10.5005/jp-journals-10028-1092

ORIGINAL ARTICLE

# Acute Respiratory Distress Syndrome: An Autopsy Study

[1]Suchet Sachdev, [2]Shobhana Pravin Pandit


## ABSTRACT

**Aim:** To find out prevalence and the associated predisposing etiologic conditions of acute respiratory distress syndrome (ARDS) amongst autopsied cases.

**Setting and design:** The present study was a retrospective analysis of 125 cases of ARDS obtained at autopsy over a span of 4 years from 2000-2003.

**Materials and methods:** Data was retrieved from the postmortem record of the pathology department and the medical record department. A review of histology slides was done with diffuse alveolar damage (DAD) as the correlate of ARDS at histopathology.

**Results:** Prevalence of ARDS amongst autopsied cases was 3.15%. There were 60% cases in adult age group and of male gender; whereas 40% were children and of female gender. Almost 90% of cases succumbed to ARDS within a week of admission. The most common presenting features were of the respiratory system. The most common predisposing etiologic association was leptospirosis, septicemia and pneumonia.

**Conclusion:** Systemic infections were the most common predisposing etiologic conditions of ARDS at autopsy.


**Keywords:** Acute respiratory distress syndrome, Diffuse alveolar damage, Leptospirosis.

**How to cite this article:** Sachdev S, Pandit SP. Acute Respiratory Distress Syndrome: An Autopsy Study. J Postgrad Med Edu Res 2014;48(1):8-13.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a life-threatening medical emergency with a poor prognosis. Despite the understanding of the pathophysiology since early nineteenth century and the advances in medical management till date, the mortality still remains around 26 to 44%.[1] The most widely used definition of ARDS was published in the American-European Consensus Conference statement in 1994.[2] It described ARDS as a syndrome of inflammation and increased permeability associated with a constellation of clinical, radiologic, and physiologic abnormalities unexplained by elevations in left atrial or pulmonary capillary pressure. The criteria included an identifiable associated condition as the first prerequisite. The present study was designed to study this identifiable associated condition predisposing to the development of ARDS obtained at autopsy by correlating the gross and histology of lungs with pathology observed in other organ systems taking into account the clinical presentation and laboratory parameters.

The annual incidence of ARDS is estimated to be around 60 per 100,000 and approximately 10% of intensive care patients suffer from acute respiratory failure, with 20% of the meeting criteria for ARDS or Acute lung injury.[1] Patients with ARDS from direct lung injury inclusive of pneumonia, pulmonary contusion and aspiration have nearly twice the mortality as compared to those caused by indirect injury which includes surgical and trauma patients.[1] The lungs are susceptible to a host of etiologic factors by the virtue of their anatomic location and the vast surface area exposed to the total cardiac output. Therefore it becomes exposed to both airborne as well as blood borne injurious insults. ARDS is not a disease entity, but rather represents a final common pathway of damage to lungs by a wide variety of injurious agents. However, despite the varied etiology the tissue response of the lung is uniform.[3,4] Pulmonary lesions correlate with the phase of alveolar damage rather than its specific cause.[5] ARDS has been described by various synonyms; however most of them are situation specific. One synonym that has stood the test of time and is also at times used interchangeably with ARDS is 'diffuse alveolar damage,' as it aptly describes the pathologic basis of this syndrome.[3,4]

## MATERIALS AND METHODS

The present study is a retrospective study of 125 cases obtained at autopsy during a span of 4 years from 2000-2003, with the final cause of death at autopsy as ARDS at histopathology. The study was carried out at the pathology department of Seth GS Medical College and KEM Hospital, Mumbai. Data regarding the cases was retrieved from the autopsy records of pathology department and the medical record department. It was retrieved taking into consideration the age, gender, duration of indoor stay, clinical presentation,

[1]Assistant Professor, [2]Ex-Professor

[1]Department of Transfusion Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India

[2]Department of Pathology, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra, India

**Corresponding Author:** Suchet Sachdev, Assistant Professor Department of Transfusion Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India Phone: 9914209487, e-mail: suchetsachdev@yahoo.com

general and systemic examination findings and laboratory parameters. Data was tabulated and analyzed. And, a clinicopathologic correlation was attempted. A minimum of 5 hematoxylin and eosin stained sections from the lungs were studied along with sections from other organs. More sections and special stains were employed as and when required. A review of histology slides was done with DAD as the correlate of ARDS at histopathology.

## RESULTS

The prevalence of ARDS obtained at autopsy was 3.15% (Table 1). Significant observation were made in the age distribution of cases, 20% cases represented in the age group of less than 1 year of age and 76% of the cases were within the first three decades of life (Table 1). The most common clinical presenting feature was fever in 86 cases (68.6%), followed by manifestations of the respiratory system in form of dyspnea in 76 cases (60.8%), cough in 35 cases (28.0%), hemoptysis in 15 (12.0%), cyanosis in 10 cases (8.0%) and chest pain in 8 (6.4%). Gastrointestinal manifestations included vomiting in 23 cases (18.4%), diarrhea in 14 cases (12.0%), icterus in 14 cases (11.2%), hematemesis and abdominal pain in 4 cases each (3.2%). Renal involvement was manifest with oliguria in 20 cases (16.0%), hematuria in 9 cases (7.2%) and edema feet in 5 cases (4.6%). Other clinical presentations included altered sensorium in 18 cases (14.4%), myalgia in 9 cases (7.2%), refusal to feed and rash in 6 cases each (4.8%), convulsions in 4 cases (3.2%) and oral thrush in one patient (0.8%). Deranged coagulation was presented as subconjunctival suffusion in 14 cases (11.2%) and purpura in 10 cases (8.0%). Coagulation abnormalities were evident on laboratory investigations and were seen consistently with leptospirosis, postoperative state, malaria, pneumonia aside from DIC, liver disease and septicemia (Table 2).

The gross morbid pathology was of bilateral hemorrhagic consolidation (Fig. 1) in all cases except one in which the consolidation was confined to the right upper lobe of the right lung. The histopathology of the lungs demonstrated hyaline membranes in 118 (94.4%), edema in 108 (86.4%), hemorrhage in 85 (68.0%), and thromboemboli in 28 cases (22.4%). All cases were in the exudative phase except, one case that was in early fibroproliferative phase. Bilateral hemorrhagic consolidation was found in all cases of leptospirosis. Histopathology revealed diffuse alveolar damage in the lungs, predominated by pulmonary hemorrhage, fibrin rich edema and hyaline membranes (Fig. 2) in leptospirosis; other organs revealed lymphocytic myocarditis, tubular necrosis, tubulointerstitial nephritis, and hepatocellular necrosis of varying severity. Viral pneumonia was noted in 15 cases (12.0%, Fig. 3), with one case each of lobar, bronchopneumonia and pneumocystis carinii pneumonia (0.8%). Lymphocytic myocarditis was noted in 36 cases (28.8%); malarial myocarditis in two cases

**Table 1:** Demography of ARDS at autopsy

| *Age (Years)* | *2000* | | *2001* | | *2002* | | *2003* | | *Total cases (n = 125)* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *M* | *F* | *M* | *F* | *M* | *F* | *M* | *F* | *M* | *F* | *M + F* |
| ≤ 1 | 3 | 1 | 4 | 5 | 2 | 3 | 4 | 3 | 13 | 12 | 25 (20.0%) |
| 1-10 | 5 | 2 | 2 | 4 | 1 | 1 | 4 | 3 | 12 | 10 | 22 (17.6%) |
| 11-20 | 6 | 0 | 1 | 3 | 5 | 1 | 2 | 4 | 14 | 08 | 22 (17.6%) |
| 21-30 | 6 | 3 | 5 | 2 | 3 | 1 | 3 | 3 | 17 | 09 | 26 (20.8%) |
| 31-40 | 3 | 2 | 0 | 2 | 1 | 2 | 1 | 0 | 05 | 06 | 11 (8.8%) |
| 41-50 | 0 | 0 | 2 | 1 | 3 | 0 | 4 | 0 | 09 | 01 | 10 (8.0%) |
| 51-60 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 02 | 02 | 04 (3.2%) |
| 61-70 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 01 | 01 | 02 (1.6%) |
| 71-80 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 02 | 01 | 03 (2.4%) |
| Cases/year | 33 | | 33 | | 23 | | 36 | | 75 | 50 | 125 |
| Prevalence | 3.3% (n = 1000) | | 3.5% (n = 933) | | 2.5% (n = 895) | | 3.1% (n = 1136) | | 3.15% (n = 3962) | | |

**Table 2:** Coagulation abnormalities associated with ARDS

| *Etiology* | *Thrombo-cytopenia* | *Increased PT*[#1] | *Increased APTT*[#2] | *Increased FDP's*[#3] | *D-dimmer positive* |
|---|---|---|---|---|---|
| Leptospirosis | 23 (n = 28) | 5 (n = 5) | TNP | TNP | TNP |
| DIC | 5 (n = 5) | 4 (n = 4) | 4 (n = 4) | 4 (n = 4) | 1 (n = 1) |
| Postoperative state | 6 (n = 15) | 3 (n = 5) | 3 (n = 3) | TNP | TNP |
| Malaria | 3 (n = 4) | 1 (n = 1) | 1 (n = 1) | TNP | TNP |
| Septicemia | 4 (n = 12) | 1 (n = 1) | TNP | TNP | TNP |
| Pneumonia | 3 (n = 3) | TNP | TNP | TNP | |

[#1]Prothrombin time; [#2]Activated partial thromboplastin time; [#3]Fibrin degradation products; N: No. of cases in which the investigation was performed; TNP: Test not performed

(1.6%) and rheumatic myocarditis along with valvulitis and libman sach's endocarditis in one case each (0.8%). Tubulointerstitial nephritis was noted in 29 cases (23.2%), acute tubular necrosis in 8 cases (6.4%) and minimal change disease, cresentic glomerulonephritis and acute as well as chronic pyelonephritis in one case each (0.8%). Centrilobular hemorrhagic necrosis of liver was noted in 15 cases (12.0%), alcoholic steatohepatitis, noncirrhotic portal fibrosis and pyogenic abscess in one case each (0.8%). One case demonstrated intimal arteritis involving heart, liver, kidneys with sparing of lungs classic of infantile PAN (Fig. 4). Focal adrenal necrosis with typical intranuclear inclusions was noted in the child with pneumocystis pneumonia presenting with oral thrush (Figs 5 and 6). Mortality was measured in terms of ward stay; 46 (36.8%) succumbed within 24 hours and 113 (90.4%) within the first week of admission. Leptospirosis in 39 cases (31.2%), septicemia in 20 cases (15.2%) and pneumonia in 18 cases (14.4%) were the common infective predisposing etiology and post-operative state in 15 cases (12.0%) and liver diseases in 7 cases (5.6%) were the common noninfective predisposing

**Fig. 1:** Voluminous right lung with diffuse congestion on pleural aspect as well as the cut surface

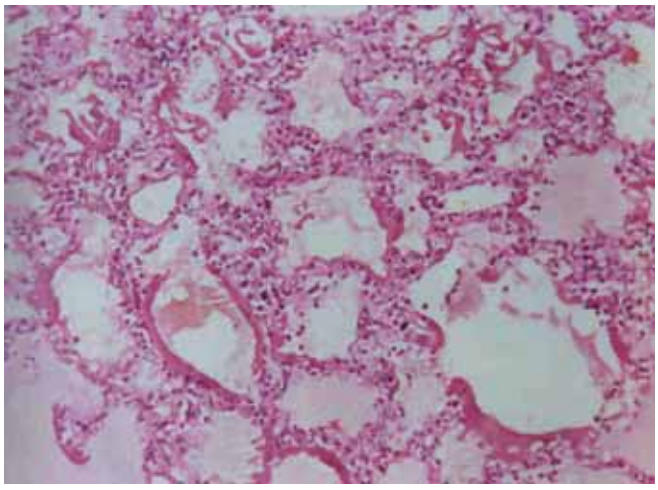

**Fig. 2:** Note thick hypereosinophilic ribbons of hyaline membranes clinging to alveolar septae, spaces contain edema fluid (H&E × 160)

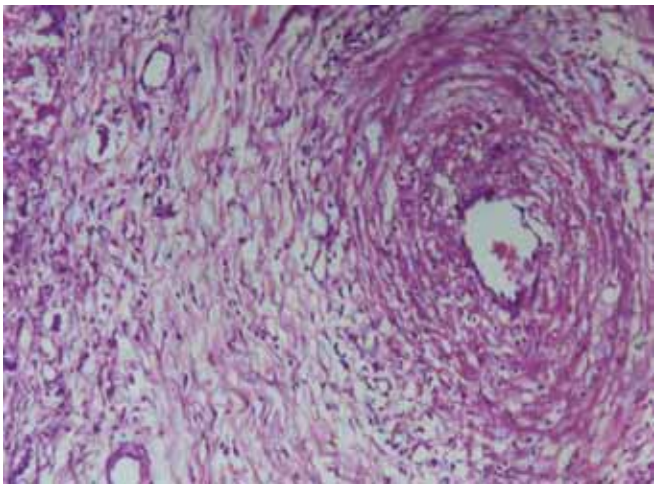

**Fig. 4:** Infantile PAN showing hepatic arteritis (H&E × 160)

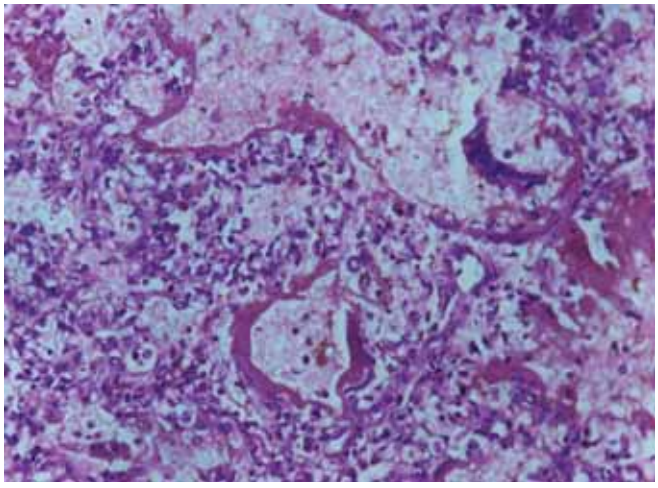

**Fig. 3:** Viral interstitial pneumonitis. Note widening of the alveolar septae with lymphocytic infiltrate (H&E × 250)

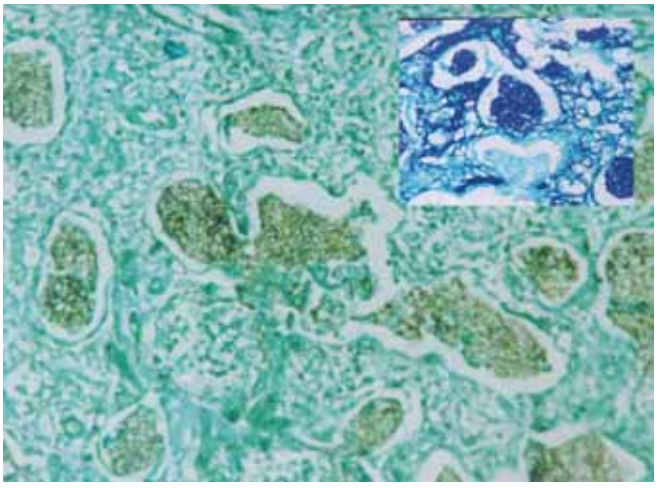

**Fig. 5:** Pneumocystis carinii pneumonia (GMS × 160, inset × 250)

etiology associated with the development of ARDS in our study (Table 3).

## DISCUSSION

There has been tremendous technological diagnostic advances over the last few decades but histopathology retains its diagnostic importance be it antemortem lung biopsy or the postmortem autopsy for making a diagnosis or understanding the etiologic basis of ARDS. Many studies have demonstrated the diagnostic disagreement between the clinical diagnosis and diagnosis arrived at after autopsy; highlighting the importance of histopathology.[6]

The prevalence of ARDS at autopsy in the present study was 3.15% which is less than that of 6.8% in a study by Fowler AA et al,[7] who studied prospectively patients at risk of developing ARDS. In the present study autopsy was performed in ARDS cases only when the clinicians requested and not in all ARDS patients and thus there may be a selection bias. The age and gender distribution correlates with the other studies in literature like the study by Fowler AA et al[7] (61.7% males, 38.3% females), Hoor TT et al[8] (51% males and 49% females) and Soeiro Ade M et al[9] (57.6% males, 42.4% females). The age distribution of cases in the present study supports the use of the term 'acute respiratory distress syndrome' terminology over the earlier 'adult respiratory distress syndrome'. Almost 90% of the patients died within a week of admission which is strikingly similar with 90% as found by Fowler AA et al,[7] supporting that ARDS is a medical emergency and has a poor prognosis. Fowler AA et al[7] observed septicemia in 16.6%, and pneumonia in 18.5%. Sloane PJ et al[10] observed septicemia in 31.3%, and pneumonia in 15.4%, whereas Seidenfeld JJ et al[11] observed septicemia in 39.0%, and pneumonia in 20.0%. The study by Soeiro Ade M et al[9] found that the patients who developed acute respiratory failure had underlying diseases such as bacterial bronchopneumonia (33.9%), cancer (28.1%), sepsis and septic shock (14.3%), liver cirrhosis (13.6%), HIV/AIDS (10.4%), pulmonary embolism (9.0%), acute myocardial infarction (4.7%), brain stroke (4.4%), chronic kidney failure (4.4%), and diabetes mellitus (4.1%). Bhadade RR et al[12] reported malaria in 16 patients (27.6%), leptospirosis in 12 (20.7%), malaria with dengue in 3 (5.2%), undiagnosed fever in 16 (27.6%), pneumonia in 8 (13.8%), urinary tract infection

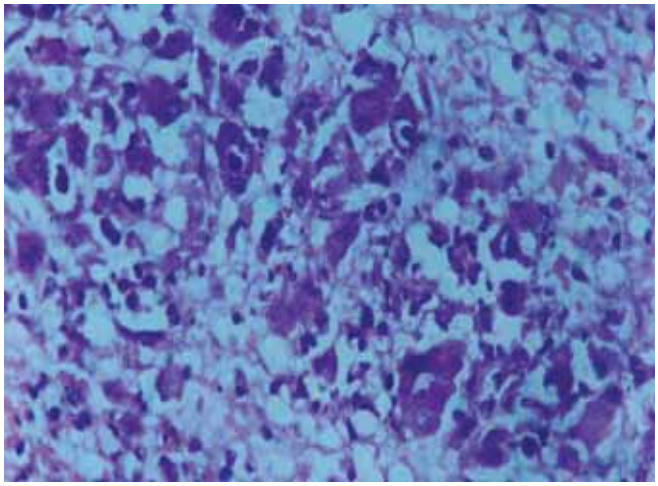

**Fig. 6:** Focal adrenal necrosis, classic nuclear inclusions of CMV (H&E × 250)

**Table 3:** Predisposing conditions (Etiology) and mortality in terms of ward stay of ARDS

| *Predisposing conditions and ward stay (n = 125)* | *Pediatrics (n = 50)* | *Adults (n = 75)* | *<24 hours (n = 46)* | *<7 days (n = 67)* | *<30 days (n = 12)* |
|---|---|---|---|---|---|
| *Infective* | | | | | |
| Leptospirosis = 39 (31.2%) | 02 (4.0%) | 37 (49.3%) | 23 | 10 | 06 |
| Septicemia = 20 (15.2%) | 08 (16.0%) | 12(16.0%) | 06 | 10 | 04 |
| Pneumonias = 18 (14.4%) | 16 (32.0%) | 02 (2.7%) | 10 | 06 | 02 |
| Malaria = 04 (3.2%) | Nil | 04 (5.4%) | 01 | 03 | Nil |
| Tuberculosis = 02 (1.6%) | 01 (2.0%) | 01 (1.3%) | Nil | 02 | Nil |
| Aspiration pneumonia = 02 (1.6%) | 01 (2.0%) | 01 (1.3%) | Nil | 02 | Nil |
| SBP[#1] = 01 (0.8%) | 01 (2.0%) | Nil | Nil | 01 | Nil |
| Rheumatic fever = 01 (0.8%) | 01 (2.0%) | Nil | Nil | 01 | Nil |
| *Noninfective* | | | | | |
| Postoperative state = 15 (12.0%) | 08 (16.0%) | 07 (9.3%) | 01 | 14 | Nil |
| Liver diseases = 07 (5.6%) | 03 (6.0%) | 04 (5.4%) | 01 | 06 | Nil |
| DIC[#2] = 05 (4.0%) | 02 (4.0%) | 03 (4.0%) | Nil | 05 | Nil |
| Shock = 04 (3.2%) | 04 (8.0%) | Nil | 03 | 01 | Nil |
| Uremia = 03 (2.4%) | 01 (2.0%) | 02 (2.7%) | Nil | 03 | Nil |
| Pancreatitis = 02 (1.6%) | 01 (2.0%) | 01 (1.3%) | 01 | 01 | Nil |
| SLE[#3] = 01 (0.8%) | Nil | 01 (1.3%) | Nil | 01 | Nil |
| Infantile PAN[#4] = 01 (0.8%) | 01 (2.0%) | Nil | Nil | 01 | Nil |

[#1]Spontaneous bacterial peritonitis; [#2]Disseminated intravascular coagulation; [#3]Systemic lupus erythematosis; [#4]Polyarteritis nodosa

in 2 (3.4%), and pancreatitis in 1 (1.7%) patient. It was also noted in the present study that the frequency of common etiologic conditions demonstrated different trends among pediatric and adult patients. Among adults, commonest was leptospirosis (49.3%), followed by septicemia (16.0%) and postoperative state (9.3%). In the pediatric age group, commonest was viral pneumonia (32.0%) followed by septicemia and postoperative state (16.0% each). Norrashidah AW et al[13] in their study of ARDS cases in pediatric intensive care unit also found septicemia and pneumonia the commonest causes. Etiology of academic interest noted in the present study was the possible causal association of pneumocystis pneumonia co-infected with cytomegalovirus,[14] vivax and falciparum malaria,[15-18] spontaneous bacterial peritonitis,[19] rheumatic fever,[20] systemic lupus erythematosis[21-23] and infantile polyarteritis nodosa[24] with ARDS. All cases at histopathology were in exudative phase, only one was in early fibroproliferative phase, the predisposing etiology being septicemia. There was one case of 'Regional' ARDS and the predisposing associated condition was lobar pneumonia.[5] The classically cited etiologic conditions in various standard text books featured as the etiology in the present study. The commonest predisposing systemic infection in the present study was one of the 'Emerging zoonotic infection' of leptospirosis[12,25-31] in 39 cases (31.2%), followed in frequency by septicemia in 20 cases (15.2%), closely followed by pneumonia[32] in 18 cases (14.4%) and then the noninfective conditions like postoperative state[33] in 15 cases (12.0%), liver disease 19,[34] (5.2%), DIC (4%) and shock (3.2%).[35] In the present study, most common clinical presentation of leptospirosis was a brief history of fever, dyspnea, icterus and oliguria coupled with bleeding tendencies like subconjunctival suffusion, petechiae and purpura. Laboratory investigations revealed thrombocytopenia in majority of cases, the usual clinical presentation of icteric type of leptospirosis in which pulmonary involvement is between 20 and 70%.[24,26] The leptospiral screening 'Dri-Dot' test was positive in 9 cases (N = 21). Thus the diagnosis of leptospirosis in 18 cases was exclusively on histopathology, and in 21 cases aided by a clinical suspicion. This rapid screening test is based on latex agglutination principle. The test is to be read within 30 seconds, as delayed positive agglutination does not carry significance. This test can also be negative in the early stage of infection. The sensitivity of the test is 67.6% and a specificity of 66.0% during the first week.[36] The test does not require special storage or sophisticated equipment and can be performed by relatively low skilled personnel, making it feasible for screening at peripheral centers. It is well known that ARDS has a varied etiology and similar varied clinical presentation was observed in the present study. ARDS is thus the pulmonary manifestation of multi organ dysfunction syndrome. The present study supports that ARDS has a varied etiology and clinical presentation; however the pulmonary lesions correlate with the phase of alveolar damage rather than its specific cause.[5]

## CONCLUSION

Systemic infections feature as the most common etiologic causal association with ARDS at autopsy. Knowledge of this can prompt a high index of suspicion toward antemortem diagnosis and facilitate institution early management of patients at risk of developing ARDS.

## LIMITATIONS

The present study was retrospective in nature and data was from the available records which had inherent limitations. Since the autopsies have not been carried out in all hospital deaths due to ARDS, there might be a bias. Furthermore, this study was limited to medical autopsies and medicolegal causes of ARDS like burns, trauma and others could not be represented, thus the entire spectrum of etiology of ARDS could not be covered. Finally, interobserver difference among pathologists exists and cannot be denied.

## ACKNOWLEDGMENT

The authors would like to express sincere gratitude to Dr Pradeep Vaideeswar, Department of Pathology, Seth GS Medical College, Mumbai for his efforts during the thesis and manuscript guidance.

## REFERENCES

1. Levy BD, Choi AMK. Acute respiratory distress syndrome. Harrison's principles of internal medicine. Longo DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J, editors. 18th ed. McGraw-Hill 2012;2205-2209.
2. Carlet J, Falke L, Bernard GR, Artigas KL, Hudson BM, et al. The American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. Am J Respir Crit Care Med 1994;149:818-824.
3. Hasleton PS. Adult respiratory distress syndrome. Spencer's pathology of the lung. Hasleton PS, editors. 5th ed. McGraw-Hill 1996;375-400.
4. Haslet C. Pulmonary edema and adult respiratory distress syndrome. Crofton and douglas's respiratory diseases. Seaton A, Seaton S, Leitch AG, editors. 5th ed. Blackwell Science 2000;770-787.
5. Tomashefski JF Jr. Pulmonary pathology of acute respiratory distress syndrome. Clin Chest Med 2000;21:435-66.
6. Pinheiro BV, Muraoka FS, Assis RV, Lamin R, Pinto SP, Ribeiro PJ Jr, et al. Accuracy of clinical diagnosis of acute respiratory distress syndrome in comparison with autopsy findings. J Bras Pneumol 2007;33:423-428.
7. Fowler AA, Hamman RF, Zerbe GO, Benson KN, Hyers TM. ARDS. Am Rev Resp Dis 1985;132:472-478.

8. Hoor TT, Mannino DM, Moss M. Risk factors for ARDS in the United States: analysis of the 1993 National Mortality Follow back Study. Chest 2001;119:1179-1184.
9. Soeiro Ade M, Ruppert AD, Canzian M, Parra ER, Farhat C, Capelozzi VL. Demographic, etiological and histological pulmonary analysis of patients with acute respiratory failure: a study of 19 years of autopsies. Clinics (Sao Paulo) 2011;66: 1193-1197.
10. Sloane PJ, Gee MH, Gottlieb JE, Albertine KH, Peters SP, Burns RJ, et al. A multicenter registry of patients with acute respiratory distress syndrome. Am Rev Resp Dis 1992;146:419-426.
11. Seidenfeld JJ, Pohl DF, Bell RC, Harris GD, Johanson WG. Incidence, site, and outcome of infections in patients with the ARDS. Am Rev Respir Dis 1986;134:12-16.
12. 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;57:286-290.
13. Norrashidah AW, Azizi BH, Zulfiqar MA. Acute respiratory distress syndrome in a pediatric intensive care unit. Med J Malaysia 1999;54:225-229(Abstract).
14. Soeiro Ade M, Hovnanian AL, Parra ER, Canzian M, Capelozzi VL. Postmortem histological pulmonary analysis in patients with HIV/AIDS. Clinics (Sao Paulo) 2008;63:497-502.
15. Tanios MA, Kogelman L, McGovern B, Hassoun PM. Acute respiratory distress complicating Plasmodium vivax malaria. Crit Care Med 2001;29:665-667.
16. Aseidu DK, Sherman CB. ARDS complicating plasmodium falciparum malaria. Heart and Lung 2000;29:294-297.
17. Valecha N, Pinto RG, Turner GD, Kumar A, Rodrigues S, Dubhashi NG, et al. Histopathology of fatal respiratory distress caused by plasmodium vivax malaria. Am J Trop Med Hyg 2009;81:758-762.
18. Taylor WR, Hanson J, Turner GD, White NJ, Dondorp AM. Respiratory manifestations of malaria. Chest 2012;142:492-505.
19. Karcz M, Bankey B, Schwaiberger D, Lachmann B, Papadakos PJ. Acute respiratory failure complicating advanced liver disease. Semin Respir Crit Care Med 2012;33:96-110.
20. Fayad G, Larrue B, Modine T, Azzaoui R, Regnault A, Koussa M, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure in postpartum woman with rheumatic mitral valve disease: benefit, factors furthering the success of this procedure and review of the literature. J Extra Corpor Technol 2007;39:112-116.
21. Kim WU, Kim SI, Yoo WH, Park JH, Min JK, Kim SC. ARDS in systemic lupus erythematosus: causes and prognostic factors: a single center, retrospective study. Lupus 1999;8: 552-557.
22. Rice AJ, Wells AU, Bouros D, du Bois RM, Hansell DM, Polychronopoulos V, et al. Terminal diffuse alveolar damage in relation to interstitial pneumonias. An autopsy study. Am J Clin Pathol 2003;119:709-714.
23. Kumar A, Marwaha V, Grover R. Emergencies in rheumatology. J Indian Med Assoc 2003;101:520-524.
24. Matsumoto T, Homma S, Okada M, Kuwabara N, Kira S, Hoshi T, et al. The lung in polyarteritis nodosa: a pathologic study of 10 cases. Hum Pathol 1993;24:717-724.
25. Goncalves AJ, de Carvalho JE, Guedes E, Silva JB, Rozembaum R, Vieira AR. Hemoptysis and the ARDS as the causes of death in Leptospirosis. Changes in the clinical and anatomicopathological patterns. Rev Med Trop 1994;25:261-270.
26. Carvalho CR, Bethlem EP. Pulmonary complications of leptospirosis. Clin Chest Med 2002;23:469-478.
27. Chawla V, Trivedi TH, Yeolekar ME. Epidemic of leptospirosis: an ICU experience. J Assoc Physicians India 2004;52:619-622.
28. Dolhnikoff M, Mauad T, Bethlem EP, Carvalho CR. Pathology and pathophysiology of pulmonary manifestations in leptospirosis. Braz J Infect Dis 2007;11:142-148.
29. Abgueguen P, Delbos V, Blanvillain J, Chennebault JM, Cottin J, Fanello S, et al. Clinical aspects and prognostic factors of leptospirosis in adults. Retrospective study in France. J Infect 2008;57:171-178.
30. Chauhan V, Mahesh DM, Panda P, Mokta J, Thakur S. Leptospirosis presenting as acute respiratory distress syndrome (ARDS) in sub-Himalayan region. J Assoc Physicians India 2010;58:390-391.
31. Paganin F, Bourdin A, Borgherini G, Dalban C, Poubeau P, Tixier F, et al. Pulmonary manifestations of leptospirosis. Rev Mal Respir 2011;28:131-139.
32. Sarmiento X, Guardiola JJ, Almirall J, Mesalles E, Mate JL, Soler M, et al. Discrepancy between clinical criteria for diagnosing acute respiratory distress syndrome secondary to community acquired pneumonia with autopsy findings of diffuse alveolar damage. Respir Med 2011;105:1170-1175.
33. Alotti N, Varro M, Gombocz K, Simon J, Wrana G, Kecskes G, et al. ARDS after open heart surgery. Orvsi Hetilap 2000;141: 493-496(Abstract).
34. Foreman MG, Hoor TT, Brown LA, Moss M. Effects of chronic hepatic dysfunction on pulmonary glutathione homeostasis. Alcohol Clin Exp Res 2002;26:1840-1845(Abstract).
35. Zhang J, Handorf C. Miliary tuberculosis presenting as acute respiratory distress syndrome, septic shock, DIC and multiorgan failure. Tenn Med 2004;97:164-166(Abstract).
36. Vijayachari P, Sugunan AP, Sehgal SC. Evaluation of lepto dri dot as a rapid test for the diagnosis of leptospirosis. Epidemiol Infect 2002;129:617-621.