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Analysis of cause of death and histopathological stages of diffuse alveolar damage in lung: An autopsy study

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Abstract
Introduction: Diffuse alveolar damage (DAD) is histopathological finding of acute respiratory distress syndrome (ARDS). ARDS is associated with disorders such as poisoning, sepsis, trauma, etc.
Aims and objective: Analysis of cause of death and histopathological stages of diffuse alveolar damage in lung autopsy
Material and method: Multiple section taken during grossing of lung specimen and processed with subsequent staining by haematoxylin and eosin, stained slide were examined by experienced pathologist under a light microscope.
Result: 34 out of 536 individuals who were diagnosed with DAD 9(26.47%) were female and 25 (73.53%) were male. Microscopic finding shows that 27(79.41%) cases were in the exudative phase, and 7 (20.59%) were in the organizing (proliferative) phase. Macrophage desquamation, pulmonary edema and alveolar epithelial cell desquamation were present in majority of patient.
Conclusion: Aged individual are frequently affected and particularly in sepsis, intoxication, poisoning, trauma and fire. Forensic autopsies may provide a platform for increasing our knowledge about DAD, acute lung damage and interstitial lung disease.

Keywords: DAD, diffuse alveolar damage, exudative phase, organizing phase, lung

Introduction
DAD is the pathologic counterpart of the acute respiratory distress syndrome (ARDS). Cases of ARDS showing DAD histology without an identified cause, previously known as Hamman-Rich syndrome, are termed acute interstitial pneumonia[1]. Histologically diffuse alveolar damage is divided into two phase exudative and organizing. Clinically, disease occurs over a wide age range without sex or smoking associations. The onset of symptoms is abrupt, generally occurring over 1 or 2 days and consisting of severe dyspnea accompanied by fever and cough, in contrast to the slow, insidious evolution of UIP (usual interstitial pneumonia). Patients have restrictive physiology along with rapidly progressive hypoxia leading to respiratory failure. Almost all patients fulfill diagnostic clinical criteria for ARDS[2]. The specific etiology of DAD may be obvious or diagnosable, for example trauma, sepsis, post operative patient, poisoning near-drowning; subsequent to cardiopulmonary bypass; following radiation therapy; or after drug therapy, such as with chemotherapeutic agents. In some patients, the cause may be multifactorial, with several factors acting either simultaneously or consecutively-particularly mechanical ventilation with high oxygen concentration[3]. Open lung biopsy sometime cause acute attacks in patients with idiopathic pulmonary fibrosis therefore executive an open-lung biopsy in patients with acute and severe respiratory distress, a few studies had been done. Thus, examination of DAD prevalence and forensic autopsy are alternative area of research.
The aim of this study was to detect frequency of diffuse alveolar damage in forensic autopsy, to identify other accompanying histopathological findings, to find out causes of death in diffuse alveolar damage, to recognize the case spectrum that are helpful in future forensic autopsy.

Materials and Methods
We received 536 number of autopsy from 1st June 2020 to 31st may 2021 at Pathology department, Surat municipal institute of medical education and research medical college. Out of which 34 were histopathologically diagnosed with DAD irrespective of age were included

in our study. Cause of death and demographic information were recorded from the autopsy reports. Multiple section taken during grossing of lung specimen and processed with subsequent staining by haematoxylin and eosin, stained slide were examined by experienced pathologist under a light microscope. The presence of any alveolar organizing fibrosis shown in figure 4 was accepted as the main criterion to distinguish exudative from organizing (proliferative) phases[4].

Results

34 individuals who were diagnosed with diffuse alveolar damage in received autopsy 25(73.53%) were male and 9 (26.47%) were female. Microscopic finding shows that 27(79.41%) cases were in the exudative phase, and 7 (20.59%) were in the organizing (proliferative) phase. Distribution of various Histopathological changes in phases of diffuse alveolar damage are illustrated in Table 1

Table 1: Distribution of histopathological lesions according to diffuse alveolar damage (DAD) phase

Histopathological lesion	Stage	Absent N (%)	Present N (%)
Hyaline membrane (HM) formation (n =25)	Exudative	06(17.65%)	21(61.76%)
	Organizing	03(8.82%)	04(11.77%)
Alveolar organizing fibrosis (*n =7*)	Exudative	27(79.41%)	00
	Organizing	00	07(20.59%)
Macrophage desquamation (*n =29*)	Exudative	04(11.77%)	23(67.64%)
	Organizing	01(2.94%)	06(17.65%)
Neutrophilic abscesses (*n = 7*)	Exudative	25(73.53%)	02(5.88%)
	Organizing	02(5.88%)	05(14.71%)
Alveolar fibrin (*n =28*)	Exudative	06(17.65%)	21(61.76%)
	Organizing	00	07(20.59%)
Alveolar epithelial cell desquamation (*n =29*)	Exudative	04(11.77%)	23(67.64%)
	Organizing	01(2.94%)	06(17.65%)
Pulmonary oedema (*n =31*)	Exudative	01(2.94%)	26(76.47%)
	Organizing	02(5.88%)	05(14.71%)
Alveolar septal fibrosis (*n =8*)	Exudative	24(70.59%)	03(8.82%)
	Organizing	02(5.88%)	05(14.71%)
Alveolar chronic inflammation (*n =20*)	Exudative	13(38.24%)	14(41.17%)
	Organizing	01(2.94%)	06(17.65%)
Type II pneumocyte hyperplasia (*n =14*)	Exudative	16(47.06%)	11(32.35%)
	Organizing	04(11.77%)	03(8.82%)
Alveolar acute inflammation (*n =23*)	Exudative	08(23.53%)	19(55.88%)
	Organizing	03(8.82%)	04(11.77%)
Intra-alveolar hemorrhage (n =20)	Exudative	11(32.35%)	16(47.06%)
	Organizing	03(8.82%)	04(11.77%)

Pulmonary edema, alveolar epithelial cell desquamation and macrophage desquamation were present in majority of patient. Histological finding like neutrophilic abscess and alveolar septal fibrosis were present in less individual. Hyaline membrane formation shown in figure 1 and 2, intra-alveolar hemorrhage shown in figure 3, inflammatory cells, type 2 pneumocytes shown in figure 5 were seen in both phase of diffuse alveolar damage. Alveolar fibrin was present in all diffuse alveolar damage having organizing phase which favour more toward organizing phase of DAD. The events causing death distribution are displayed in Table 2. Major common causes include sepsis and poisoning. Other causes are post-operative, fire, traffic accident, physical trauma, drug intoxication, cancer patient taking radiochemotherapy.

Table 2: cause of death and phase of diffuse alveolar damage distribution

Causes of death	Total cases N (%)	Exudative Phase	Organizing phase
Sepsis	10	08	02
Alcohol poisoning	04	03	01
Aluminium phosphide poisoning	03	03	00
Unknown substance poisoning	03	02	01
Pesticide poisoning	01	00	00
Fire accident	03	02	01
Post operative	03	03	00
Traffic accident	03	01	02
Physical trauma	01	01	00
Cancer patient taking Radiochemotherapy	01	01	00
Drug intoxication	01	01	00
Unidentified	01	01	00

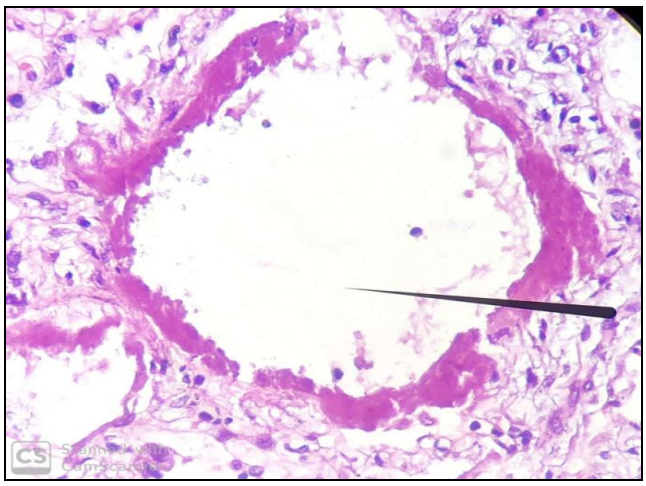

Fig 1: Hyaline membrane formation (40x)

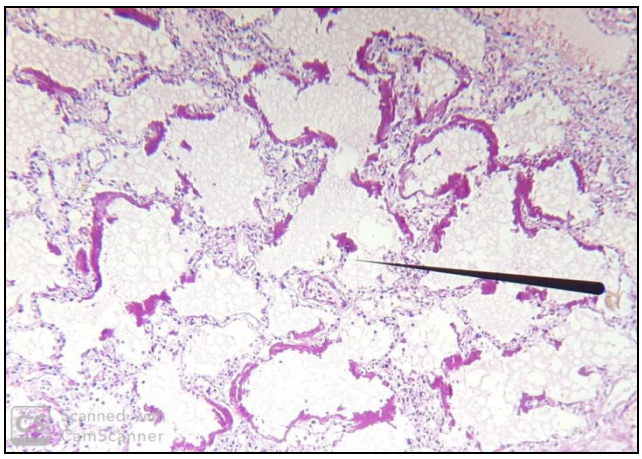

Fig 2: Hyaline membrane formation (10x)

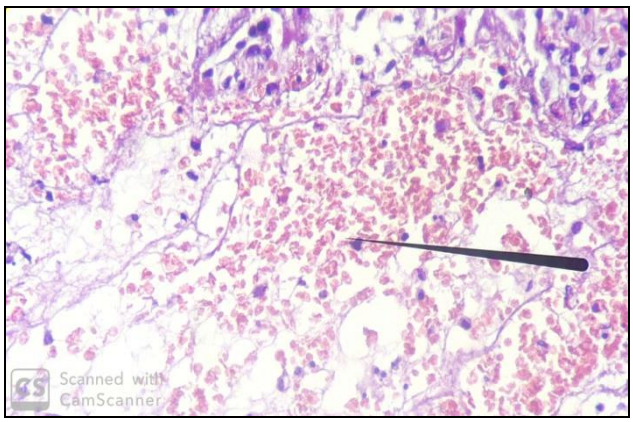

Fig 3: Intra-alveolar hemorrhage

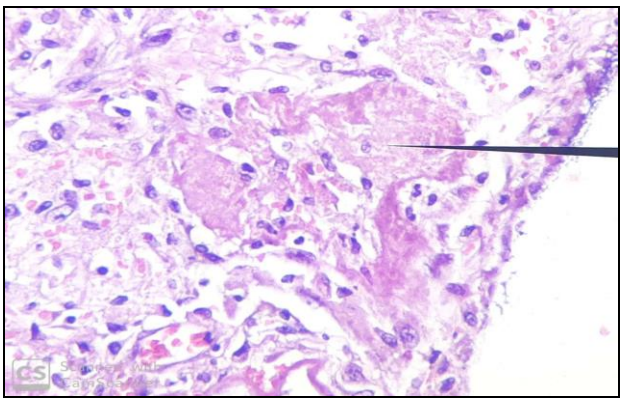

Fig 4: Alveolar organizing fibrosis

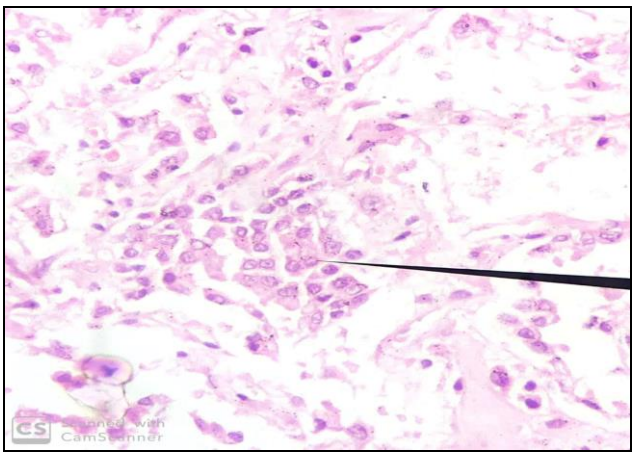

Fig 5: type 2 pneumocytes proliferation

Discussion

DAD is difficult to diagnose due to the severity of pre-operative histopathological ARDS, but may be diagnosed at autopsy. Individuals more than 50 years of age are more frequently involved by diffuse alveolar damage [5]. In our study mean age was 48 year which is in compared to Halide nur urer *et al.* [7] mean age was 53. In forensic autopsies, Ferrer *et al.* [6]. Detected HM (hyaline membrane) development in 12% of exudative-phase cases and 62% of proliferative-phase cases. In Halide nur urer *et al.* [7] the prevalence of HM was higher in the proliferative phase than in the exudative phase. In our study HM are present in 77.78% exudative phase and 57.14% organizing phase the histologic pattern of DAD is characterized by an early exudative phase that develops into an organizing phase. The term *diffuse* refers to complete involvement of the pulmonary lobule and not necessarily the entire lung sample. The early reaction shows rounded organizing plugs of exudate in the terminal bronchioles and protein-rich edema in the alveolar space, with fibrin-rich eosinophilic hyaline membranes along the surface of the alveolar septa [8].

Type II pneumocytes are reactive with nucleomegaly and atypia. Interstitial edema is usually accompanied by scant numbers of lymphocytes, plasma cells, and a few neutrophils. Intra-alveolar hemorrhage may be present focally but is generally not severe. Thrombi may be seen within pulmonary capillaries and small- to medium-sized pulmonary arterioles. Large numbers of acute inflammatory cells may indicate that DAD is superimposed on another process, such as bacterial pneumonia or alveolar capillaritis [9].

In lesions of one to several weeks' duration, a phase of organization may ensue that can result in complete resolution of the process or that may progress to interstitial fibrosis. Histologically, the picture is usually uniform, but some biopsy specimens may show a mixed pattern of acute exudation along with areas of organization indicative of repeated bouts of lung injury. When fibrosis is established, the alveolar septa are densely fibrotic, and the late changes are difficult to differentiate from other causes of diffuse interstitial pulmonary fibrosis. However, residual hyperplasia and atypia of alveolar lining cells and remnants of hyaline membranes may be a clue to preexisting DAD.

Regardless of the inciting cause, a sequence of events, including the damaging effects of leukocyte enzymes, inactivation of pulmonary repair mechanisms, depletion of surfactant, activation of blood coagulation factors, and fibrinolysis, result in damage to the endothelial cell

basement membrane and alveolar type I cells10. The presence of hyaline membranes help distinguish DAD from other interstitial pneumonias; however, organizing DAD can be mistaken for organizing pneumonia if one does not appreciate the more diffuse nature of the process and impressive alveolar septal fibrosis. Although fibrosis in DAD may resemble fibrotic NSIP or even honeycomb change in UIP pattern, clinical and radiologic features should discern the entities [11, 12]. DAD may fully resolve either in the acute, protein-rich phase or even after biopsy shows organization and fibrosis [10]. Death occurs in roughly 40% to 50% of cases, usually after several weeks or months
This study had some limitation like inter-observer variation and autolysis of some lung biopsy in which DAD may be missed due to autolytic changes.

Conclusion

In DAD both exudative and proliferative lesions may be identified during forensic autopsies. However, many histopathological changes can seen in both phase of DAD. Individual of older age are frequently affected particularly in sepsis, intoxication, poisoning trauma and fire may play a role in the etiology of DAD. Death due to sepsis and poisoning are more common in our study. The cause of death must be determined in forensic autopsy cases to evaluate the event within the context of possible mechanisms and available histopathological findings during the final assessment. If consent is obtained from the relatives of the deceased and ante-mortem information is obtained properly, forensic autopsies may provide a favourable means for increasing our knowledge about DAD, acute lung damage and interstitial lung disease.

References

1. Olson J, Colby TV, Elliott CG. Hamman-Rich syndrome revisited. Mayo Clin Proc 1990;65(12):1538-1548.
2. Bernard GR, Artigas A, Brigham KL *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(3 Pt 1):818-824.
3. Nash G, Blennerhassett JB, Pontoppidan H. Pulmonary lesions associated with oxygen therapy and artifical ventilation. N Engl J Med 1967;276(7):368-374.
4. Corrin B. Pathology of the lung, in Diffuse Alveolar Damage, the Pathological Basis of the Adult Respiratory Distress Syn- drome, JM. Houston, Ed., Churchill Living- stone 2000, 121-135.
5. De Hemptinne Q, Remmelink M, Brimioulle S, Salmon I, Vincent JL. A clinicopathological confrontation, Chest 2009;135(4):944-949.
6. Ferrer A, Castellano M, Plaza L. Pathological spectrum of the lung in cases of violent death: part II. Clinicopathologic correlation, Journal of Forensic Sciences 1988;33(2):490-497.
7. Halide Nur Urer, Gokhan Ersoy *et al*. Diffuse Alveolar Damage of the Lungs in Forensic Autopsies: Assessment of Histopathological Stages and Causes of Death The Scientific World Journal 2012, Article ID 657316, 6 pages doi:10.1100/2012/657316
8. Tomashefski JF, Jr. Pulmonary pathology of the adult respiratory distress syndrome. Clin Chest Med 1990;11(4):593-619.
9. Gaudin PB, Askin FB, Falk RJ *et al*. The pathologic spectrum of pulmonary lesions in patients with anti-neutrophil cytoplasmic autoantibodies specific for anti-proteinase 3 and anti myeloperoxidase. Am J Clin Pathol 1995;104(1):7-16.
10. Ware LB, Matthay MA. The acute respiratory distress syndrome. N Engl J Med 2000;342(18):1334-1349.
11. Katzenstein AL, Fiorelli RF. Nonspecific interstitial pneumonia/fibrosis. Histologic features and clinical significance. Am J Surg Pathol 1994;18(2):136-147.
12. Rice AJ, Wells AU, Bouros D *et al*. Terminal diffuse alveolar damage in relation to interstitial pneumonias. An autopsy study. Am J Clin Pathol 2003;119(5):709-714.