ISSN: 2037-4445

Histogenesis of Human Lung with Special Histochemical Stains in Aborted Fetuses at Different Weeks of Gestation

Mrs. S. Savitha[1], Dr. N. Vishali[2], Dr. G. Ramulu[3], Dr. B. Swapna Kumari[4], Dr. N. Hima Bindu[5], Dr. L. Peter[6]

[1]PhD Scholar, Department of Anatomy, Meenakshi Academy of Higher Education and Research, Chennai, Tamil Nadu, India

[2]Associate Professor, Department of Anatomy, Vel's Medical College, Tiruvallur, Tamil Nadu, India

[3]Associate Professor, Dept. of Respiratory Medicine, Gandhi Medical College, Secunderabd, Telangana, India

[4]Assistant Professor, Dept. of Pathology, Gandhi Medical College, Secunderabd, Telangana, India

[5]Professor & HOD, Dept. of Anatomy, Mamata Academy of Medical Sciences, Bollaram, Hyderabad, Telangana, India

[6]Professor & HOD, Dept. of Anatomy, KAMS & RC, Hyderabad, Telangana, India

Corresponding author: Mrs. S. Savitha, PhD Scholar, Department of Anatomy, Meenakshi Academy of Higher Education and Research, Chennai, Tamil Nadu, India;

Abstract

Background: The lungs play a crucial role in gas exchange, supported by specialized cells and tissues. While many studies have focused on the development of the human lung, limited research exists on the histogenesis of the human lung, particularly with the use of specific histochemical stains like Masson's Trichrome. Our study aims to address this gap by employing hematoxylin and eosin staining, along with Masson's Trichrome staining, on sections of aborted fetal lungs.

Materials & Methods: This cross-sectional observational study conducted at KAMS&RC, Hyderabad, and TS involved 77 aborted fetuses without congenital anomalies, aged between 12 to 40 weeks of gestational age. Lung tissues from the fetuses were collected after inevitable abortion, spontaneous miscarriage, stillbirth, or medical termination of pregnancy (MTP). The lung tissues were fixed in 10% neutral buffered formalin and subjected to Haematoxylin-Eosin (H&E) staining for general observations, and Masson's Trichrome staining to assess connective tissue deposition during lung development. The study aimed to provide insights into lung histogenesis in aborted fetuses using specific histological

techniques.
Results: At 12-16 weeks of gestation, the lungs have abundant mesenchymal tissue, and the bronchi are lined by columnar epithelium. Between 17-20 weeks, bronchi are surrounded by hyaline cartilage. At 21-24 weeks, bronchial tubes are lined by simple cuboidal epithelium with cartilaginous islands in their walls. From 25-28 weeks, the mesenchyme reduces, and multiple branching bronchi with cartilaginous plates and lymphatics are evident. At 29-32 weeks, numerous air spaces with an increased capillary network are observed. At 33- 36 weeks, bronchioles with developing alveoli are seen. By 37-40 weeks, many alveoli separated by thin septa and a single layer of alveolar capillary network are present. Masson's trichrome stain was used to highlight connective tissue elements such as collagen and smooth muscle fibers around bronchi and blood vessels at various gestational ages. The study provides important insights into the morphological progression of fetal lung development throughout gestation.
Conclusion: In the present study, multiple staining methods were employed to document the appearance and organization of lung tissue during development in aborted fetuses at different gestational ages. As the gestational age advanced, a gradual decrease in the amount of mesenchymal tissue and the height of the epithelium was observed. Additionally, the study planned to investigate the expression of FGF-10 in the specimens. FGF-10 is a growth factor that plays a critical role in lung development, and its examination may provide further insights into the molecular mechanisms underlying fetal lung maturation at different stages of gestation.
Keywords: Human fetal lung, bronchial tubes, alveoli, cartilage, Hematoxylin and Eosin stain, Masson’s trichrome.

Introduction

The lungs, a pair of respiratory organs located in the thoracic cavity, play a vital role in gas exchange facilitated by specialized cells and tissues. Congenital lung diseases often stem from developmental defects during gestation, making lung development a complex and critical process influencing the fetus's independent survival.

Respiratory system development commences in the fourth week of gestation from the ventral foregut endoderm. The formation of the lung begins with cells evaginating from the foregut endoderm into the splanchnic mesenchyme, forming the respiratory diverticulum or lung bud. The respiratory system has a dual origin, with the foregut endoderm differentiating into various epithelial cell types lining the lung and trachea's inner surface, while the lung mesenchyme originates from the lateral plate mesoderm. The mesenchyme gives rise to multiple lung components, including connective tissue, endothelial cell precursors, smooth muscle surrounding airways and blood vessels, tracheal cartilage, lymphatics, and mesothelial cells covering the lung's outer surface and pleura.

Human lung development is categorized into five stages based on histological criteria: Embryonic, Pseudoglandular, Canalicular, Saccular, and Alveolar stages. Postnatally, lung growth mainly involves an increase in the number of respiratory bronchioles and alveoli, rather than their size. New alveoli continue to form during the first ten years of postnatal life. Although many studies have investigated human lung development, few have explored the histogenesis of the lung using special histochemical stains like Masson's Trichrome. In our study, we examined sections of aborted fetal lungs using hematoxylin and eosin, along with Masson's Trichrome staining to gain further insights into their histological characteristics.

Aim Of The Study:

To study the histoarchitecture of human fetal lung with H&E and Special histochemical stains in aborted fetuses at different weeks of gestation

Objectives

The objective of this study is to analyze the micro-development and determine the timing of appearance of various functional components in the developing lung. Additionally, the chronological pattern of histogenesis will be observed.

Another aim of this study is to examine the appearance of connective tissue elements in the fetal lung at different gestational ages.

Materials & Methods

Study Design & Duration of Study

This cross-sectional observational study was conducted at the Department of Anatomy, Kamineni Academy of Medical Sciences & Research Centre (KAMS&RC) in Hyderabad, TS. Ethical clearance was obtained from the institutional ethics committee to perform autopsies and conduct additional studies. The study was carried out over a period of three years, from 2020 to 2023.

Sample size

This study included 77 aborted fetuses without any apparent congenital anomalies, ranging in age from 12 weeks to 40 weeks of gestational age (GA). The fetuses were obtained from the Obstetrics & Gynecology department (OBG) after experiencing inevitable abortion, spontaneous miscarriage, stillbirth, or medical termination of pregnancy (MTP). Prior to participation, informed consent was obtained from the parents and/or legal guardians.

Inclusion Criteria

The study included aborted fetuses of various gestational ages (GA) obtained from medical termination of pregnancy (MTPs), stillbirths, or spontaneous miscarriages. All fetuses selected for the study did not have any obvious congenital anomalies.

Exclusion Criteria

Abnormal aborted fetuses with gross congenital anomaly.
Macerated fetuses.
Maternal history of infections such as TORCH, HIV.
Mothers below 18 years of age.

Methodology

The duration of amenorrhea and ultrasound fetometry were collected from medical records. Fetal weight, Crown Rump Length (CRL), Head Circumference (HC), and Biparietal diameter (BPD) measurements were also recorded and computed using the chart from the textbook "Human Embryology" by Boyd, Hamilton, and Mossman. The fetuses were well-preserved, and a thorough examination was conducted to identify any gross congenital malformations. To estimate fetal age accurately, different fetal parameters, such as CRL, BPD, and ultrasound data, were used, along with the last menstrual period of the mother. This approach aimed to minimize errors in the estimation of fetal age.

In this study, lung specimens were collected by dissecting the thoracic cage following standard protocol. The dissected lungs were then fixed in 10% formalin for 24-48 hours. Two sections were taken from each lung. Subsequently, the fixed lung tissues were embedded in paraffin. Serial paraffin sections, 5µ thick, were cut for further analysis. The following staining methods were employed in this study for histological examination and characterization of the lung tissues.

In this study, two staining methods were used for the analysis of lung specimens:

Hematoxylin and eosin staining were employed to demonstrate the microscopic structure of the lungs. This staining technique provides detailed information on cellular and tissue morphology, aiding in the examination of lung maturation.

Masson's trichrome staining was used to visualize and assess connective tissue deposition in the developing lung. This staining method specifically highlights collagen and other connective tissue elements, allowing for a comprehensive evaluation of lung development.

All stained sections were examined under a microscope to observe lung maturation, and images were captured for further analysis. The study samples were categorized into 7 groups based on gestational age, and fetuses from each age group were studied to understand the developmental changes at different stages of gestation.

Results

The present study involved a total of 77 fetuses, ranging in gestational age from 12 to 40 weeks. The fetal lungs were grouped based on both gestational age and gender. Out of the total fetuses,

43 were male, and 34 were female (Table-1). The highest number of study samples was observed in fetuses with a gestational age of 21 and 23 weeks, with 5 cases each. On the other hand, there was only one case each in gestational ages 19, 25, 35, and 39 weeks, and no representation in gestational ages 13, 15, 24, 30, and 37 weeks.

The study analyzed various parameters, including head circumference (HC), Bi-parietal diameter (BPD), fetal weight, and crown-rump length (CRL), and their means were observed to increase as gestational age increased, except in cases suspected of intrauterine growth retardation (IUGR) (Table-2).

The study population consisted of 77 pregnant females, with 3 (3.90%) in the first trimester, 44 (57.14%) in the second trimester, and 30 (38.96%) in the third trimester. The age range of the females included in the study was from 20 to 36 years, and their gravidity ranged from 1 to

Among them, there were 41 cases in gravida-1, 20 cases in gravida-2, 13 cases in gravida-3, 2 cases in gravida-4, and one case in gravida-5.

Table -1: Grouping of fetal lungs according to gestational age & gender

Groups	GA in weeks	No of fetuses	Lung specimenslung Male:	specimens Female:
I	12-16	8	05	03
II	17-20	13	08	05
III	21-24	13	08	05
IV	25-28	13	07	06
V	29-32	09	05	04
VI	33-36	14	06	08
VII	37-40	7	4	3
	Total	77	43	34

Table-2: Showing the fetal anthropometric measurements and their mean as per groups

Groups	GA in weeks	Range of birth weight grams	Mean of birth inweight	Range of CRL mm	Mean of inCRL	Range of HC mm	Mean of inHC	Range of BPD in mm	Mean of BPD
I	12-16	22-145	88.94	52-105	73.56	66-132	98.13	18-34	26.5
II	17-20	160.5-370	253.81	94-149.5	129.67	130-183	155.00	32-50	41.08
III	21-24	250-650	463.85	144-196.5	172.73	187-222	201.46	48.5-58	53.36
IV	25-28	414-1210	868.77	191-230.5	214.92	186.2-271	252.63	54-75	68.23
V	29-32	1050-2250	1569.44	258-315	284.13	275-302	287.56	73-82.2	77.23
VI	33-36	1950-3100	2540	284-380	336.20	290-330	317.93	80.5-91	86.54
VII	37-40	2240-3750	3150.71	380-415	407.93	329-350	339.86	87-96.5	91.79

Table-3: Showing the distribution of pregnancies as per gravida

Groups	GA in Weeks	Total Aborted foetuses	Gravida				
			Primi	Gravida- 2	Gravida- 3	Gravida- 4	Gravida- 5
I	12-16	8	3	3	2	0	0
II	17-20	13	9	3	1	0	0
III	21-24	13	9	2	1	0	1
IV	25-28	13	7	3	2	1	0
V	29-32	9	4	1	3	1	0
VI	33-36	14	7	5	2	0	0
VII	37-40	7	2	3	2	0	0
	total-	77	41	20	13	2	1

Table-4: Showing the Distribution of foetuses as per trimester

Stages of Pregnancy	**No Foetuses**
First Trimester	3
Second Trimester	44
Third Trimester	30

The observations in our study are as follows Group I (12-16 weeks of gestational age):
During the gestational age of 12-16 weeks, the lung tissue showed an abundance of mesenchymal tissue. The bronchus was initially lined by pseudostratified ciliated epithelium in the early weeks and later by columnar epithelium with subnuclear vacuoles (Fig: 1a). Additionally, a few blood vessels and cartilaginous plates began to appear during this stage. Smooth muscle fibers were observed around blood vessels and the bronchus. Masson's trichrome stain was utilized to highlight the presence of smooth muscle fibers surrounding the bronchus and blood vessels (Fig: 1b).

Group II (17-20 weeks of gestational age):

During the gestational age of 17-20 weeks, the bronchi were surrounded by mesenchymal tissue. The lining epithelium of the bronchus appeared cuboidal and non-vacuolated. There was an observed increase in branching of the bronchus (Fig: 2a). Additionally, cartilaginous plates were identified in this stage. Masson's trichrome stain effectively highlighted thin collagenous interlobular septae (Fig: 2b).

Group III (21-24 weeks of gestational age):

During the gestational age of 21-24 weeks, there was a notable decrease in mesenchymal tissue. An increasing number of bronchi were observed to be lined by cuboidal non-vacuolated epithelium (Fig: 3a). Furthermore, well-formed cartilaginous plates and blood vessels were clearly highlighted by Masson's trichrome stain (Fig: 3b). This stage of lung development indicates the maturation and formation of key structural elements essential for proper respiratory function.

Group IV (25-28 weeks of gestational age):

During the gestational age of 25-28 weeks, there was a significant decrease in mesenchymal tissue observed around the bronchus. This period showed an increase in complex air spaces with flattened epithelium lining (Fig: 4a), and a few primitive alveoli were present. Smooth muscle fibers around blood vessels were increased, and there was an apparent rise in collagen fibers in the interlobar septae (Fig: 4b). This stage indicates a more advanced lung development, with the establishment of intricate air spaces and structural components essential for proper respiratory function.

Group V (29-32 weeks of gestational age):

During the gestational age of 29-32 weeks, there was almost negligible mesenchymal tissue observed. This stage demonstrated an increase in the number of bronchioles with alveolar ducts and developing alveoli, along with a rich capillary network (Fig: 5a). The bronchus was surrounded by blood vessels, and cartilaginous plates were evident as seen in the Masson's trichrome stain (Fig: 5b). This stage of lung development indicates a significant advancement towards a more mature respiratory system, with a well-developed network of bronchioles and alveolar structures essential for gas exchange.

Group VI (33-36 weeks of gestational age):

During the gestational age of 33-36 weeks, the bronchioles exhibited numerous outpouchings known as saccular crests, which represent primitive alveoli (Fig: 6a). These structures were accompanied by a thin capillary network and smooth muscle. A marked decrease in mesenchymal tissue was noted at this stage, indicating a further advancement in lung development. Well-formed blood vessels surrounded by collagen and smooth muscle were observed (Fig: 6b), along with the presence of cartilaginous plates. This stage signifies the maturation of the respiratory system, with well-developed alveoli and vascular structures essential for gas exchange and proper lung function.

Group VII (36-40 weeks of gestational age)

During the gestational age of 37-40 weeks, the lung parenchyma exhibited marked vascularization. There was a prominent presence of respiratory bronchioles, alveolar ducts, and well-arranged alveoli (Fig: 7a). The lung parenchyma showed well-formed blood vessels with increased smooth muscle and collagen (Fig: 7b), contributing to the establishment of a mature vascular network essential for gas exchange.

In addition to the vascularization, lymphatics and cartilage were observed around the bronchus, indicating a fully developed respiratory system with all necessary components for efficient gas exchange and proper lung function. This stage signifies the final stages of lung maturation, ensuring the fetus is ready for independent breathing after birth.

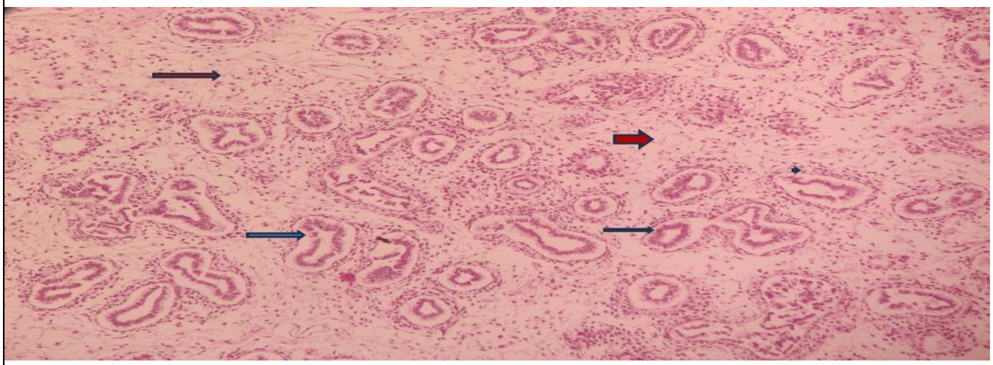

Fig -1a: Lung (14 weeks GA, H&E, x10) Mesenchymal tissue is more (red arrow) and bronchi are lined by columnar epithelium with sub nuclear vacuoles (blue arrow)

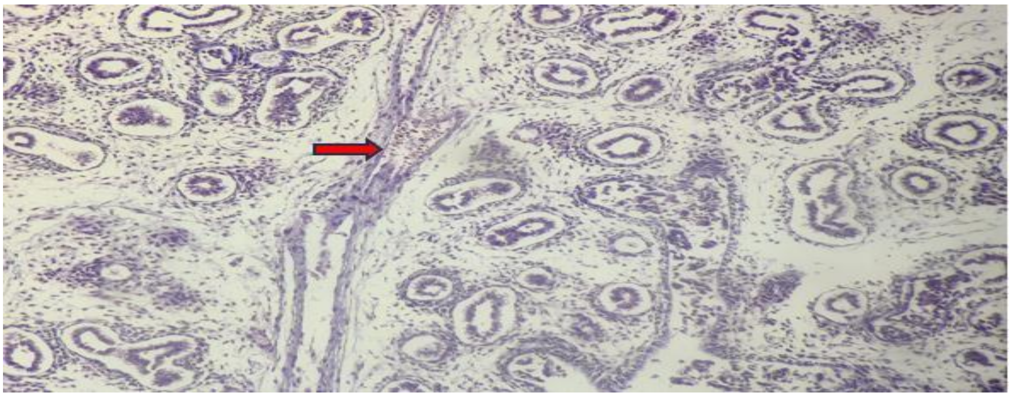

Fig -1b: Lung (14 weeks GA, Masson's trichrome, x10) Masson's trichrome staining highlighting the smooth muscle fibres around blood vessels (red arrow).

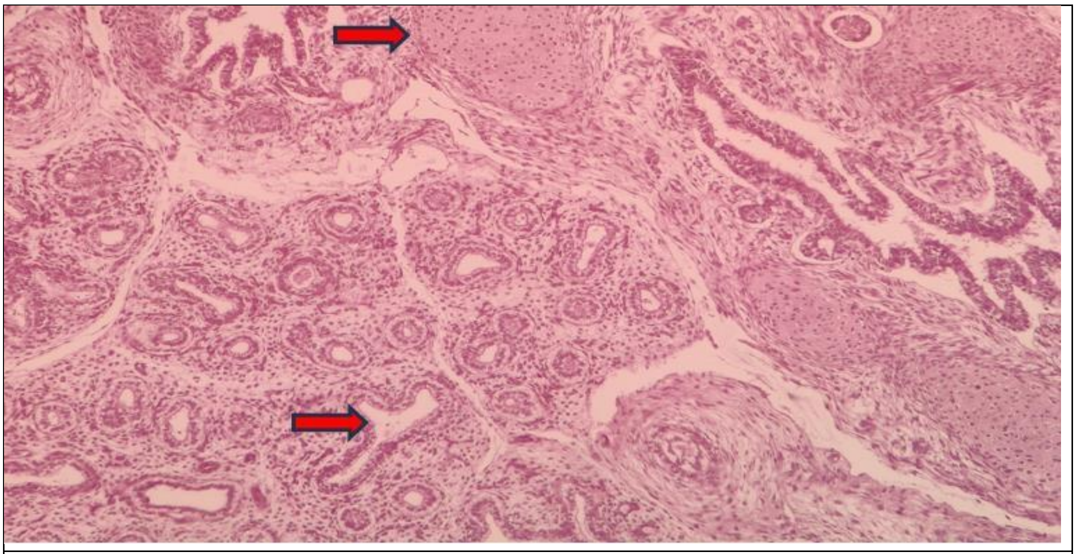

**Fig-2a: Lung (GA:18 weeks, H&E, x10) Bronchi are lined by cuboidal epithelium
with increased branching of bronchi (red arrow) & appearance of cartilage (blue arrow) is seen**

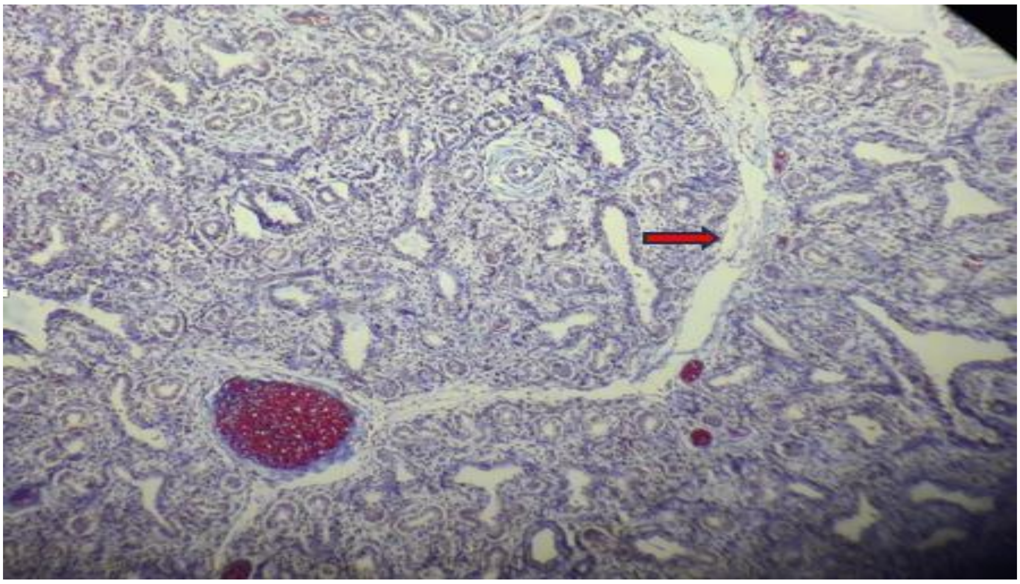

Fig 2b: Lung (GA:18 Weeks, Masson's trichrome, x40) Masson trichrome showing dividing bronchi separated by thin collagenous interlobular septae (red arrow)

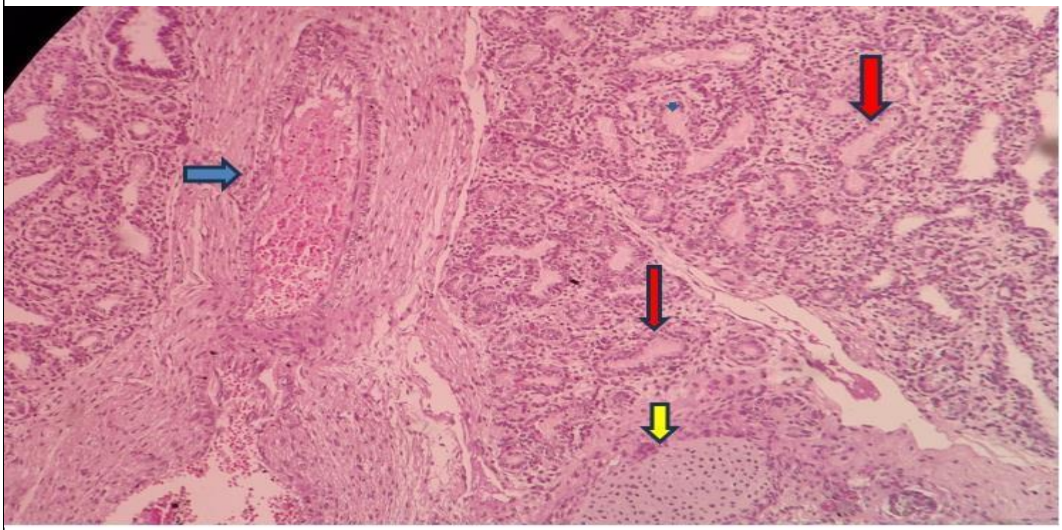

Fig 3a: Lung (GA:21Weeks, H & E, x10) Bronchial tubules lined by cuboidal non-vacuolated epithelium (red arrow) in the mesenchyme along with appearance of blood vessels (blue arrow),
smooth muscle and islands of cartilage (yellow arrow)

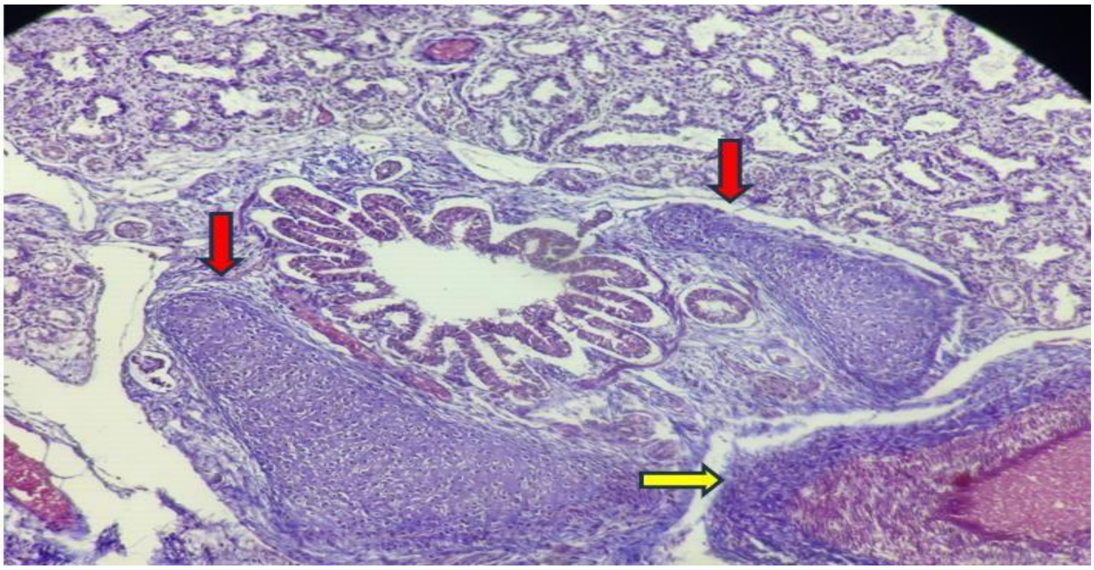

Fig 3b:(GA:21 Weeks, Masson's trichrome .x10): Well-formed cartilaginous plates (red arrow) & blood vessels (yellow)around bronchus surrounded by collagen & smooth muscle fibres.

ISSN: 2037-4445

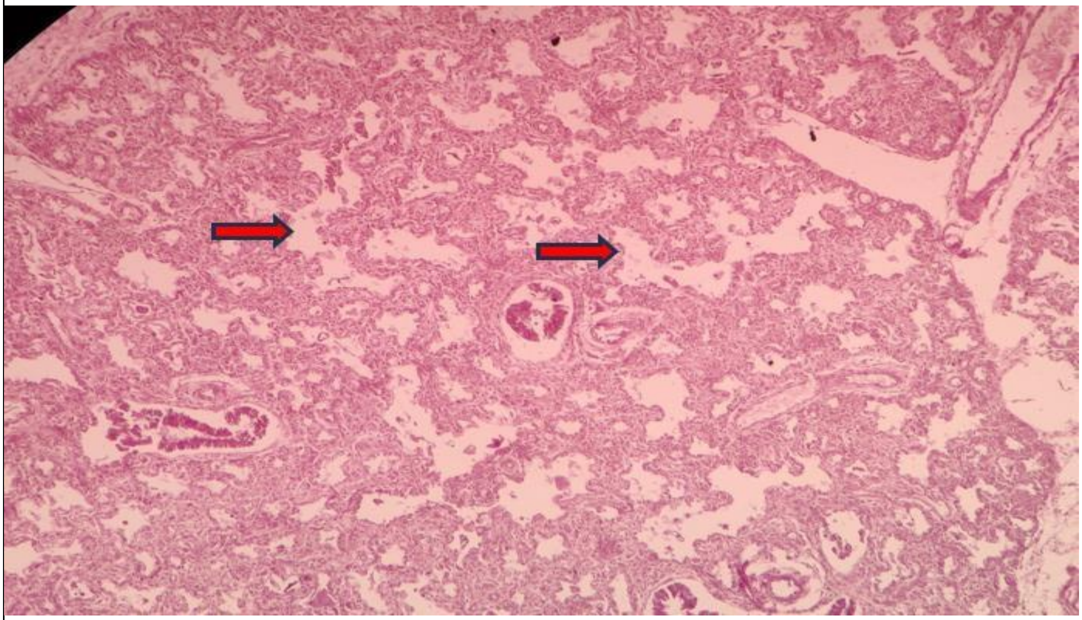

Fig 4a: Lung (GA: 26 Weeks, H & E, x10) Bronchial tubules are lined by flattened epithelium

(red arrow) with appearance of capillary network in decreasing mesenchymal tissue.

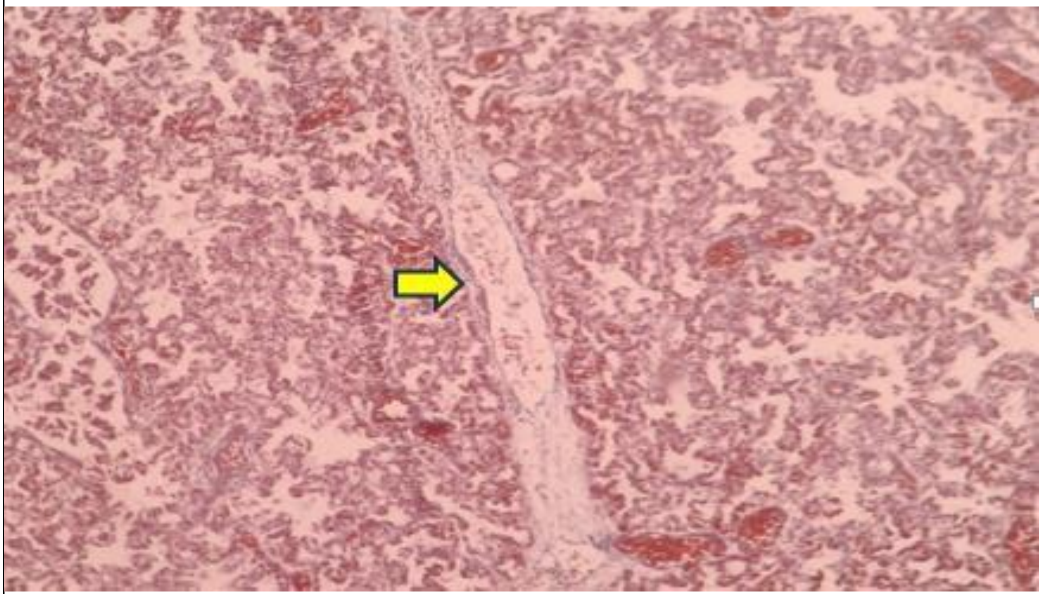

Fig 4b: Lung (GA: 26 Weeks, Masson's trichrome, x10) Masson's trichrome highlights interlobular septae with blood vessels (yellow arrow) and increased collagen fibres.

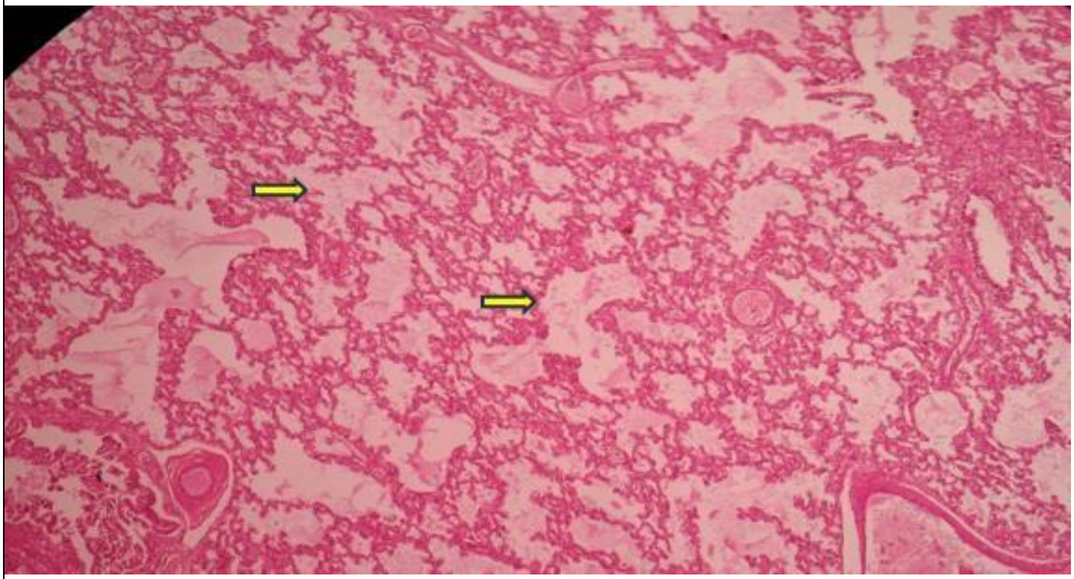

Fig 5a: Lung (GA: 30 Weeks, H &E, x10) Increased respiratory bronchioles with alveolar duct, alveoli in rich capillary network (yellow arrow) & markedly reduced mesenchymal tissue.

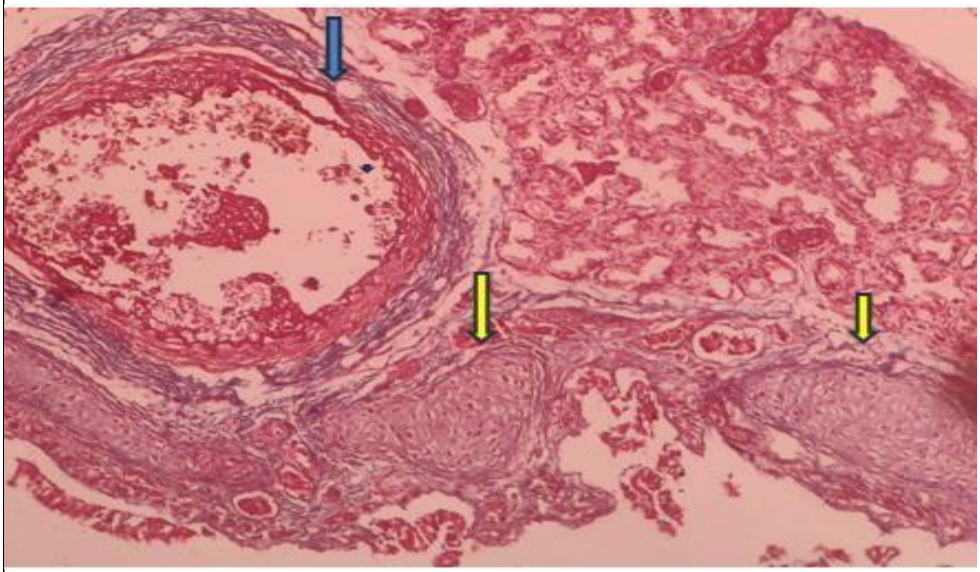

Fig 5b: Lung (GA: 30 Weeks, Masson's trichrome, x10) Masson's trichrome showing bronchus and respiratory bronchioles surrounded by vessels (blue arrow) and cartilage nests (yellow arrow).

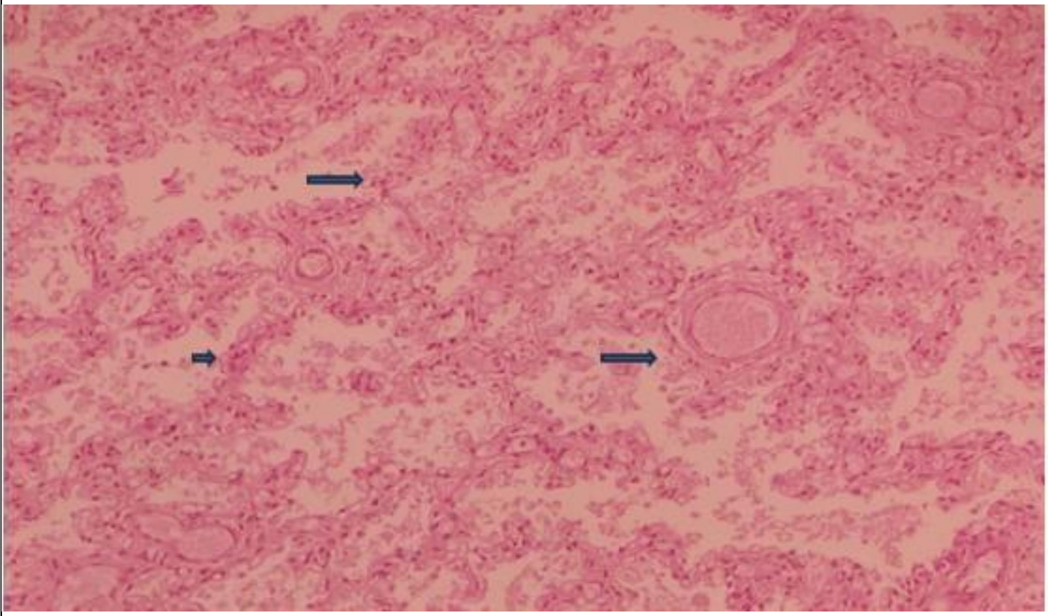

Fig 6a: Lung (GA:35 Weeks, H&E, x10) Alveolar sacs showing saccular outpouchings of alveoli (blue arrow) with increased capillary network

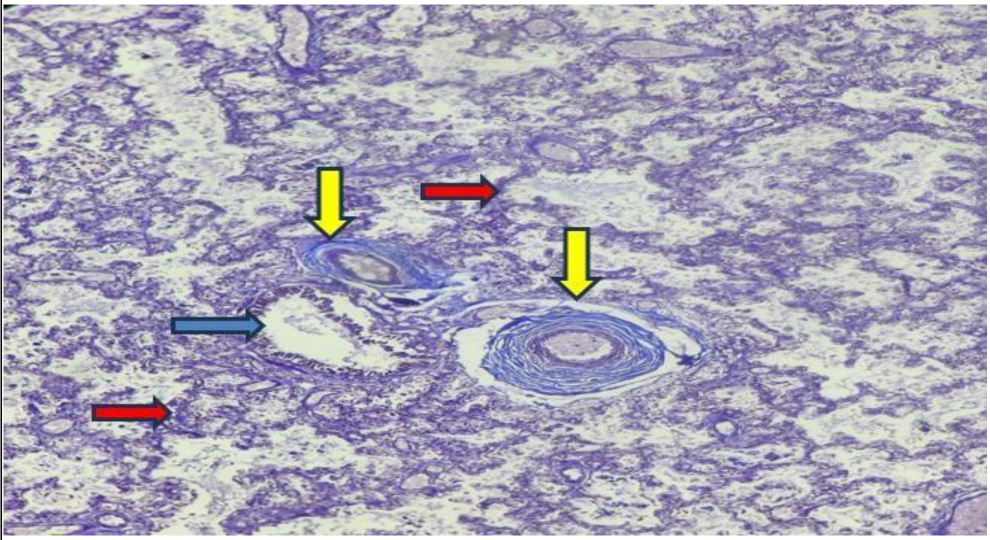

Fig 6b: Lung (GA: 35 Weeks, Masson's trichrome, x10) Masson's trichrome showing bronchi (green arrow) & bronchioles (red arrow) surrounded by smooth muscle &vessels (yellow arrow) surrounded by collagen & smooth muscle.

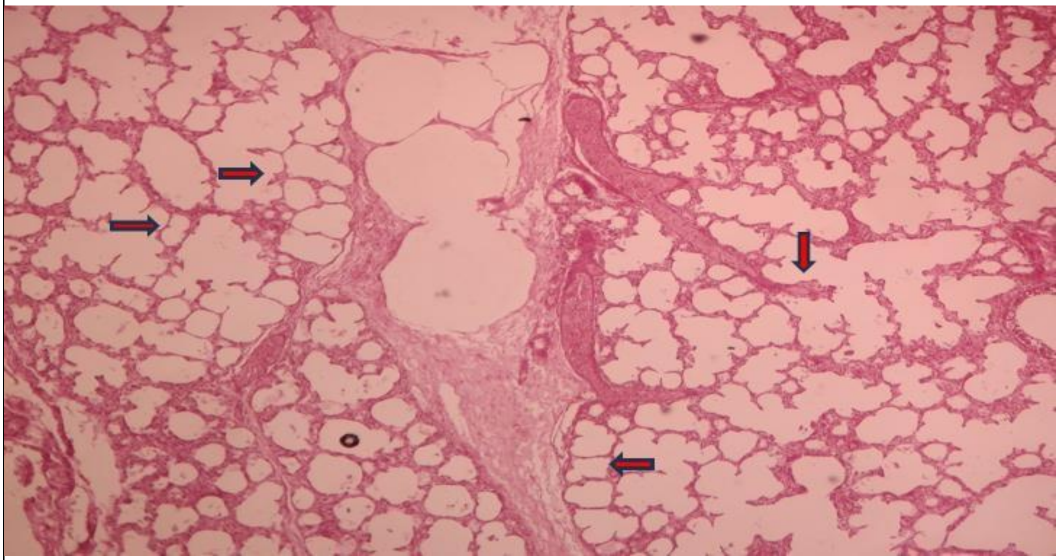

Fig 7a: Lung (GA: 37 Weeks, H &E, x10) Back to back arranged alveoli (red arrow) with single layer of flattened epithelium with increased vascularisation and mesenchymal tissue is completely reduced.

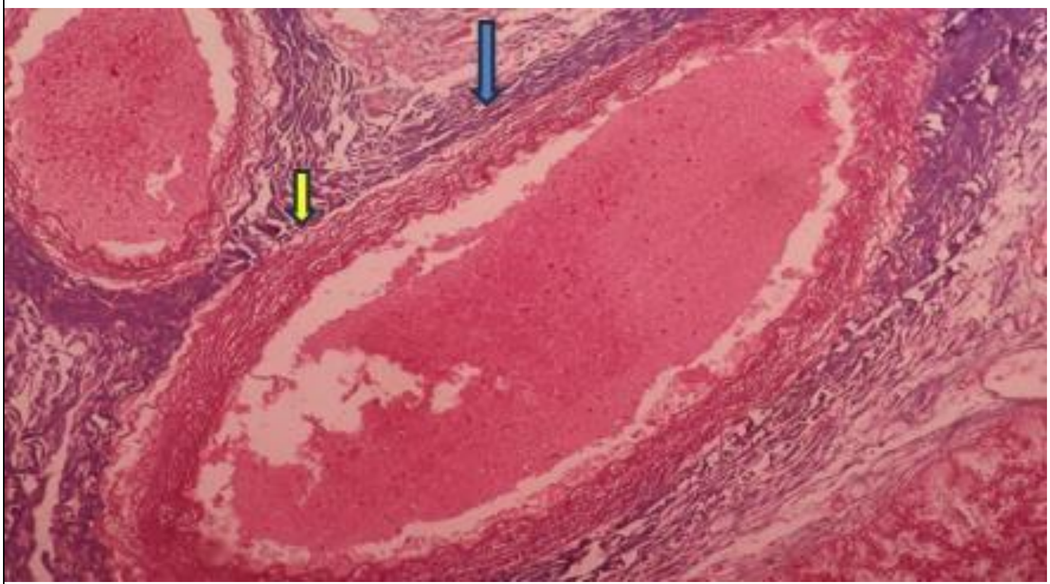

Fig 7b: Lung (GA:37 Weeks, Masson's trichrome, x10) MT stain highlighting the collagen (blue arrow) and smooth muscle (yellow arrow) around the well-formed blood vessel

Discussion

Histogenesis is a crucial series of integrated processes that take place during embryonic development. In this complex phenomenon, undifferentiated cells acquire the specific characteristics of various tissues found in the human body and attain functional maturity. For the lungs, the process of histogenesis is particularly significant as it directly impacts the fetus's ability to survive independently.

In this present study, we categorized fetal lung specimens into seven groups based on their gestational age. By using Hematoxylin and Eosin (H&E) staining, we examined the maturation of lung tissue, enabling us to observe its microscopic structure and cellular development. Additionally, we utilized Masson's trichrome stain to evaluate the connective tissue deposition in the developing lung. This comprehensive approach allows us to gain valuable insights into the developmental progression of the lung, which is crucial for understanding proper lung function and respiratory health.

Mesenchymal tissue:

During the gestational age of 12-16 weeks, the lung parenchyma exhibited a significant amount of mesenchymal tissue. However, as the gestational age progressed, we observed a replacement of the lung parenchyma by an increasing number of bronchi. These bronchi eventually differentiated into alveoli, completely replacing the mesenchymal tissue in the developing lung (ref: 8).

These findings in our study were consistent with the results reported in other studies by Nagajyothi et al (ref: 9) and Jessy et al (ref: 10). Additionally, the mesenchymal tissue surrounding the bronchi showed spindle-shaped nuclei with round to oval vesicles in the periphery, which was in agreement with the findings reported by Tanaka et al (ref: 11).

These correlations with previous studies validate the reliability of our findings and contribute to a better understanding of lung development during different stages of gestation.

Epithelium:

In the present study, during the gestational age of 12-16 weeks, the bronchi were observed to be lined by columnar epithelium with subnuclear vacuoles, which was consistent with the findings reported by Sanjukta et al (ref: 12) and Kate et al (ref: 13). Additionally, pseudostratification of the epithelium was observed at certain locations, in line with the findings reported by Edward et al (ref: 14).

Moving on to the gestational age of 21-24 weeks, the lining epithelium of the bronchi was identified as cuboidal and non-vacuolated, which also correlated with the observations made by Kate et al (ref: 13). At around 25-28 weeks, air spaces within the lung were found to be lined by flattened epithelium.

These correlations with the studies mentioned above help to strengthen and validate the findings of our present study. The similarities in observations across multiple studies contribute to a more comprehensive understanding of lung development during different stages of gestation.

Development of bronchi, bronchioles and alveoli:
In the present study, as the gestation advanced, the lung parenchyma demonstrated a progression of developing bronchi that further differentiated into bronchioles, alveolar ducts, and alveoli. The epithelium of the air spaces also transitioned from columnar with subnuclear vacuolation to cuboidal and eventually to flattened epithelium.

At 12-16 weeks of gestation, the bronchi were surrounded by pre-cartilaginous plates, with very few smooth muscle fibers seen around bronchi and vessels, as highlighted by Masson's trichrome stain, which agreed with the findings reported by Jessy et al (ref: 10). At 17-20 weeks, the bronchioles were lined by columnar to cuboidal epithelium, consistent with the observations made by Nagajyothi et al (ref: 9). After 20 weeks of gestational age, smooth muscle fibers around the bronchus increased along with a few collagen fibers highlighted by Masson's trichrome.

Around 21-24 weeks, the bronchioles were lined by a single layer of cuboidal epithelium, and thin collagen fibers were observed in the interlobar septae along with vessels, correlating with Jessy et al (ref: 10). After 25 weeks, more respiratory bronchioles appeared, similar to Bucher et al (ref: 15).

Around 25-28 weeks, the airways were lined by flattened epithelium, and primitive alveoli were observed, in line with the findings of Keith Moore et al (ref: 16) and Kate et al (ref: 13). Alveolar ducts with alveoli increased from 32 weeks onwards, and a capillary network was evident around 29-32 weeks of gestation, which continued to increase after 32 weeks.

At 36-40 weeks of gestational age, there was marked vascularization of the lung parenchyma, correlating with the findings reported by Nagajyothi et al (ref: 9). These observations provide a comprehensive understanding of lung development during different stages of gestation and are consistent with findings from other studies, reinforcing the reliability and significance of our present study.

Cartilage and smooth muscle:

In our study, we observed cartilaginous plates at around 12-16 weeks of gestational age, in agreement with the findings reported by Bucher and Reid et al (ref: 15) and Edward et al (ref: 14). At this stage, very few smooth muscle fibers were seen around the bronchi, consistent with the observations made by Jessy et al (ref: 10).

After 18 weeks of gestational age, well-formed cartilage was noted in our study. Smooth muscle fibers were observed around bronchial tubules at 21-24 weeks, similar to the findings reported by Jessy et al (ref: 10) and highlighted by Masson's trichrome stain. Furthermore, smooth muscle and collagen content increased around vessels and the bronchus from 23 weeks onwards in our study, as shown by Masson's trichrome staining.

These findings contribute to a better understanding of lung development during different stages of gestation and are consistent with the results reported in previous studies, validating the reliability and significance of our present study.

Glands:

In our study, we observed the appearance of glands surrounding the bronchi at around 21 weeks of gestational age. This finding indicates a developmental milestone in the lung, where glandular structures begin to form and surround the bronchial tubes. The presence of glands is significant as they play a role in producing mucus and other substances that help in maintaining the health of the respiratory system. The development of glands around the bronchi is an essential part of lung maturation and is crucial for proper respiratory function.

Blood vessels and lymphatics:

In our study, we observed a few blood vessels at around 16 weeks of gestational age, which is consistent with the findings reported by Reid and Histop (refs: 18, 19) and Nagajyothi et al (ref: 9). As the gestational age increased, the number of vessels also increased, indicating the progressive development of the vascular network in the lung. Additionally, a few vessels were seen in the interlobular septa in our study, further contributing to the lung's vascularization.

Capillaries began to appear around airspaces at 24-28 weeks in our study, which is similar to the findings reported by Reid and Hislop (refs: 18, 19). By 34-36 weeks, a double capillary layer wall was observed in the walls of alveoli, resembling the findings reported by Nagajyothi et al (ref: 9). Lymphatics were also observed at 24-28 weeks of gestational age, indicating the establishment of a functional lymphatic system in the developing lung.

The use of Masson's trichrome stain in our study highlighted various components, including smooth muscle fibers around vessels and bronchus, cartilaginous plates around bronchi, and collagen fibers around vessels, interlobular septae, and bronchi. These observations provide valuable insights into the development and composition of the lung during different stages of gestation, supporting the findings of previous studies and reinforcing the importance of our present study in understanding lung histogenesis.

Conclusion

The usage of multiple staining methods in the present study allowed us to document appearance and organization lung tissue during development. As the gestational age advances, gradual decrease in the amount of mesenchymal tissue and the height of epithelium
was seen. A better understanding of human fetal lung histogenesis will help the anatomists and the pathologists for studying the histopathological abnormalities. Developmental delay of lung leads to histopathological abnormalities. This information may use full for future research activities in lung transplantation and the clinicians during the clinical procedures and the management of premature infants.

We have also planned to look into the immunohistochemistry (expression of FGF-10; the factor for onset of branching morphogenesis). This may help in the development of targeted therapeutic strategies to combat lung diseases.

Conflicts Of Interest

None

Acknowledgements

We would like to acknowledge Dr. N. Vishali, Associate Professor & Guide and Dr. L. Peter, Professor & HOD for their support, guidance and contribution to complete this study on time. We would also special thanks to give special thanks to Dr. B. Swapna Kumari for histopathological analysis. We would like to thank Dr. G. Ramulu, associate professor for helping in analysis of results and write up of dissertation and publications. We also sincerely thank the HOD of the department of obstetrics and gynecology for allowing to collect fetuses and relevant data as required and those who donated their fetuses.

References

1. Shah P, Johnson D, Standring S. Thorax. In: Standring S, editor. Gray's Anatomy: The Anato mical Basis of Clinical Practice. 39th ed. Edinburgh: Churchill Livingstone;2005. p. 1068-10 69.
2. Rosse C, Gaddum-Rosse P. Hollinshead's textbook of anatomy. Philadelphia: Lipincott Willia ms & Wilkins;1997. p. 441-461.
3. Sharma G, Vijayvergiya T. Anatomical variations in lobar pattern of the lungs: anatomical study and clinical significance. J Pharm Biomed Sci. 2013; 26:301-303.
4. Agorastos T, Vlassis G, Zournatzi B, Papaloukas A. Fetal lung maturity and skin maturity: 2 distinct concepts and the clinical significance of their differences. Z Geburtshilfe Perinatol. 1983;187(3):146-50
5. Langman’s medical embryology. — 12th ed. / T.W. Sadler. Chapter 14;page no 201-207.
6. Swarr DT, Morrisey EE. Lung endoderm morphogenesis: gasping for form and function. Annu Rev Cell Dev Biol. 2015; 31:553-73. doi: 10.1146/annurev-cellbio-100814-125249.
7. Burri, P.H.(1997) Structural aspects of prenatal and postnatal development and growth of the lung. In McDonald, J.A.(ed.), Lung Growth and Development. Marcel Dekker, New York,p 1
8. Baskerville A. Histological and ultrastructural observations on the development of the lung of the fetal pig. Acta Anat (Basel). 1976;95(2):218-33. doi: 10.1159/000144615
9. D. Nagajyothi, Gayathri Pandurangam, K. Kshitija, S. Saritha. Histogenesis Research of Lung in Human Foetuses In Different Weeks of Gestation A Light Microscopic Study. Int J Acad Med Pharm 2022; 4 (5); 690-695
10. Jessy J P, Kanchan Kapoor, Mahesh K Sharma. Histogenesis Of Human Lung - Retrospective Fetal Autopsy Study. Int J Anat Res 2019, Vol 7(1.2):6211-19. ISSN 2321-

4287

11. Tanaka O, Oki M, Shimatsu A. Histogenetic study on fetal lungs. Shimane J. Med. Sci 1980; 4:81-90.

12. Sanjukta Sahoo, Arpan Haldar et al. Histogenesis of Lung in human fetuses at different weeks of gestation in eastern India. International Journal of Medical and Health Research ISSN: 2454- 9142.Volume 4; Issue 7; July 2018.

13. Dr.Deepali.R.Kate, Dr.Sudhir.M.Sant. Histogenesis of Human Foetal Lung: A Light Microscopic Study. (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 9, Issue 2 (Jul. - Aug. 2013), PP 01-08.

14. Edward Edward L, Charmock Carl Doershuk,et al.Developmental aspects of human lung,paediatric clinics of North America.1973;20:275-292.

15. U.Bucher and L.ReidBucher.U and Lynne Reid.,Development of Intra segmental Bronchial Tree-The pattern of branching and Development of Cartilage at various stages of Intrauterine Life, Thorax,1961, 16: 207-218

16. Keith Moore, T. Persaud.1998, Developing Human in Development of Bronchi and Lungs6th edn, W.B Saunders Co. 262-266

17. Charnock EI, Doershuk CF. Developmental aspects of Human Lung. Pediat Clin N Am. 1973; 20:275-292

18. Hislop A, Reid L. Intra-pulmonary arterial development during fetal life-branching pattern and structure. J Anat. 1972;113(Pt 1):35-48.

19. Hislop A, Reid L. Fetal and childhood development of the intrapulmonary veins in man- branching pattern and structure. Thorax. 1973;28(3):313-9. doi: 10.1136/thx.28.3.313.