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Original Research Article

Fetal Dissection of Human Lungs Morphological Analysis.

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Abstract:

Background: The vital components of breathing are the lungs. They take up the majority of the thoracic cavity and are located on either side of the heart and other mediastinal structures. Except for where it is linked to the mediastinum at the hilum and pulmonary ligament, each lung is free within its pleural cavity. A fresh normal lung that has been removed from the thorax is spongy, may float in water, and crepitates when handled due to the air in its alveoli. Additionally, it is quite elastic, thus when taken out of the thorax, it retracts. The locations of contact between its most periphery lobules and the pleural surface are indicated by thin, black lines that cut through its smooth, shining surface to form numerous small polyhedral domains. As a result, the current study offers extensive information about the morphological features of typical fetal and fetal lung development as well as the histogenesis of the fetal lung in the general population. In relation to body size, men's lungs are heavier than women's, while boys' lungs are larger than those of females. Air volume, pulmonary tissue volume, and lung volume all rise linearly with body length. A rare fetal anomaly known as pulmonary agenesis, which is linked to congenital heart disease, causes the absence of pulmonary arteries, bronchi, and lung parenchyma.

Aim: Fetal dissection of human lungs morphological analysis. To establish standard reference morphometric data for developing human fetus as well as fetal lungs. Gaining a more substantive insight into the normal events and characteristics of human prenatal development.

Material And Method: This study was carried out in the Department of Surgery of Civil Hospital with the proper approval of the ethics committee, the medical director, and the department head. The abortus/fetus used in this study were gathered from the Department of Obstetrics and Gynecology. 40 fetuses between the ages of 14 and 40 weeks were gathered. For the benefit of the parents and close relatives, the consent form was written in both Hindi and English. Once we receive information from sister-in-charge of labor room about availability of fetus, we immediately rushed to the labor room.

Results: the mean fetal weight and means of weight of right and left lungs as per the group distribution. It was observed from the data that the rate of increase in weight of the lungs were similar to the increase in the body weight for the initial weeks of development. But during the last weeks of gestation i.e., 33 – 40 weeks, the increase in weight of lungs slows down as compared to the fetal weight increase. It is observed that increase in the width of both of the lungs is suddenly increased during the gestational age of 33 – 40 weeks. The width of both of the lungs is almost double for the group for as compared to group 3. Similar pattern was also observed in other parameters like thickness as well as circumference of right and left lungs.

Conclusion: It was concluded that in the present study that fetal weight in the population is lower than the same from Nepal as well as Eastern India. Up to second trimester end, the Gujarati fetuses were found to be heavier than the American fetuses. At terms, the Dennis, the Australian and the Gujarati fetuses were comparable in weight. In the last trimester, fetuses of Gujarati population weigh lighter than the same from the French.

Keywords: Fetal Weight, Gestational Week, Crown-Rump Length, Crown-Heel Length Occipito-Frontal Diameter.

Introduction

Lungs are the respiratory organs of the human body. [1] To complete the essential task of air exchange, lungs are equipped with an extensive airway system and a large inner surface. The functional lungs are comprised of a tree of tubes conducting the air for the gas exchange, a large, blood vessel rich surface area for the effective gas exchange and a surfactant system to maintain the stability of the inflation system. [2] The embryological development of the lungs has been studied in as detailed fashion as the other larger organs of the body. [3]

As the lungs are developing, the airway tubes are formed first which is followed by the development of air exchange surface. The alveoli formation continues until adulthood.2 Lungs develop in the form of a diverticulum from the foregut during 3 – 4 weeks of gestational age. [4] As lungs are having a dual origin, the parts of the lungs originating from foregut diverticulum like larynx, trachea, bronchi, bronchioles and part of respiratory bronchioles are found to be lined with cuboidal epithelium, whereas the remaining part of respiratory bronchioles, alveolar ducts, sacs and alveoli arise from the mesenchyme present adjacently. [5]

The acquired developmental abnormalities occurring during pregnancy are the primary cause of congenital lung disorders. Some of the frequent developmental anomalies include agenesis, accessory lung, ectopic lung, persistence of fetal lobulation, and congenital lung cysts. Different stages of the vascular and morphological formation of the human lung are closely related to many physical, environmental, and biological elements in a complex yet intimate way. In antenatal diagnosis and interventional therapy for life-threatening congenital disorders including congenital diaphragmatic hernia and pulmonary hypoplasia, the expanding understanding of lung development will be helpful. [6] Understanding the stages of lung development might help explain the lung issues suffered by premature newborns whose lungs were still in the embryonic stage when they were born. Human in vitro experimental systems will be improved with a better understanding of how the human lung normally develops. [7] During the embryonic development of a baby, there is a series of interrelated processes that are taking place which involves formation of specialized, differentiated tissue from undifferentiated cells. This process is known as histogenesis. Lung histogenesis is a crucial process since it affects the fetus' ability to survive on its own. Despite extensive research and illustrations on human lung formation, the majority of papers only cover a few areas of histogenesis. The care of premature newborns is anticipated to benefit from knowledge of the prenatal developmental morphology and histology of the human lung. [8]

Between the conclusion of the fourth month and the start of the fifth month, the mesenchyme near the epithelium began to proliferate with capillaries. After that, at the seventh month, the capillaries started to penetrate the closest section of the terminal buds and were thus directly exposed to the air gaps. The proximal portion of the terminal buds had mesenchymal condensation and uneven epithelial organization. [9] The alveolar wall was found to be resembling the adults at the age of 36 week in terms of its thinning. The pre-acinar branching pattern of both conventional and supernumerary arteries was found to be completed by half-way through fetal life and corresponds with the bronchial branching pattern. Later changes in the arteries were in dimension and wall structure. The wall structure of the proximal vessels was established by 19 weeks' gestation and was the same as in the adult, though the arteries were smaller. The wall thickness was found to be greater during fetal life than in the adult or child but muscle extends to vessels of the same size as in the adult. [10]

This study was conceptualized to study the various embryonic developmental stages of human lungs and establish the correlation of the same with the gestational age at the same time to study the histogenesis of the human lung in the Indian population.

Material and Methods

This study was carried out in the Department of Surgery of Civil Hospital with the proper approval of the ethics committee, the medical director, and the department head.

Sample selection:

40 fetuses at gestational age from 14 to 40 weeks were collected. Specimens will be selected on the basis of the inclusion and exclusion criteria mentioned below.

Inclusion criteria:

- 14-40 weeks of gestational age
- Normal obstetric history
- Clinical history available
- Free from observable and detectable abnormalities.
- Patients willing to participate in study (parents have to fill consent form which is available in Hindi & English language.

Exclusion criteria:

- Aborted fetuses below the gestational age of 14 weeks
- Fetus with any observable and detectable congenital anomalies
- Clinical history not available
- Formalin fixation before examination
- Hydrops fetalis
- Known abnormal karyotype or any other genetic disease
- Macerated fetuses
- Presence of congenital malformation
- Maternal or fetal infection
- Multiple pregnancies
- Patients not willing to participate in the study

Type of study: Comparative study

Consent:

Consent form was prepared in two different languages (Hindi and English) for better understanding of the parents and near relatives. Once we receive information from sister-in-charge of labor room about availability of fetus, we immediately rushed to the labor room. We have team of 3 people including principle researcher, secondary researcher and one laboratory technician trained in histopathology lab who is aware about handling of freshly received specimen.

Primary handling of the Specimen:

Fetus collected in sterilized container after cutting umbilical cord. Placenta was not the part of study, so we had not collected placenta. Fetus collected from the labor room were brought to department of Anatomy and immediately washed in to tap water. After washing plastic coin with

embossed number, had been attached to the specimen. Each specimen has been provided with unique ID

Instruments/Equipment required for study:

Special instruments must be used when performing a perinatal autopsy, because of the small size of the fetus. Ophthalmic instruments are excellent for these small dissections.

- Charts providing normal weights and measurements for newborns and still borns
- Sterile and nonsterile syringes and needles (multiple sizes)
- Sterile packs including scissors and forceps (tooth forceps, blunt forceps) for cultures and karyotype
- Stout scissors for cutting bone
- Small scissors with at least one sharp point (one)

Prenatal (USG) and Postnatal findings:

The gestational age was estimated by measuring Crown Rump Length (CRL) and referring to the chart given in the text book of Human Embryology by Boyd, Hamilton and Mossmann.11

Microscopic examination:

Routine microscopic exam is an important part of the autopsy, particularly in well-preserved fetuses. The lungs were procured and were processed for histological examination with hematoxylin and eosin stain.12

Result

The total number of non-macerated cases studied was 40. Total 90 families were identified and asked for consent, out of which 30 families were refused permission for an autopsy.

Table 1: Group wise mean of FW, CRL, CHL and HC

GROUP	FW in gm	CRL in mm	CHL in mm	HC in mm
1	142.3	128	195.31	141.11
2	402.74	200.33	298.64	201.53
3	1021.22	223	342.4	252.12
4	2356.42	231.44	396.82	310.44

All the samples were divided into four groups as mentioned previously as group 1, 2, 3 and 4 which comprised of fetuses of the gestational ages between 14 – 18, 19 – 26, 27 – 32 and 33 – 40 weeks respectively.

Table 2: Group wise fetal weight and fetal lung weight

Group	Age of fetus	Mean FW	Mean RL weight	Mean LL weight
1	14 – 18 weeks	138.2	1.4	1.9
2	19 – 26 weeks	497.82	4.32	4.05
3	27 – 32 weeks	1042.23	10.54	10.33
4	33 – 40 weeks	2365.52	17.74	14.3

Table 2 shows the mean fetal weight and means of weight of right and left lungs as per the group distribution. It was observed from the data that the rate of increase in weight of the lungs were similar to the increase in the body weight for the initial weeks of development. But during the last weeks of gestation i.e., 33 – 40 weeks, the increase in weight of lungs slows down as compared to the fetal weight increase.

Table 3: Group wise right fetal lung parameters

Group	Mean RL weight	Mean RL Length	Mean RL width	Mean RL thickness	Mean RL circumference
1	1.4	13.24	7.29	7.79	40.73
2	3.32	22.15	13.20	20.48	54.11
3	10.32	38.14	16.66	29.01	83.66
4	11.74	69.58	38.21	53.01	121.11

Table 4: Group wise left fetal lung parameters

Group	Mean LL weight	Mean LL Length	Mean LL width	Mean LL thickness	Mean LL circumference
1	1.50	12.65	7.54	10.61	35.22
2	4.09	20.56	13.02	12.11	59.61
3	8.44	33.41	11.34	26.22	77.82
4	13.5	64.25	37.18	62.03	155.42

Table no 3 and 4 show various morphological parameters of both of the lungs individually. It is observed that increase in the width of both of the lungs is suddenly increased during the gestational age of 33 – 40 weeks. The width of both of the lungs is almost double for the group for as compared to group 3. Similar pattern was also observed in other parameters like thickness as well as circumference of right and left lungs.

Discussion

A total of 40 fetuses of gestational age ranging from 14 – 40 weeks were studied in the present study. Various morphological features of fetus like fetal weight, crown to heel length (CHL), crown to rump length (CRL) and head circumference (HC) were studied. The morphological features of both right and left lung like lung weight, length, thickness and circumference at base were also studied.

The mean CRL of the fetuses of the gestational age between 33 – 40 weeks in present study was found to be slightly lower than same from Australia, Denmark and France, whereas Cussen L 1990 [13] (Australia) recorded the CRL in similar age group to be slighter lower than the present study. The mean CHL of the fetuses of the age group of 14 – 18, 19 – 26 and 27 - 32weeks in present study was observed to be higher than all the previous researchers. In the fetuses of 33 – 40 weeks of age, the CHL in present study was seen to be found to be lower than the previous researcher except the results of Cussen L 1990 [13] who recorded the CHL in the same age group to be lower. The mean HC of the fetuses of gestational age of 14 – 18 and 33 – 40 weeks in present study was observed to be higher than the same from previous all researchers. The HC in the age group between 19 – 27 weeks in present study was higher than all the previous workers except Cussen L 1990 [13] who recorded the same parameter to be lower than the present study.

Hansen K 2003 [14] studied fetal lung weight of fetuses of 14 – 18 and 19 – 26 weeks of gestational age. The lungs of fetuses of 14 – 18 weeks of age of American population weighed lower than the lungs of the fetuses of the similar age group from the Gujarati population but as the age advanced the weight of the lungs of the fetuses of 19 – 26 weeks of age in American population were seen to be weighing more than those of the Gujarati population.

In the fetuses of 14 – 18 weeks of gestational age, we reported the light microscopic appearance of the fetal lung to be similar to an exocrine gland. Similar

findings were also reported by AK Dutta 2005 [15]. Kate DR et al 2013 [8] observed the epithelial linings of the proximal bronchi to be of pseudostratified columnar variety which was not observed in the present study. They also observed the appearance of cuboidal and low columnar epithelium lining the developing bronchial tubes which was in agreement with the findings of the present study.

De Paepe et al 2014 [16] undertook study of human fetal lung in two sets of samples from population of Rhode Island. Only in one study, the fetuses were found to have lower lung weight as compared to present study. Rest all the samples of all the age group were seen to be having larger lung weight as compared to the present study.

Kate DR et al 2013 [8] noted the same epithelial lining to be present at the age of 16 weeks. The fetuses of this groups also showed presence of respiratory bronchioles already formed in the present study, also the presence of developing air saccules lined by the squamous cells was observed too. This finding was in agreement with the stages reported by Schittny JC 2017 [2] and Mastumoto S 1957 [17] who also noted the present of branching in the intrapulmonary bronchial tree. Mantraratnam PP 2012 [18] reported the presence of respiratory bronchioles in the fetuses of 24 weeks which we observed in the fetuses 25 weeks of gestational age. The presence of the primitive alveoli and developing air saccules were also reported by Kate DR [8] and Mantraratnam PP et al 1957 [17] which was in agreement with the observations of the present study. Schittny JC 2017 [2] quoted the differentiation of the epithelial lining cells in to type I and type II pneumocytes established in the fetus of the same age group which was differing from the results of the present study as we didn't find the appreciable differentiation in the pneumocytes.

Naik SK et al 2014 [3] also reported the bulging of the developing alveolar wall due to budding blood vessels in the fetuses of the age of 30 weeks which is comparable with the findings of the present study. Mastumoto S 2012 [18] also observed the dilation of alveoli in the fetuses of eight months of age which in agreement with the present study where observed the further development of the alveolar structures. Mantraratnam PP et al 1957 [17] reported the presence of squamous and cuboidal lining epithelium in the developing alveoli which was in agreement with the findings of the present study. Mantraratnam PP et al 1957 [17] also reported the epithelial lining alveoli to be of simple squamous variety which again was in agreement with the observation of the present study. [19]

Conclusion

It was concluded that in the present study that fetal weight in the population is lower than the same from Nepal as well as Eastern India. Up to second trimester end, the Gujarati fetuses were found to be heavier than the American fetuses. At terms, the Dennis, the Australian and the Gujarati fetuses were comparable in weight. In the last trimester, fetuses of Gujarati population weigh lighter than the same from the French. The present study provides the first of its kind Indian data for the morphometric analysis of the developing lung. These data can be used as a reference standard for the developing lung in obstetric practice to refer the lung development. These data of the normal growth pattern of human fetal lung and its dimensions will also be useful as to provide a subtle background for future autopsy and other related studies.

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