Micrococcus luteus, enterococcus faecium, Staphylococcus hominis, E. coli and Staphylococcus aureus.

Table 8: Distribution of patients according to survival (N=40)

Survival Status	Number	Percentage
Death	17	42.5
Survived	23	57.5
Total	40	100.0

The above table shows the distribution of patients according to survival. Of the 40 patients in our study, 17 (42.5%) had expired, while 23 (57.5%) had survived.

Table 9: Distribution of patients according to hospital stay (N=40)

Hospital stay	Death (n=17)		Survived (n=23)	
	No.	%	No.	%
1-3 days	7	41.2	3	13.0
4-7 days	4	23.5	9	39.1
7-14 days	3	17.6	8	34.8
14-21 days	1	5.9	2	8.7
>21 days	2	11.8	1	4.3
Total	17	100.0	23	100.0

The above table shows the distribution of patients according to hospital stay in both the death and survival patients. There were 17 deaths in our present study and rest 23 was survivors. In the death group, 7 (41.2%) patients had a hospital stay of 1-3 days, 4 (23.5%) had a hospital stay of 4-7 days, 3 (17.6%) patients had a hospital stay of 7-14 days, 1 (5.9%) patient had a hospital stay of 14-21 days and 2 (11.8%) patients had a hospital stay of >21 days.

In the survival group, 3 (13.0%) patients had a hospital stay of 1-3 days, 9 (39.1%) had a hospital stay of 4-7 days, 8 (34.8%) patients had a hospital stay of 7-14 days, 2 (8.7%) patient had a hospital stay of 14-21

days and 1 (4.3%) patients had a hospital stay of >21 days. Most of the patients had a hospital stay of 1-14 days in our study.

Table 10: Association of etiology with survival status (N=40)

Etiology	Survival Status		
	Death	Survived	Total
Acute pancreatitis	1	0	1
Complicated malaria	1	1	2
H1N1 infection	5	3	8
Pulmonary infection	3	6	9
Sepsis	6	11	17
Transfusion related ALI	0	1	1
Trauma	1	1	2
Total	17	23	40

$\chi 2$=4.164, DF=6, P value = 0.654, Not significant

The above table shows the distribution survival status in relation to etiology. The test of association (Chi-square) was applied. The chi-square value obtained was 4.164, with a degree of freedom of 6 and P value obtained was 0.654, which is statistically not significant. Thus, no association could be established between survival status with etiology. Survival status is independent of the etiology.

Table 11: Association of survival status with organism (N=40)

Organism	Survival Status		
	Death	Survived	Total
Not done	9	7	16
No growth	4	9	13
Candida	2	3	5
Gram negative bacilli	2	2	4
Pseudomonas aeruginosa	0	2	2
Klebsiella pneumoniae	0	2	2
E. coli	0	1	1
Enterococcus faecium	1	0	1
Micrococcus luteus	0	1	1
Staphylococcus aureus	1	0	1
Staphylococcus hominis	0	1	1
Total	19	28	47

$\chi 2$=10.017, df=10, P value = 0.439, Not significant

The above table shows the distribution survival status in relation to organism. The test of association (Chi-square) was applied. The chi-square value obtained was 10.017, with a degree of freedom of 10 and P value obtained was 0.439, which is statistically not significant. Thus, no association could be established between survival status with organism. Survival status is independent of the organism seen on culture.

Table No. 12: **Association of survival status with hospital stay (N=40)**

Hospital stay	Survival Status		
	Death	Survived	Total
1-3 days	7	3	10
4-7 days	4	9	13
7-14 days	3	8	11
14-21 days	1	2	3
>21 days	2	1	3
Total	17	23	40

$\chi 2$=5.691, df=4, P value = 0.223, Not significant

The above table shows the distribution survival status in relation to hospital stay. The test of association (Chi-square) was applied. The chi-square value obtained was 5.691, with a degree of freedom of 4 and P value obtained was 0.223, which is statistically not significant. Thus, no association could be established between survival statuses with hospital stay. Survival status is independent of the hospital stay.

Table 13: Mean age, WBC counts and hospital stay (N=40)

Parameter	Mean ± SD
Age (Years)	42.00 ± 16.65
WBC Count	17476.92 ± 13119.98
Hospital stay (Days)	9.28 ± 9.00

The above table shows the mean age, mean WBC counts and mean hospital stay in the present study.

The mean age was 42.00 ± 16.65 years.

The mean WBC count was 17476.92 ± 13119.98 / cumm.

The mean hospital stay in days was 9.28 ± 9.00 days.

Table 14: **Mean PEEP comparison according to survival status (N=40)**

Survival Status	N	PEEP Value Mean ± SD	't' value	P value
Survived	23	6.83 ± 1.99	0.760, df=38	0.452, NS
Death	17	7.29 ± 1.83		

Unpaired 't' test. P > 0.05, Not Significant

The above table shows the mean PEEP value between the survived and death cases. The mean PEEP value for survived patients was 6.83 ± 1.99, while in the death cases it was 7.29 ± 1.83. The unpaired 't' test was applied to find out the statistical difference, the 't' value obtained was 0.760, while P value obtained was 0.452, which is statistically not significant. Thus, PEEP value in both the survived and deaths are comparable.

Table 15: Mean PaO2 / FiO2 comparison according to survival status (N=40)

Survival Status	N	PaO2 / FiO2 Value Mean ± SD	't' value	P value
Survived	23	230.56 ± 44.83	0.711, df=38	0.481, NS
Death	17	217.92 ± 67.55		

Unpaired 't' test. P > 0.05, Not Significant

The above table shows the mean PaO2 / FiO2 value between the survived and death cases. The mean PaO2/FiO2 value for survived patients was 230.56 ± 44.83, while in the death cases it was 217.92 ± 67.55. The unpaired't' test was applied to find out the statistical difference, the 't' value obtained was 0.711, while P value obtained was 0.481, which is statistically not significant. Thus, PaO2/FiO2 value in both the survived and death are comparable.

DISCUSSION

A total of 40 patients that met the Berlin definition of ARDS were studied. The mean age was 42.00 ± 16.65 years. The males compromised slightly more than half the study group at 17 (42.5%), the rest were 23 (57.5%) female. Longitudinal epidemiologic studies have shown consistent differences in mortality amongst ARDS patients as a group. Males with ARDS have a persistently higher mortality rate than females with ARDS. Data would also suggest that African-American males with ARDS have a higher mortality rate than males of other racial backgrounds. Similarly, females of African-American race have a higher ARDS mortality rate than females of other racial backgrounds [97].

This study show 42.5% patients who had sepsis, 22.5% had pulmonary infection, 20% patients had H1N1 infection. Bakowitz *et al.;* found that in patients developing ARDS, the rate of pneumonia approached 50% with crude mortality of 19%. Patients spent on average 20 days on the ventilator, 22 days in the ICU, and 32 days in the hospital [15].

A 2006 retrospective review of trauma ICU data at the University of Southern California showed an overall complication rate of 43% in patients with ARDS. Complications included pneumonia, DVT, pulmonary embolism, ARF, and DIC.

Evidence clearly illustrates that early transfusion of packed red blood cells (PRBCs) is an independent predictor of ARDS and increases with increasing units of transfused blood [99,100]. Fresh

frozen plasma (FFP) has also been independently associated with a greater risk of developing ARDS, whereas platelets and cryoprecipitate were not [16]. Pre-storage leuko reduction has been attempted in an effort to minimize the pro-inflammatory effects of residual leukocyte contamination of stored PRBCs, with the hopes of decreasing post-transfusion ARDS rates. However, randomized controlled trials have failed to show any difference in the risk of ALI or ARDS in patients receiving leuko reduced versus standard PRBCs at 28 days [17].

Cultures showed no growth in 32.5% of the patients, 12.5% each had candida and gram negative bacilli, 5% had pseudomonas aeruginosa, while the rest 2.5% each had Klebsiella pneumonia, Micrococcus luteus, enterococcus faecium, Staphylococcus hominis, E. coli and Staphylococcus aureus. Bacterial or viral pneumonia is the most common cause of ARDS.

Sepsis due to nonpulmonary infections, aspiration of gastric contents, and major trauma with shock also commonly precipitate the injury. Less commonly, acute pancreatitis, transfusions, drug reactions, and fungal and parasitic lung infections are linked to ALI and ARDS [6].

A study conducted by Vigg *et al.;* [18] in Hyderabad had observations with Primary pulmonary infection being the most common etiology of ARDS.

Our study can not show any statistically significant association between etiology and mortality. There (42.5%) patients who had sepsis, (22.5%) had pulmonary infection, (20%) patients had H1N1 infection, (5%) had complicated malaria, (5%) had trauma, (2.5%) each had TRALI and acute pancreatitis. Majority of the patients had etiology of sepsis, pulmonary infection or H1N1 infection. No association could be established between survival statuses with organism. Survival status is independent of the organism seen on culture.

A total of 42.5% Patients expired in this study. In a prospective study in Spain, despite use of lung-protective ventilation, overall ICU and hospital mortality of ARDS patients is still higher than 40% [19]. ICU mortality rates ranged between 33 and 55% among participating centers in the ALIEN study.

Phua *et al.;* [20] found that the pooled mortality for ARDS from 1994 to 2006 was 44%. They also found that the definition of ARDS was not an independent predictor of mortality and that this mortality rate is consistently higher than that reported in randomized control trials [21]. In a review published of 101 cases of ARDS the average mortality was 50 %, with reported mortality varying from 30 to 70 % [22]. A study conducted in a RICU in North India noted a mortality rate of 47.8% [23]. The group of patients, who developed ARDS due to sepsis, had a significantly higher mortality when compared to the group in whom the etiology was factors other than sepsis. These findings corroborate well with a retrospective study conducted at the Post Graduate Institute of Medical Education and Research [23].

In the patients who survived, 13.0% patients had a hospital stay of 1-3 days, 39.1% had a hospital stay of 4-7 days, 34.8% patients had a hospital stay of 7-14 days, 8.7% patients had a hospital stay of 14-21 days and 4.3% patients had a hospital stay of more than 21 days. Most of the patients had a hospital stay of 1-14 days in our study. No association could be established between survival statuses with etiology. Survival status is independent of the etiology (p-0.654) and so is duration of hospital stay (p-0.223).

In analysis performed by Kraft and his colleagues [22] showed that statistical comparisons of the PaO2/ FiO2 ratio of survivors and non survivors were not significant on the ARDS. In our study PaO2/FiO2 ratio in both the survived and death are comparable (P-0.481) and statistically not significant. PEEP value in both the survived and death are statistically not significance and comparable (P-0.452).

SUMMARY

This was a prospective observational study aimed at identifying the major etiological factor of ARDS and comparative analysis of the clinical course, ICU stay and final outcome in different etiological situations.

Majority of the patients had etiology of sepsis, pulmonary infection as causes for ARDS in this study. No association could be established between survival statuses with etiology. Total 40 patients in our study, 42.5% had expired. Most of the patients had mean hospital stay in days was days in 9.28 ± 9.00 days in our study. No association could be established between survival status with hospital stay.No association was observed between survival status with infective organism. Survival status was independent of the organism seen on culture.

The mean PaO2/FiO2 value for survived patients was 230.56 ± 44.83, while in the death cases it was 217.92 ± 67.55. The statistical difference, the't' value obtained was 0.711, while P value obtained was 0.481, which is statistically not significant. PaO2/FiO2 value in both the survived and death are comparable.

CONCLUSIONS

The study show that the most common etiology responsible for ARDS is sepsis 42.5%,

pulmonary infection 22.5%, Patients had H1N1 infection 20%. No association could be established between survival statuses with etiology. No association could be established between survival statuses with hospital stay. No association could be established between survival statuses with infective organism. Survival status is independent of the organism seen on culture. The mean PEEP value and mean PaO2/FiO2 value for patients who survived were statistically not significant.

Limitations

Demographic, cultural, economical, and health-care system differences between the USA and Europe may also account for the order of magnitude difference between our study (as well other European studies) and Rubenfeld's. It is plausible that variations in the number of ICU beds, hospital policy on ICU bed utilization, ICU staffing, and burden of disease requiring ICU admission influenced the number of patients admitted into the ICU and diagnosed as having ARDS.

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