WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 6, Issue 3, March- 2025

A METHOD FOR DETERMINING PATHOMORPHOLOGICAL CHANGES IN PULMONARY HYALINE MEMBRANE DISEASE

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Abstract
This article is devoted to the analysis of scientific literature and practical research on respiratory distress syndrome and hyaline membrane disease. One of the most urgent problems in pediatrics is neonatal respiratory distress syndrome and its morphological manifestation, the hyaline membranes. The growing importance of this problem is associated with the increase in premature births. Hyaline membrane (HM) disease is one of the most common diseases among newborns and usually develops against the background of prematurity; morphologically, it is characterized by a hyaline-like, dense, eosinophilic formation in a circular shape inside the respiratory spaces of the lungs. The hyaline membrane is formed from various components: plasma proteins, hemoglobin, fibrin, nucleo- and mucoproteins.

Keywords: Newborn, lung, breathing disorder, respiratory distress syndrome, hyaline membrane, surfactant.

Introduction

Respiratory disorders rank second (8.8%) among neonatal morbidity indicators, frequently occurring in premature infants whose lungs are morphologically and functionally immature. Hyaline membrane disease in newborns makes up 6-12% of cases, whereas among infants with extremely low birth weight, it is found in 0.6-0.7% [1,3,5,15,18]. The primary cause of this disease is a primary deficiency of endogenous surfactant in the lungs of newborns, coupled with weak respiratory muscles and difficulties in independent breathing. In such infants, primary atelectasis is also common alongside hyaline membrane disease. Hyaline membrane syndrome is the most severe form of pneumopathy; it is detected in 39-50% of newborns and 15-25% of premature infants, with a higher prevalence in males.

Materials and Methodology

Autopsy data from 52 premature infants of varying degrees, who died due to respiratory failure, were used as the material for this study. First, the clinical histories and autopsy findings of these deceased infants were analyzed. They were divided into

groups according to gestational age (Table 1). From these, Group 1 consisted of deeply premature infants with extremely low birth weight who died within the first hour after birth and served as the control group. The purpose was to identify early morphological changes in the lungs that lead to the development of hyaline membrane disease in these infants. The main cause of death in this group was postnatal asphyxia. In all cases, prenatal and intranatal risk factors from the mother, as well as placental and umbilical cord pathologies, were identified. The anthropometric indicators of the examined infants are presented in Table 1.

Table 1: Anthropometric Indicators of Premature Infants, M±m

No.	Group of Premature Infants	n	Gestational (weeks)	Age Birth Weight (g)	Length (cm)
1	22–27 weeks	12	25.2±0.4	654±24.3	29.5±1.6
2	28–32 weeks	18	29.8±0.6*	1067±84.7*	38.4±4.6*
3	33–37 weeks	22	35.3±0.7**	1986±124.6**	43.2±8.5**

Note: * -p≤0.05 – Statistically significant difference in gestational age, birth weight, and length of Group 2 compared to Group 1.
** - p≤0.05 – Statistically significant difference in gestational age, birth weight, and length of Group 3 compared to Group 1.
A clinical and anamnestic analysis showed that the shortest survival times and the most severe heart–respiratory failure were observed in Group 1 infants, whereas those in Group 3 survived relatively longer.
For histological examination, tissue samples were taken from various regions of both lungs during pathological autopsy. The macroscopic appearance of the lungs was assessed at autopsy by examining their external aspects. The tissue samples of the lungs were fixed in 10% neutral formalin, passed through graded alcohols, and embedded in paraffin. Histological sections were stained with hematoxylin and eosin, by the PAS (Periodic Acid-Schiff) reaction, and using the van Gieson method.
The following morphometric measurements were carried out:
1. The percentage of aerated alveolar area relative to the total lung area.
2. Counting the number of alveoli with hyaline membranes within one field of view.
3. Measuring the thickness of the hyaline membrane.
4. Measuring the height of the alveolar epithelium.
5. Measuring the thickness of the alveolar septal tissue.

Each parameter was measured 10 times, and the arithmetic mean and standard error of the mean were calculated. Statistical processing of quantitative indicators was carried out using descriptive and variation statistics; differences at $p \leq 0.05$ were considered statistically significant.

Results

Group 1 (Control Group)

Group 1 infants had a very severe condition at birth, with profound morphofunctional immaturity and severe cardiopulmonary failure. Macroscopically, the lungs were consistent with the gestational age. Histological examination generally showed enlarged alveolar epithelial cells with rounded, normochromic nuclei. In some cases, alveolar epithelial damage was observed, with deformed nuclei. In certain lung areas, a small number of alveoli were air-filled and dilated, taking on a round shape, which caused the alveolar epithelial cells to become flattened and elongated. Most alveoli remained almost collapsed, appearing as various holes and cracks. Their septa were thick and consisted of tissue and cells packed due to the lack of air (Figure 1). The capillaries in the alveolar septa were dilated and full of blood, and in some areas, diapedetic hemorrhages were observed (Figure 2).

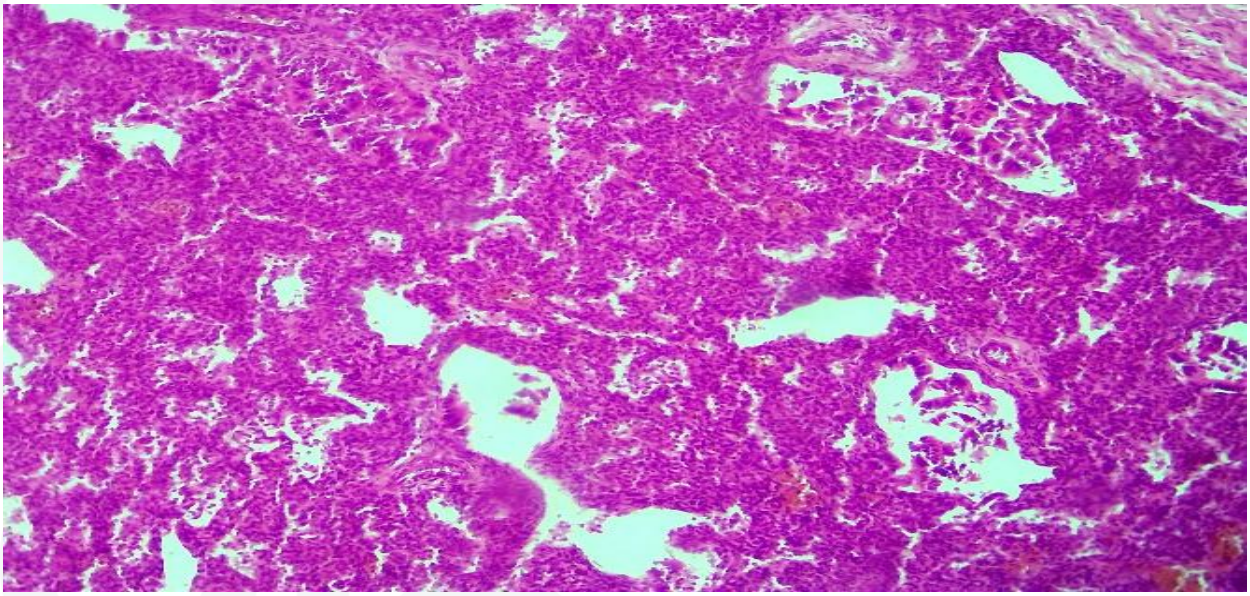

Figure 1. Infant born at 25 weeks of gestation. Most alveoli are not opened. Staining: H&E. Magnification: 10×10.

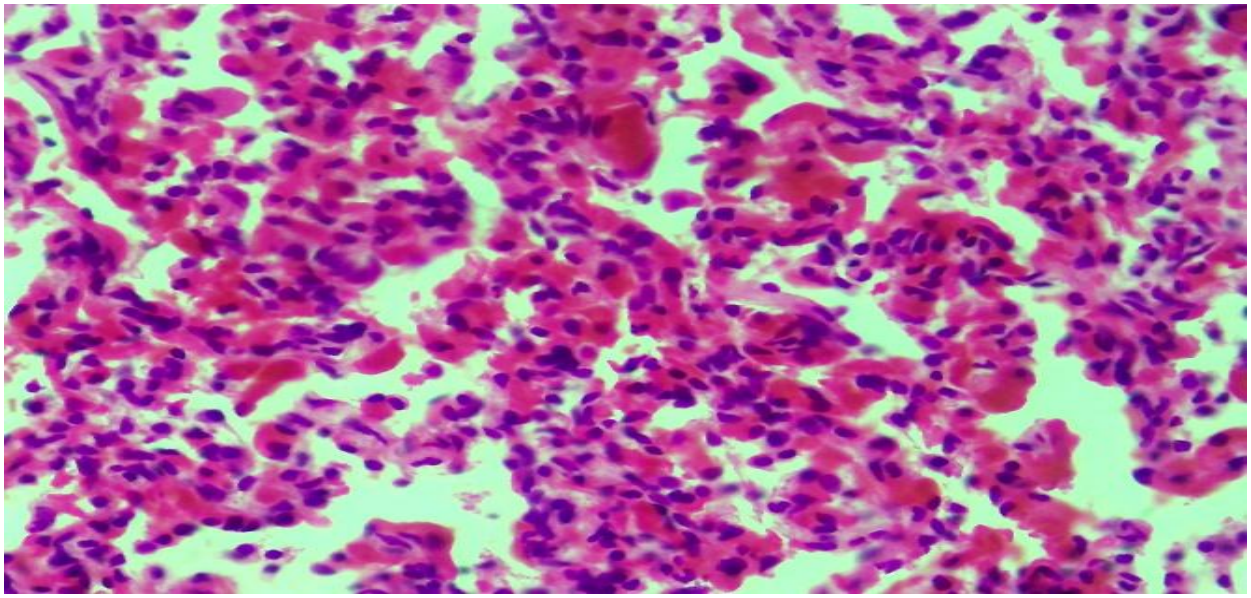

Figure 2. Fragment of Figure 1. The capillaries are blood-filled, and hemorrhages are present. Staining: H&E. Magnification: 10×40

Morphometric measurements showed that in Group 1, the area of aerated alveoli was 28.5±3.6% of the total lung area. Within one field of view, the average number of alveoli containing hyaline membranes was 5.8±1.4. The average height of alveolocytes was 9.34±3.4 μm (ranging from 2.4 to 14.8 μm). The thickness of the alveolar septa averaged 32.3±5.2 μm (with the thinnest area at 9.6 μm and the thickest at 54.2 μm). Hyaline membranes were found in 22.8% of the Group 1 infant lungs. These membranes varied in thickness and formed a reticular pattern in certain areas. Measurement of the hyaline membrane thickness averaged 9.6±2.7 μm (Table 2), with the thinnest regions at 2.6 μm and thickest at 16.8 μm. According to clinical and anamnestic analyses, most of these infants suffered from intranatal asphyxia, cerebral edema and hemorrhages, which are significant risk factors for developing hyaline membrane disease.

Among the Group 2 premature infants, 3 died within the first 6 hours after birth; 6 infants (33.3%) died between 12 and 24 hours, 5 (27.7%) between 72 hours, and another 4 (22.2%) by 120 hours. In the lungs of the 3 infants who died within the first 6 hours, hyaline membranes with homogeneous structures were detected in certain areas. The alveoli containing hyaline membranes were primarily located in the peribronchial region. These membranes were arranged in a ring-like manner, firmly adhered to the inner alveolar surface. In addition to hyaline membranes, the alveolar spaces contained fragments of amniotic fluid, meconium particles, and maternal erythrocytes. In infants who died between 12 and 24 hours, hyaline membranes were found throughout most of the lung tissue, filling relatively small alveolar spaces. Many

alveoli appeared dilated and contained dense, purple-colored clumps of hyaline membranes. No membranes were found in collapsed alveoli. The alveolar septa displayed a mild reaction to the presence of hyaline membranes.

In infants who died between 72 hours, alveoli varied in size; in some, hyaline membranes were found. The alveolar shape ranged from triangular and elongated to star-shaped. In addition to hyaline membranes, amniotic epithelium, fibrin-like masses, and segmented leukocytes were observed in the alveolar spaces. There were areas of distal atelectasis around blood vessels and bronchioles, vascular dilation, and signs of serous edema in both the interstitial tissue and alveolar spaces.

Infants who died up to 120 hours had lung tissue with most alveoli filled with air and dilated. Some areas showed emphysematous changes; the hyaline membranes in the alveolar spaces had fragmented and partially disintegrated. A strong inflammatory response to the membranes was observed in the interstitium (a lymphohistiocytic infiltration). Small foci of atelectasis and distal atelectasis were found around blood vessels (perivascular) and bronchi (peribronchial).

Morphometric measurements of Group 2 infant lungs showed that the aerated alveolar area was 48.7±6.2% of the total. On average, 7.8±1.4 alveoli within each microscopic field contained hyaline membranes. The average height of alveolocytes was 7.18±3.6 µm, ranging from 3.4 to 12.8 µm (Table 2). The average thickness of the alveolar septa was 25.3±3.2 µm (thin areas 6.6 µm; thickest 42.4 µm). Hyaline membranes were present in 27.8% of Group 2 lungs. As in Group 1, the membranes varied in thickness and had a reticular pattern in places. The average measured thickness was 11.6±2.8 µm, ranging from 3.6 µm in thinner parts to 21.8 µm in thicker ones.

Table 2: Morphometric Indicators of Hyaline Membrane Disease (M±m)

No.	Structures Examined	Group 1	Group 2	Group 3
1	Aerated alveolar area (% of total area)	28.5±3.6	48.7±6.2*	78.4±8.5**
2	Alveolar epithelium height (µm)	9.34±3.4	7.18±3.6*	6.15±2.4**
3	Thickness of alveolar septal tissue (µm)	32.3±5.2	25.3±3.2*	18.3±2.3**
4	Number of alveoli with hyaline membranes (per FOV)	5.8±1.4	7.8±1.4*	6.9±1.3**
5	Thickness of hyaline membranes (µm)	9.6±2.7	11.6±2.8*	12.7±3.6**

Note: *- p≤0.01 – Statistically significant difference for Group 2 compared to Group 1.

** - p≤0.01 – Statistically significant difference for Group 3 compared to Group 1.

In Group 3, 8 infants (36.3%) died between 12 and 24 hours, 6 (27.3%) by 72 hours, and 8 (36.3%) by 120 hours. In those who died between 12 and 24 hours, most of the lung tissue showed hyaline membranes filling the largely dilated alveolar spaces (Figure 3). Many alveoli contained shed alveolocytes, segmented leukocytes, cellular fragments, bronchial epithelial cells, and lymphocytes. In the lungs of those who died by 72 hours, alveoli varied in size; some contained hyaline membranes. The alveolar septa appeared thickened, with proliferating fibroblasts and lymphoid cells (Figure 4). The bronchi were dilated, and their lumens contained leukocytes, shed epithelium, and erythrocytes. In infants who died by 120 hours, most alveolar spaces were aerated and dilated, with some emphysematous foci; the hyaline membranes in the alveoli had disintegrated into fragments. A robust lymphohistiocytic infiltration was observed in the interstitium, representing a pronounced reaction to the hyaline membranes.

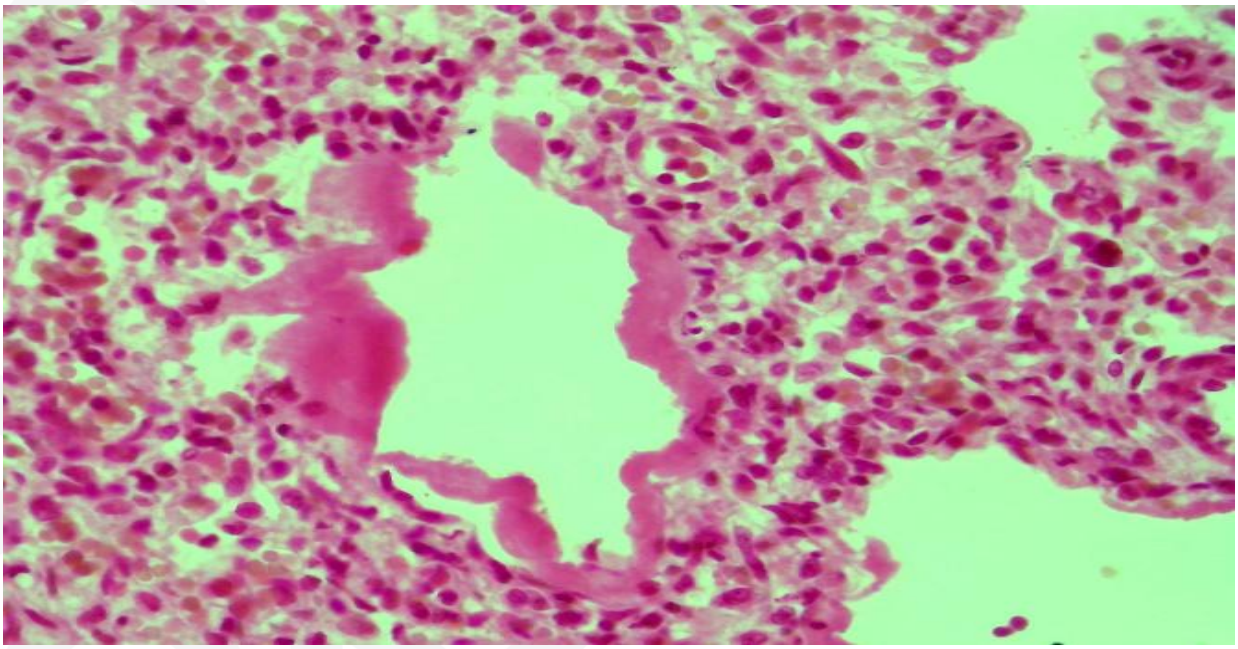

Figure 3. Infant born at 34 weeks of gestation. Dilated alveoli with thick hyaline membranes.
Staining: H&E. Magnification: 10×40.

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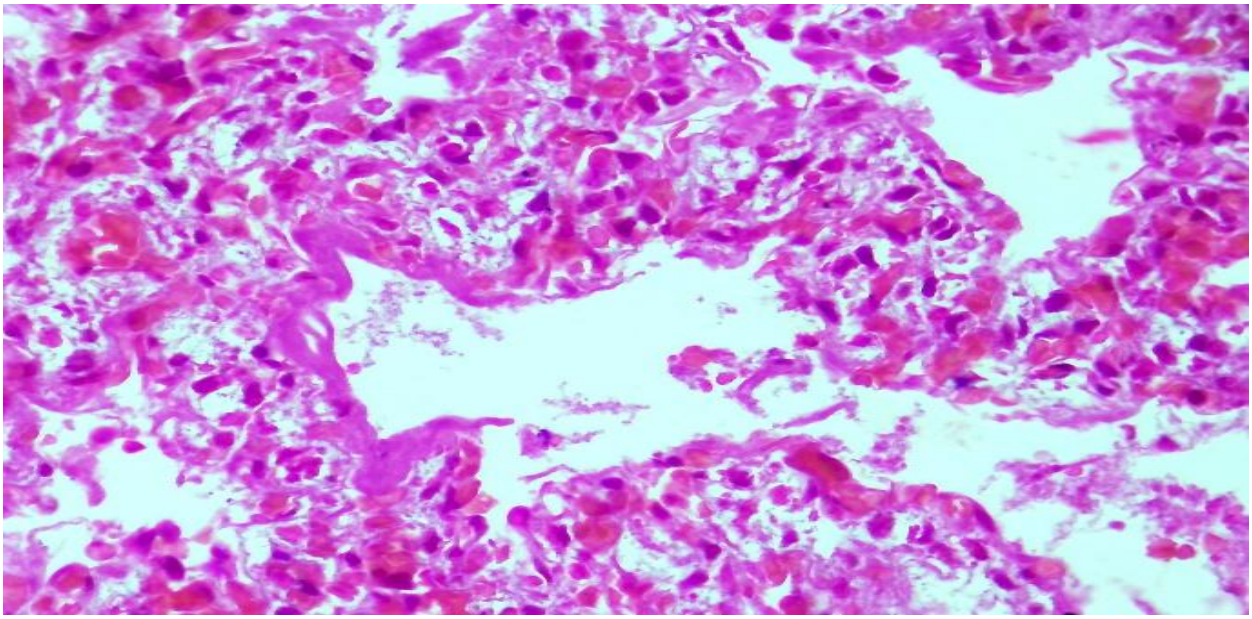

Figure 4. Infant born at 36 weeks of gestation. Dilated alveoli with proliferated fibroblasts in the interstitial tissue.
Staining: H&E. Magnification: 10×40.

Morphometric measurements of Group 3 lungs showed that the aerated alveolar area reached 78.4±8.5% of the total. Within one microscopic field, an average of 6.9±1.3 alveoli contained hyaline membranes. The average thickness of the alveolar septa was 18.3±2.3 μm (ranging from 4.7 μm to 38.4 μm). The average thickness of the hyaline membranes was 12.7±3.6 μm, with the thinnest region at 5.6 μm and the thickest at 27.6 μm. The average height of alveolocytes was 6.15±2.4 μm (ranging from 5.2 μm to 14.8 μm) (Table 2).

DISCUSSION

The morphological and morphometric features of the hyaline membrane structure were studied during the study. The materials of a clinical and anamnesis study conducted on 22-37 patients aged 18 to 24 years were used as the material. The results showed that with insufficient blood supply to hyaline membranes, circulatory disorders, circulatory disorders and damage to the alveolar epithelium of the bronchi are possible. The results of morphometric studies have shown that within 22-27 BC, about 1/3 of the total number of alveoli, oral alveoli, alveolar epithelium, and hyaline fibers were found in the alveoli. The membranes consist of relatively thick fibers. In 28-32 and 33-37 BC, the Gurkhas, whose alveoli were interconnected by channels, had their oral alveoli dilated and their hyaline membranes dilated.

Conclusion

This article presents an analysis of scientific literature and practical research findings regarding respiratory distress syndrome (RDS) and hyaline membrane disease. The main problem in neonatology is respiratory distress syndrome and its morphological hallmark, hyaline membranes. The principal reason for the growing incidence of this condition is the increased rate of prematurity worldwide. Hyaline membrane disease is one of the most common disorders encountered in pediatrics, occurring against the background of prematurity. Morphologically, it is characterized by hyaline-like, dense, eosinophilic formations in a circular shape within the respiratory spaces of the lungs. It has been determined that hyaline membranes are composed of various substrates such as plasma proteins, hemoglobin, fibrin, nucleo- and mucoproteins.

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