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Study of histology of lungs in aborted fetus- A tool to limit premature deaths.

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Abstract

Introduction: Many deaths take place in premature babies because of immature development of lungs. Therefore, it's important to study histology of lungs and see its maturity. Many studies are based on gross anatomical features of lungs but very few on histology. Therefore, we are hereby conducting study based on histology and which will be helpful to prevent death of premature babies. Aim of study was to study microscopically stages in development of fetal lung and its comparison with adult stage.

Material and methods: Fifty aborted fetus more than 16 weeks were collected. Fetus were obtained within 1-2 weeks of abortion and were stored in 10% formalin. After processing tissues, slides were fixed and stained using hematoxylin and eosin staining.

Results: At 16 weeks epithelial lining of proximal bronchi was pseudo stratified columnar. By 18th week blood vessels were found in connective tissue septae and lung parenchyma. By 22nd week lymphatic elements with bulging nuclei were seen. Mucous and serous glands appeared by 23rd week. At 25th week of gestational age respiratory bronchioles made their appearance. Many primitive alveoli appeared by end of 28th week. 33rd week onwards sections were seen showing all features resembling that of adult lung.

Conclusion: Many deaths occur due to respiratory distress in premature babies. When histology of lungs is known according to week of gestation, development at that particular stage can be known. So, treatment modalities can be done according to development of lung till that particular week. If treatment will be started accordingly, it will definitely help to prevent premature deaths.

Keywords: Aborted fetus, histology, hematoxylin and eosin, lungs, premature deaths

Introduction

The development of human organ system is an ongoing process which begins with fertilization and continues into the postnatal life. It is well known fact that function of

organ depends on histological maturation of organ.[1] Although development of human lung has been widely studied and illustrated, most of the articles deal with few aspects of histogenesis. [2] Histologically, lung development and maturation has been divided into four stages:

1. The pseudo glandular stage (5–16 weeks).
2. The canalicular stage (17–25 weeks).
3. The terminal saccular stage (25 weeks) and
4. The alveolar stage (late fetal period to childhood) [3]

With the recent advances in medical field, it is now possible that the premature babies can survive successfully. For this purpose, it is essential to have knowledge regarding histological maturity of lung and its functional status at the given gestational age. In this regard, our study gives information about histological development of human lung and the time sequence in which it develops.

Aims and objectives

1. To study microscopically the stages in the development of fetal lung and its
2. Comparison with adult stage.

Material and methods

Sample size

50 aborted human fetuses (29 females and 21 males) of different gestational ages from 16thweek onwards were collected from the department of Obstetrics and Gynecology.

Duration of study: 2years

Inclusion criteria

1. Spontaneously aborted fetuses from 16th week onwards.
2. Stillborn fetuses.
3. Those in good condition without any Congenital Anomalies or signs of decomposition.
4. Terminated fetuses under the Medical termination of Pregnancy Act of India 1971.

Exclusion criteria

1. Fetuses less than 16 weeks.
2. Presence of any congenital anomalies
3. Post mortem decomposition

Procedure

Fetuses were obtained within 1-2 hours of abortion to avoid post-mortem decomposition changes and kept in jars of 10% formalin.

The observations were divided under:

Histological parameters (Development and appearance of various tissue elements):

1. Development of bronchi
2. Epithelium
3. Glands
4. Cartilage
5. Lymphatic element
6. Development of Bronchioles
7. Respiratory Bronchioles
8. Development of Alveolar ducts and Alveoli
9. Development of Blood Vessels

For dissection of lungs 10% formalin was injected in thoracic and abdominal cavity. Lungs were fixed using Bouins fluid. Tissues were dehydrated using ascending grades of alcohol. Clearing was done to remove alcohol from tissue. Tissues were placed in xylene for about 30 minutes. Later, tissues were subjected to two changes of paraffin wax each for three hours. In this process the blocks were prepared by pouring molten paraffin wax (melting point 55-60C) into a mold. Slides were fixed and were stained using hematoxylin and eosin staining.

Results

External Appearance of lungs: All the lungs observed were soft, smooth, pyramid shaped, pinkish brown in color. All borders were appreciated.

On histological findings changes were

16 to 18 Weeks

Development of Bronchial Tree

The youngest fetus studied was of 16 weeks. Its tissue which was sectioned

Resembled to an exocrine gland. Centrally placed gland like tissue was peripherally covered by thin layer of pleura. Pale recolored connective tissue septae were seen running from pleura isolating the lung parenchyma into number of lobules. Mesenchymal tissue showed presence of bronchial tubes of varying sizes.

Epithelium

A) Some parts of bronchial tubes - simple cuboidal epithelium

B) Remaining parts of bronchial tube- low to high columnar epithelium.

C) Overall developing bronchial tubes- low tall columnar cells.

D) Epithelial lining- pseudo-stratified columnar near hilum.

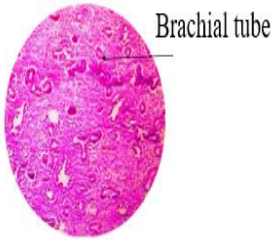
Glands*:* Few glandular cells were observed as gathered mass with large oval bulging nuclei. These cells were found without lumen.

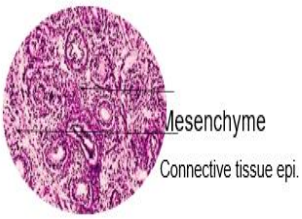
Cartridge*:* The walls showed presence of developing cartilages with large polygonal cells.

Development of bronchioles, alveoli*:* Bronchioles showed infoldings. The epithelium lining bronchioles was simple tall columnar. Increase in number and size of bronchioles along with further branching was observed in successive sections of the tissues from fetuses of this age group.

Well-developed plates of cartilages, lymphoid tissue, different types of glands, connective tissue and smooth muscle were absent.

Development of Lung Vasculature: Blood vessels were found in the connective tissue septa as well as lung parenchyma. Proximal to the developing lung bronchi, thick-walled artery and thin-walled vein were noted. Vessels were lined by endothelial flat cells while their walls showed few spindles and few polygonal cells.





Photomicrograph 1: Lung of foetus of 16 weeks: 10X; Haematoxylin and Eosin

Photomicrograph 2: Lung of foetus of 16 weeks: 10X; Haematoxylin and Eosin

19 to 22 Weeks

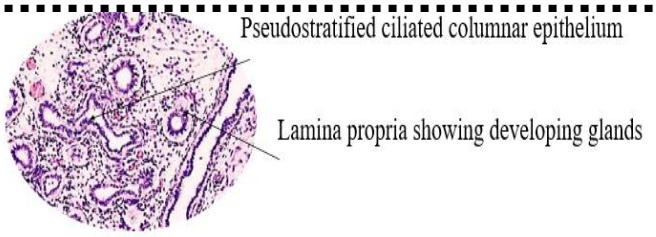
Epithelium: Most of the bronchial mucosa was lined by cuboidal to low columnar epithelium. The large upper while the simple columnar type of epithelium with cilia was observed in distal narrower bronchi.

Glands: At this stage lamina propria of bronchi showed presence of many developing glands. Few glands showed lumen leading to primitive tubular pattern.

Cartridge: Cartilaginous matrix of proximal bronchus showed diffuse central basophilic staining while in distal bronchi eosinophilic matrix was seen

Lymphatic elements: Also, the additional lymphatic elements with dark nuclei were seen.

Development of bronchioles, alveoli: Fetus at 20th week of gestational age showed numerous bronchial tubes and large lumen with profuse branching. The quantity of mesenchymal cells was found to be less compared to sections from earlier age group. Few ducts among these were visible penetrating the lamina propria and opening in epithelial crypts. By the end of 22 weeks, the ducts were found to be lined by simple cubical epithelium.



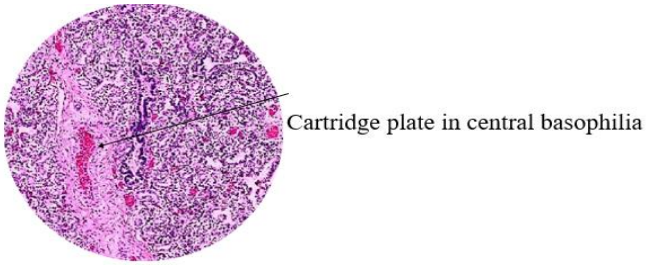
Photomicrograph 3: Lung of fetus of 20 weeks: 40X; Haematoxylin and Eosin

23 to 26 Weeks

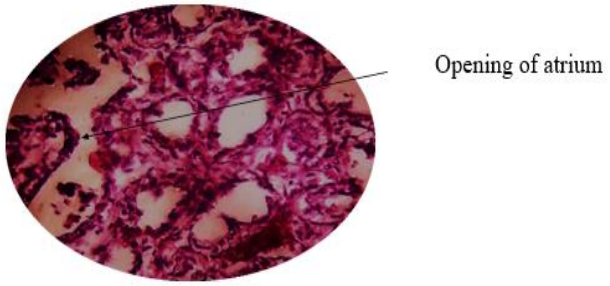
Epithelium-The bronchi were lined with pseudo stratified columnar epithelium

With numerous infoldings while the distal part of bronchi was found to be lined by cuboidal epithelium by spindle shaped cells.

Bronchi, bronchioles and alveoli- At 23 weeks abundant mucous glands with hazy cytoplasm flat nuclei and few but mature serous glands which resembled adult type were observed in the walls of large bronchus. In this stage, bronchi showed presence of matured cartilage plates, mucous and serous glands, muscles and connective tissue in their walls. At 25th week of gestational life, respiratory bronchioles made their appearance. These primitive alveoli resembled matured alveoli in their microscopic structure. Primitive alveoli were observed at terminal ends of respiratory bronchioles while true alveoli are seen at the ends of ducts of alveoli. The main difference between alveolar sacs and the true alveoli is the proportion of pneumocytes i.e., Type I and Type II cells. The true alveoli showed more percentage of Type II pneumocytes which are also called as surfactant producing cells.



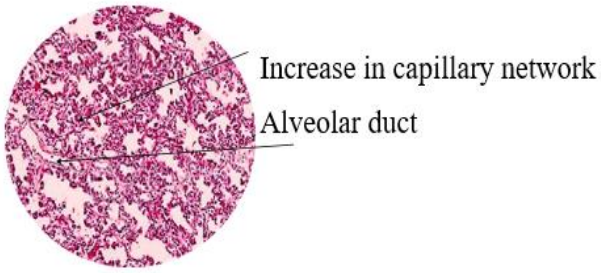
Photomicrograph 4: Lung of foetus of 24 weeks: 10X; Haematoxylin and Eosin



Photomicrograph 5: Lung of foetus of 24 weeks: 40X; Haematoxylin and Eosin

27 to 30 weeks

The section of tissue obtained from 28 weeks old fetus showed numerous alveolar pouching from respiratory bronchioles and well differentiated bronchi as well as bronchioles. Alveoli were lined by flattened squamous epithelium along with surrounding capillary network. Abundant primitive alveoli were seen by 29th week. These alveoli showed further divisions in alveolar ducts which looked like narrow tubular passage lined by low cubical epithelium.



Photomicrograph 6:Lung of foetus of 31 weeks:10X; Haematoxylin and Eosin

Development of Bronchial Tree

Fetus of 31st week showed alveolar sacs opening in alveolar ducts. In subsequent sections of tissue and procured from 33-week-old fetus, the components of intrapulmonary bronchial tree were developed. The alveoli showed extremely thinned out walls which were lined by simple squamous type of epithelium. Meshwork

of capillaries were observed surrounding the alveolar walls. Sections of tissues 33 weeks onwards showed all the features resembling that of adult lung.

Development of Lung Vasculature

Number of branches of pulmonary artery was observed nearby the respiratory bronchioles. Meshwork of capillaries was observed surrounding the alveolar walls in the thin inter-alveolar septa. Hence as gestational age advanced, the vascularization of lungs increased and was proved by differentiation of a greater number of capillaries in late ages

Discussion

The present study was conducted over a period of 2 years on dead fetuses with gestational age more than 16 weeks.

Epithelium

In the present study, the simple tall columnar epithelium was observed at 16th week of gestation along with few pseudos stratified cells lining near hilum. This finding was compared to the study of Edward et al, according to him the pseudo stratified epithelium is lining the bronchi by 10th week of gestation.[4] In the present study the sample started at 16 week onwards hence appearance before 16 week could not be ascertained however at 16-week tall columnar epithelium is seen. In our study, the cilia were evident only after 18 weeks which is later than the previous study done by Edward et al who noted cilia by 10 weeks spreading to periphery by 13th week. [4]

Glands

In the present study glands were observed as early as 16th week as mass of cells around the epithelium. This finding is corroborative with the finding of Brites G and Bernek who described appearance of glands by 15th week.[5] In our study tubular glands with lumen were found only after 19th week and their ducts made appearance by 22nd week. Mucous and serous acinar pattern was distinguishable by 24 weeks. While according to the study carried out by U.Bucher and L.Reidglands with lumen were visible by 14th week while mucous and serous acinar pattern can be differentiated by 26th week. [6]

Cartilage

Edward et al described presence of primitive cartilaginous plates in bronchi as early as 11th week of gestation.[4] They also stated that by 16th week numerous airways were having cartilage of adult type. U.Bucher and L.Reid found pre-cartilaginous zones in bronchial walls by 12th week.[6] According to them few eosinophilic cartilaginous plates were converted to basophilic by then. While matrix of almost whole of the proximal cartilage plates showed marked basophillia near term. In accordance with these studies, we found few pre-cartilaginous plates in the bronchi by 16th week. These plates showed eosinophillic matrix. Basophillic matrix in the proximal parts were evident by 21st week while the cartilaginous plates in periphery were eosinophillic even after 34th week.

Lymphatic elements

According to Reid and Robino lymphatic elements in the walls of bronchi were seen at 20th week. While in present study lymphatic aggregation with darkly stained nuclei were observed by 23rd week which was 3 weeks later.[7]

Development of Bronchioles

Bronchioles are the tubes without cartilage. In the present study the bronchioles were found to be lined by simple columnar epithelium at the end of 20th week. Most of the distal tubes were lined by cuboidal epithelium by 20th week.

Development of Respiratory Bronchioles and Primitive Alveoli

As described by Keith L. Moore [in] his text book on embryology, terminal bronchiole gives rise to respiratory

bronchioles which ultimately leads to alveoli by 24th to 25th week. [3] U.Bucher also noted similar features. In the present study respiratory bronchioles were first observed by 25th week and this number increased with increasing gestational age.[6] Saccular outpouchings were observed in the bronchiolar walls where it was lined by flat cells without cilia. Rest of the respiratory bronchioles was lined by ciliated cuboidal cells. The saccular outpouchings were precursors of primitive alveoli. Hence our findings regarding structure, time of appearance of respiratory bronchiole are similar with Keith L.Moore and U.Bucher.[3,6] Osamu Tanakaand Misturu Oki observed that the epithelium of respiratory saccules was low columnar by 17th week, columnar to cubidal by 20th week, cubidal to squamous by 25th week.[8] These findings were corroborative with our study.

Development of Alveolar ducts and Alveoli:

According to Keith L. Moore**,** terminal bronchioles give rise to respiratory bronchioles and in turn respiratory bronchioles divides into subsequent alveolar ducts by 24th week.[3] The development of respiratory bronchioles from primordial alveoli takes place by 25th week. In the present study the alveolar ducts were observed for the first time by 29th week and their number increased subsequently up to 33rd week. By then the alveolar walls were extremely thinned out.

Development of Blood Vessels

According to the study carried out by Reid and Hislop (1973) all pre-acinar arteries and veins appeared by 17th week of gestation and intra-acinar vessels grew in later fetal life as the respiratory airways developed.[9] Due to further divisions and re-divisions of bronchioles during canalicular stage of development (16-27 weeks) epithelium was extremely thinned out. This thinning of respiratory airways lead to formation of blood gas barrier that is sufficient to bear the stress of oxygenation in premature infants. Cup shaped alveoli with double layered capillaries in the walls beneath the epithelial cells were evident by 34th week. These findings were similar with the present study. [9] Large blood vessels were seen in proximity to developing bronchi by 21st week. Vascularization of lung increased considerably by 33rd week in septa near squamous epithelium and branches of artery increased towards term.

Conclusion

At 16 weeks the epithelial lining of proximal bronchi was pseudo stratified columnar, while the distal bronchi and bronchioles were lined by low columnar epithelium. By 18th week blood vessels were found in connective tissue septae and lung parenchyma as well. Around 21st week bronchial mucosa was found to be cuboidal. By 22nd week lymphatic elements with bulging nuclei were seen. Mucous and serous glands appeared by 23rd week. At 25th week of gestational age respiratory bronchioles made their appearance. Many primitive alveoli appeared by the end of 28th week. These were lined by flattened epithelium. 33rd week onwards sections were seen showing all the features resembling that of adult lung. The bronchi were also fully differentiated.

References

1. Jobe A. Antenatal Associations with Lung Maturation and Infection. Journal of Perinatology. 2005; 25: S31-S35.
2. Pramila Padmini, Mantraratnam and Narasinga Rao Bhattam. Cytoarchitecture of Human Fetal Lung. International Journal of Basic and Applied Medical Sciences. 2012; 2 (1): 22-2
3. Keith Moore, T.Persaud. Developing Human in Development of Bronchi and Lungs. 1998.6th ed.262-266.

4. Edward A. Boyden. Segmental Anatomy of the Lungs. A Study of the Patterns of the Segmental Bronchi and Related Pulmonary Vessels. RSNA Radiology.1956; 66 (6):895-903.
5. Brites.G (1929) and Brenek Brites.G, Social Biology (Paris), 1929:102.
6. Bucher ureid L. Development of the Intrasegmental Bronchial Tree: The Pattern of Branching and Development of Cartilage at Various Stages of Intra-uterine Life. Thorax. 1961; 16(3):207-218
7. Reid L, Rubino M. The Connective Tissue Septa in The Fetal Human Lung. Thorax. 1959; 14 (1):3-13.
8. Osamu Tanka, Mitsuru Oki, Histogenetic study of Human Fetal lungs, Shimane Journal.Med.Sci, 1980; 4: 81-90.
9. Hislop areid L. Fetal and Childhood Development of the Intrapulmonary Veins in Man--Branching Pattern and Structure. Thorax. 1973; 28(3):313- 319.