

## Original Research Article

# Study of pulmonary functions with DLco in acute respiratory distress syndrome/acute lung injury syndrome

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### ABSTRACT

**Background:** The objective of this is to study the lung functions with DLco in ARDS/ALI survivors; to study and analyse the lung functions in different diseases causing ARDS/ ALI survivors and to analyse the effect of treatment strategies on lung functions with DLco in survivors.

**Methods:** All patients who survived ARDS/ALI illness from January 2008 to July 2009 are selected and follow up for pulmonary function at discharge, 3 months and 6 months were performed post illness were recorded and compared.

**Results:** In the study period, 37 cases were enrolled in the prospective cohort study, out of which 9(24.3%) were suffering from ALI according to American European Consensus definition. There was varied infections etiology causing ARDS/ ALI. Pulmonary function test at discharge were showing normal flow rates and volumes (94.6%), mild restriction in some cases (8.4%) as the patients included in the study does not have any past respiratory illness out of 37(100%) patients of ARDS/ALI discharged from Hospital 21(56.8%) had low DLco and 16 (43.2%) had normal DLco.

**Conclusions:** Diffusion defect is found to be more common in the patients who had mixed infections than the patients who had single infection. There was no effect of steroids on the outcome of the patients in terms of diffusion defect.

**Keywords:** Acute Respiratory Distress Syndrome (ARDS), Acute Lung Injury (ALI), Pulmonary Function Test (PFT)

### INTRODUCTION

The acute respiratory distress syndrome (ARDS) is a clinical disorder characterized by injury to the alveolar epithelium and endothelial barriers of the lung, acute inflammation and protein rich pulmonary edema leading to respiratory failure.<sup>1</sup> It is characterized by dyspnoea, tachypnea, arterial hypoxemia, diffuse bilateral infiltrates on chest radiographs and reduced pulmonary compliance. ARDS and acute lung injury (ALI) are the two ends of a spectrum of the same clinical disorder with ALI being at

the lower end of the spectrum. Ashbaugh and colleagues provided the first description of ARDS in 1967.<sup>2</sup> They termed clinical syndrome of tachypnoea, hypoxemia resistant to supplemental oxygen, diffuse alveolar infiltrates and decreased pulmonary compliance as "Adult Respiratory Distress Syndrome" But there are few limitations as the definition was not specific and hence was liable to a wide variety of interpretations and the etiology of syndrome was not specified. So, in 1988 Murray and colleagues proposed an expanded definition of ARDS depending on calculation of lung injury score.<sup>3</sup>

But score is unable to predict outcome in first 24 to 48 hours after onset and cannot exclude cardiogenic pulmonary edema.<sup>4,5</sup> In 1994, the North American-European Consensus Conference (NAECC) on ARDS proposed a revised definition for ALI and ARDS where Panel Changed definition “adult” to” acute” So, for the first time a milder form of syndrome was defined in the form of ALI so as to detect patients in the early stages of syndrome.<sup>6</sup>

The incidence of Acute Lung Injury and Acute respiratory distress syndrome has been difficult to establish. In 1972 the National Heart and Lung Institute Task force estimated and incidence of 75 cases of ARDS per one lac population per year.<sup>7</sup> Several Subsequent studies have estimated much lower annual incidence of 1.5 to 13.5 cases per one lakh population.<sup>8-13</sup> There are several reasons why the number of cases may have been overestimated. The task for force predated the widespread acceptance of the definition of ARDS and used a broad definition of lung injury that included conditions such as renal failure and volume overload. Most of the studies on ALI/ ARDS, its etiology, pathogenesis, treatment outcomes and the long-term effects in survivors have been in the developed countries. The high prevalence of tropical diseases like malaria, leptospirosis and dengue added new dimension in the study of ALI/ ARDS. The initial assessment and prediction outcomes in ALI/ ARDS patients due to this disorder have not been studied as extensively as compared to other etiology of ALI/ARDS.

**METHODS**

A retrospective study which included all patients with ALI/ ARDS (as per inclusion criteria) admitted in intensive respiratory care unit who survived the illness. The study was conducted in the intensive respiratory care unit in Mumbai in India. All patients who survived ARDS/ ALI illness from January 2016 to July 2017 are selected and follow up for Pulmonary function assessment at discharge, 3 months and 6 months were performed post illness were recorded and compared. This study uses a prospective cohort (analytical epidemiology) study design to collect baseline clinical interpretation of cases of ALI/ ARDS attending tertiary care hospital. All patients fulfilling the inclusion criteria as per American European consensus conference on ARDS/ ALI definition of ARDS/ ALI were included in the study which includes.<sup>14</sup>

1. PaO<sub>2</sub> / FiO<sub>2</sub><300 for ALI and PaO<sub>2</sub> / FiO<sub>2</sub>< 200 FOR ARDS regardless of presence or level of PEEP.
2. Chest X-ray with bilateral pulmonary infiltrates.

All chest X-rays were evaluated by the same researcher, who has experience in the area. The patients were admitted, a detailed history was taken, and a clinical

examination was carried out. Patients were monitored during treatment and recovery phase. The detailed clinical history included the onset, duration and the progress of presenting complaint. It also included a search in the etiology of the condition leading to ALI/ ARDS such as history of trauma or any surgery or blood transfusions, fractures. The details of treatment prior to admission in IRCU were also taken into account. For each patient a clinical proforma was used to collect data. The severity of illness was measured by acute physiology and chronic health evaluation (APACHE) score.<sup>15</sup> Multiple organ dysfunction score (MODS and sequential organ dysfunction assessment (SOFA score).<sup>16,17</sup>

These scores were calculated on admission to present intensive care unit. The details of past history were also included in this, including history of tuberculosis, chronic respiratory diseases, hypertension and diabetes and alcohol consumption were also taken into account. On clinical examination the vital parameters were recorded. The respiratory system, abdominal, cardiovascular and central nervous system were examined in detail. The patient was investigated initially with x-ray chest PA view and an arterial blood gas to look for parameters satisfying the inclusion criteria of the study. Further investigation included work up for pyrexia including a peripheral smear for malarial parasite, tridot test for leptospirosis, liver function tests and renal function test were carried out. A coagulation profile including levels of APTT (Activated partial thromboplastin time), PT (Prothrombin time), INR (International Normalised Ratio), fibrinogen and FDP (fibrin degradation product) was recorded. Authors Studied following infections leading to ALI/ ARDS- Dengue, Dengue and leptospirosis, influenza, leptospirosis, *Plasmodium falciparum* and leptospirosis, *Plasmodium falciparum*, *Plasmodium vivax* and leptospirosis, *Plasmodium vivax* and *Plasmodium falciparum* and leptospirosis, Widal and *Plasmodium falciparum*, unknown. Authors studied following risk factors Pneumonia, post op septicemia, polytrauma, poisoning, PTB, malignancy, neurological disorders, tropical diseases. Data was entered in MS-Excel, coded and analysed using SPSS-18 software.

**RESULTS**

**Table 1: Incidence of ARDS/ ALI in patients.**

	Frequency	Percentage
ARDS	09	24.3
ALI	28	75.7
Total	37	100

It was seen from Table 1 that, 37 cases were enrolled in the study, out of which 9(24.3%) were suffering from ALI according to Arterial European Consensus definition. 25(68%) were males and 12 (32%) were females. Nearly more than half (54.04%) of all the cases enrolled were below the age of 25 years and one quarter (24.32%) were in the age group of 25-35. There was no

much difference in age distribution of cases between two sexes. The mean age of the case was 29 years. Fever was most common symptom as it was found in all cases. Three fourth of total cases had a history of wadding through water. Almost all cases had dyspnea. There was varied infections etiology causing ARDS/ALI- major underlying infections were leptospirosis (60%), plasmodium (11%), S. typhi (10%) and dengue (8%). Apart from the above common infections causing ARDS, other infection found were influenza and in nearly 8% cases the underlying cause/ infection could not be substantiated with common routine tests used in investigation.

**Table 2: Risk factors for developing ALI/ ARDS.**

Risk factors	Frequency	Percentage
Dengue	01	2.7
Dengue and Lepto	02	5.4
Influenza	01	2.7
Leptospirosis	22	59.5
P. falci and Lepto	01	2.7
P. Falciparum	01	2.7
P. vivax and P. lepto	01	2.7
P. vivax, P. falci and Lepto	01	2.7
Widal Test	03	8.1
Widal Test and P. Falci	01	2.7
Unknown	03	8.1
Total	37	100

It was seen from Table 2 that the commonest risk factor is leptospirosis 22 (59.5%) and that the incidence of mixed infections 27%, followed by salmonella typhi 8.1% and malaria as a single infection 5.4% in a decreasing order of frequency. In comparison with the risk factors associated with ARDS/ALI in the other studies, in present tertiary care centre where the study has been conducted, majority of patients are related to acute febrile illnesses and mainly due to disease affecting mainly in particular season, the data available from different studies are mainly from western literature with having different set of etiology.

## DISCUSSION

Much of available data on clinical course, disease etiology, effects on lung function in survivors are from western literature, the relatively higher prevalence of tropical diseases in India as compared to western countries adds a new diversion in the study ARDS/ALI. The limitation of resources and ignorance along with restricted financial resources add more challenges in the management of ALI/ARDS. In the study of patients with ALI/ARDS by Vigg A et al the risk factors were as follows: primary pulmonary infection (30%), recent abdominal surgery (10%), severe sepsis with multiorgan failure (18%), peritonitis (5%), polytrauma (12%), thermal burns (6%), pancreatitis (10%), *Plasmodium falciparum* malaria (4%), acute fulminant viral hepatitis

(2%) and organophosphorus poisoning.<sup>17</sup> A study by Zilberg MD et al the most prevalent predisposing conditions for ALI/ARDS were pneumonia (40%), sepsis (32%) and aspiration of gastric contents (9%).<sup>5</sup>

In present study authors use the 1994 AECC definition of ARDS/ALI as the inclusion criteria. In present study, authors had total 37 patients, out of which 9 (24.3%) were suffering from ARDS and 28 (75.7%) were suffering from ALI out of which 25 (68%) were male and 12 (32%) were females as compared to gender difference in a study done by Herridge MS et al where 66% were males and 44% females.<sup>18</sup> The surviving age group of the patients in present study was young adults (15-25 years) compared to many studies that had been done.

An attempt was made to analyze the presenting clinical features of the patient and the impact they had on the outcome. It was observed that most of patients presented within 10 days of the onset of the symptoms. Fever was the most common presenting symptom with duration of 2 to 4 days being most common occurrence (50%), the duration of fever does not show any statistically significant correlation with pulmonary function changes. Dyspnoea was present in almost all cases as all patients were hypoxic at presentation. History of wadding through water was present in 27 (73%) cases, this can be attributed to the similar frequency of leptospirosis 22 (59.5%) which is water borne infection. 11 (29.7%) patients had history of haemoptysis, which is mainly due to thrombocytopenia which is common occurrence in these diseases. The relationship between the duration of symptoms (before presenting to us) of cough, fever, breathlessness and haemoptysis and outcome was examined in present study. The incidence of these symptoms was as follows; fever, breathlessness, cough in almost of all cases and haemoptysis-29.7%. It was observed that the patients who had duration of cough of less than 10 days were associated with a better prognosis than those who had cough present for more than 10 days. Hence early detection of symptoms like cough could help alter the outcome of disease. A detailed clinical examination was carried out to look for physical signs that may help determine the outcome with respect to lung functions, the clinical parameters such as temperature, respiratory rate, pulse rate did not show major variations amongst case with low and normal DLco at discharge. There is no statistical difference between the patients having and not having pallor, petechie, icterus in respect to the pulmonary function tests.

Laboratory Tests: Organ Dysfunction can alter the outcome of ALI/ARDS and hence various clinical and laboratory parameters were examined in present study. Haematological dysfunction was present in almost all cases in the form of thrombocytopenia 31 (83.78%), haematological picture among both the groups having normal or low DLco at discharge showed that mean haemoglobin was low in cases having low DLco (10.4%) and with normal DLco the mean haemoglobin was

11.4%. This collaborates with the majority of patients presenting with pallor. It was observed that 31 (83.78%) of all the patients had haematological dysfunction, 46% had renal dysfunction, 11 (29.72%) had liver dysfunction during the course of disease. 8 patients out of 11 patients who had abnormal liver function tests had low DLco at the time of discharge correlating with multiorgan failure in cases of severe ARDS/ALI patients. There was no statistical difference among both the groups with respect to LFT abnormality. Cardiogram was abnormal in 13.5% case, with majority having T wave inversion and 1 patient having Brugada syndrome signifies underlying myocarditis component. Cardiogram reverted to normal at the end of 3 months. There were 5 patients out of 37 showing electrocardiogram abnormality, out of which 4 had low DLco and 1 (20%) had normal DLco. Present study has correlated clinical signs and symptoms along with the pulmonary function tests, authors have not taken mortality into consideration as authors have followed up patients pertaining pulmonary function tests. Different other studies mainly from western literature had taken mortality into consideration. In the study by Zilberg et al preceding organ dysfunction was present in 46% of all patients of which 22% had haematological dysfunction, 7.4% had liver dysfunction, 21.4% had renal dysfunction, 14.9% had neurological dysfunction and 10.8% had gastrointestinal dysfunction while the rest had other dysfunction, Doyle and co-workers<sup>4</sup> found preceding organ dysfunction in 21% of medical and surgical ALI patients and its presence was associated with 88% mortality rate.<sup>5</sup> Herridge et al also found that preceding organ dysfunction had an incidence of 72% in patients of ALI/ARDS with a mortality of 88%.<sup>18</sup>

**Treatment:** In present study 22 (86.5%) patients required mechanical ventilation. Out of which 20 (54.1) managed with non-invasive ventilation 12 (32.4%) required invasive ventilation using ACMV (assist control mechanical ventilation) of control mode and lung protective strategy with tidal volume of 6 ml/kg was given and PEEP whenever required. Inverse ratio ventilation and prone pressure ventilation were also attempted in few cases. 5 (13.5%) patients managed with oxygen supply through venturi mask out of 37 patients who performed pulmonary function at discharge 21 had low DLco and 15 were normal and 1 had raised DLco. Out of 21 patients 17 had followed up at the end of 3 months, 3 had normal DLco and 14 had still low DLco. Out of 14 patients having low DLco, 11 had followed up at the end of 6 months only 1 patient had normal DLco, 10 had still low DLco. Patients who had low and normal DLco and variables were compared for the difference.

## CONCLUSION

The mean age of patients with low DLco at discharge was found to be 27 years and that with normal DLco was 32 years. This suggests that ARDS/ALI not only affects young adults but also DLco is low among young adults. There was no difference in height amongst the cases with

low and normal DLco at discharge. Leptospirosis was found to be the most common underlying cause but there was no statistical difference among both the groups having low or normal DLco. The same type of association was found with other underlying infections such as malaria, dengue, *Salmonella typhi*. In patients who needed invasive support out of 12, 11 patients had low DLco, out of 20 patients who needed NIV support 9 had low DLco at discharge.

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