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The Correlation of the Aborted Human Foetal Lung to Body Weight Ratio in Relation with the Gestational Age

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KEYWORDS
Gestational Age; Human Foetuses; Lung Weight; Foetal Weight; fetal lung to birth weight ratio

ABSTRACT:
Respiratory system is made up of specialized cells and tissues that play a vital role in the gas exchange and the development of lung is a very significant as it influences the independent viability of the fetus .There are only few studies on the growth of human lung in relation with fetal body weight. In this study we have assessed the Correlation of the aborted human foetal lung to body weight ratio in relation with the gestational age.This study involved 77 human aborted normal fetuses collected from the OBG (Obstetrics & Gynaecology) department of KAMS&RC, Hyderabad, Telangana after institutional ethical committee [IEC]approval and informed consent.The weight of the fetal lung and fetuses was measured in grams on digital weighing machine. The range ,mean values of all parameters by gestational age [GA]was calculated and analyzed. The data was represented graphically by using appropriate statistical analysis. The data suggest a steady increase in lung weights[LW] with advancing gestational age from 12th week to 40th weeks of gestation. The close similarity between the right and left lung growth rates implies symmetrical lung development.The weight of left lung was seen less than the weight of right lung throughout the gestational weeks.The results in this study indicate a statistically significant decrease in the fetal lung to birth weight ratio [LW/BW]as gestation progresses from 12th week (0.0945) to 40th week (0.0155).The findings could be used as reference values for normal lung development. Deviations from these trends could indicate potential growth anomalies, which may necessitate further medical evaluation

Introduction

Lungs made up of specialized cells that play a vital role in the gas exchange and the development of lung influences the independent viability of the fetus.[1]Lung development and growth is a complex , significant and intricate process with a host of regulatory factors. During the fourth week of pregnancy, the respiratory system development begins from the ventral foregut

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endoderm as respiratory diverticulum .The respiratory system has a dual origin, i.e. from endoderm and mesoderm.[2,3]Based mainly on histological criteria the lung maturation events are divided into four stages; the pseudo-glandular, canalicular, terminal sac, and alveolar stages .[2,4]The lung development defects affecting the structure and function of the lung can have fatal consequences.[5]

The lungs occupy the thoracic cavity on either side of mediastinum.[1]The right and left lung anatomy are similar but asymmetrical as both lungs do not have an identical lobular structure .The right lung by its oblique and horizontal fissures is divided into three lobes (superior, middle and inferior lobes).[6] The left lung by its oblique fissure is divided into two lobes (superior and inferior lobes).[6] The adult right lung weighs 625 gms and left lung weighs 50-100 gms lesser or approximately 525 gms.[7]In proportion to body stature, the lungs are heavier in men than in women, and boys have bigger lungs than girls(Thurlbeck 1982).[8] Most of previous studies on growth of fetal lung were done in animals but less on humans .Hence the present study was done to find out the Correlation of the foetal lung to fetal body weight [LW/BW]ratio in relation with the different gestational age in human aborted fetuses.

Materials and Methods

This is a cross sectional observational study involved 77 human aborted fetuses collected from the department of anatomy at Kamineni Academy of Medical Sciences & Research Centre (KAMS&RC) ,LB Nagar , Hyderabad, T.S after obtaining approval from the Institutional Ethical Committee [IEC] ,KAMS&RC to conduct autopsies and further process of autopsies tissues as per the study requirements **[IEC:EC/NEW/INST/2021/1676,Dated:22/03/2022]**T he study was carried out over a period of 18 months [March 2022 to August-2023].The study included aborted normal fetuses with a gestational age (GA) between 12 to 40 weeks.

Fetuses for the present study collected after inevitable/spontaneous abortions or stillbirth, or medical termination of pregnancy (MTP) for contraception failure/unwanted pregnancy. Prior to participation, informed consent was taken from the patient, husband/parents or legal guardians if the patent is a minor.Macerated fetuses and congenital anomalous fetuses are excluded from the study.

At the time of collection of aborted fetal specimen from labour room , parameters related to obstetric history, mother and fetus has been recorded in data collection form. Fetus collected from the labor room were brought to department of Anatomy and immediately washed with tap water. After applying identity tag with unique ID(e.g. S-001,First character says 'Specimen', next three characters for numbering of the specimen) complete external examination of the specimen was done in adequate light source the demographic parameters of fetuses (like as gender, gestational age ,weight and other anthropometric measurements).All the morphometric measurements were recorded in millimeters to the nearest 0.01 decimal by using standard metric rulers, tapes ,calipers and by nylon thread as per autopsy protocol .Fetal Weight in grams was recorded with the help of electronic weighing machine. [Figure 1a]

The fetuses were well preserved in 10% formalin and a thorough examination was conducted to identify any gross congenital malformations. The duration of amenorrhoea and ultrasound fetometry were collected from medical records. To estimate fetal age accurately, different fetal parameters such as CRL, BPD, and ultrasound data, were used, along with the LMP (last menstrual period) of the mother.

Abdomino-thoracic wall was opened by Y-shaped incision .By using midline sternotomy the thorax was opened.The ribs were cut from midaxillary line and removed to expose whole thoracic cavity[Figure-1b and 1c] .In this study, after opening rib cage the lungs were dissected out along with heart according stranded autopsy procedure [Figure-1d] . The dissected lungs were then fixed in 10% neutral buffered formalin for 24-48 hours after measuring lung weight by electronic weighing machine [figure 2a & 2b]. All the statistical analysis is done in Python 3.11.4 version and for simple and multiple linear regression scikit-learn version 1.3.0 are used.

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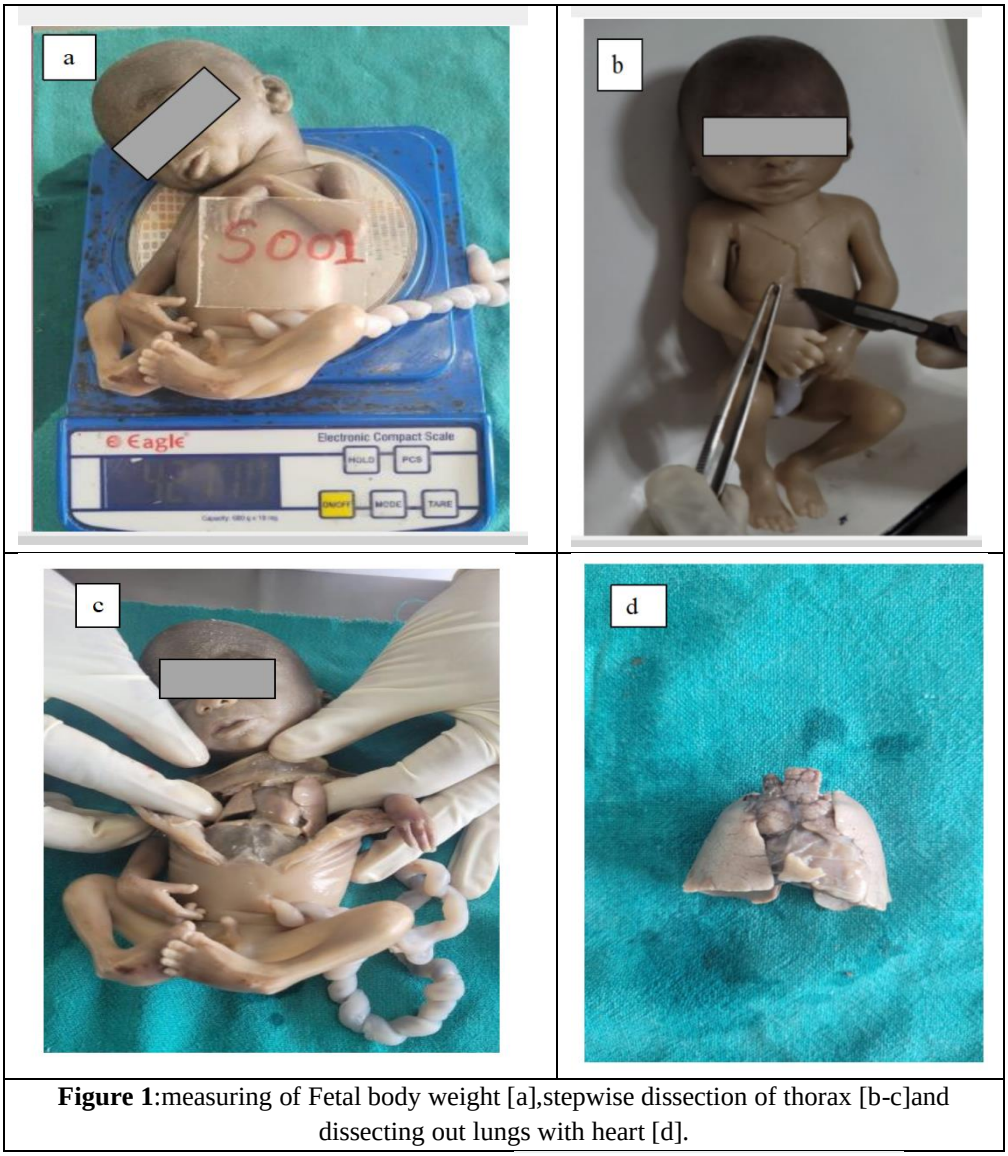

Figure 1:measuring of Fetal body weight [a],stepwise dissection of thorax [b-c]and dissecting out lungs with heart [d].

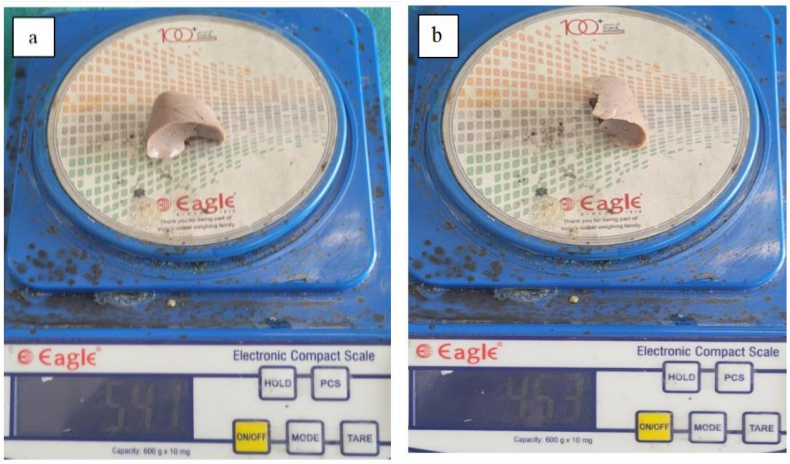

Figure 2: Measuring the weight of right lung [a] and left lung[b].

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Results:

Total 90 families were identified and asked for consent, out of which 13 families were refused permission for an autopsy. The present study compromised of seventy seven (77) aborted normal fetuses, ranging in gestational age from 12 to 40 weeks on the basis of the inclusion and exclusion criteria. Even though our sample size is less, we had representation from all the fetal ages except 13, 15, 24, 30 and 37 weeks. Out of the 77 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. Regarding fetal gender distribution, males were slightly predominant, accounting for 55.84% of the sample, whereas females represented 44.16%.The fetuses were grouped into seven groups based on gestational age.

Comorbidities

In the assessment of maternal health within our cohort, a notable proportion of participants (27) did not report any Comorbidities, indicating a significant segment of mothers with no underlying health conditions during their pregnancy.However, for those who did present with health concerns, the most prevalent Comorbidities were Anemia, found in 6 mothers, followed by Hyperemesis Gravidarum in 3 mothers. Additionally, Hypothyroidism and Scar Rupture were each identified in 2 participants. Beyond these primary health conditions, the study also highlighted the presence of several other Comorbidities, albeit in fewer numbers, such as pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM), and more.The above Comorbidities are according to data collected from the department of obstetrics and gynecology in the present study [Figure 3]

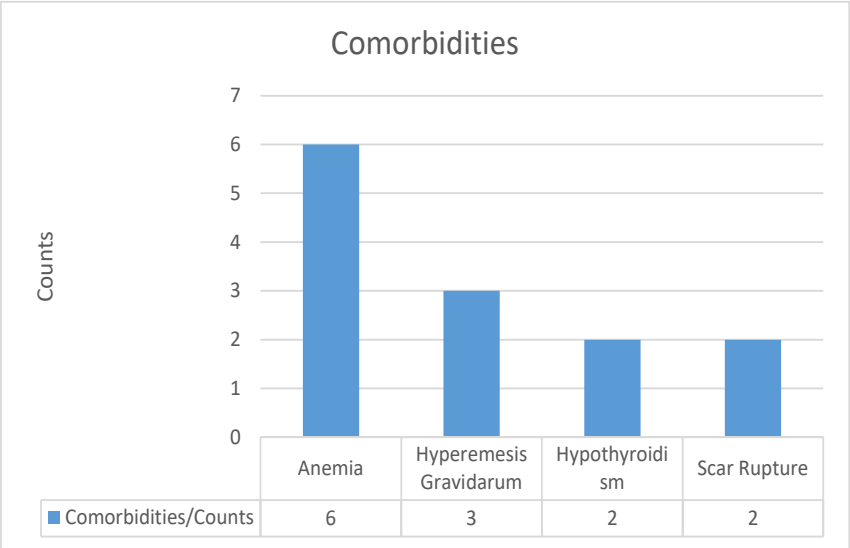

Figure 3:Bar diagram showing distribution of Comorbidities among study group

The results of mean fetal body weight, fetal lung weights (right &left) and ratio of fetal lung & body weight as per gestational week from 12th to 40th week is shown in [Table-1]. In the present study the body weight of foetuses showed gradual increase from 12th week to 40th week of gestation. The range of fetal weight in the study extended from a mere 22.0 grams to 3750.0 grams. Column chart showing mean weight of right and left lung in gram against gestational age in weeks is shown in [Fig-4].We also noticed that average birth weights of fetuses born to mothers with severe anaemia were significantly associated with low birth weight compare to normal hemoglobin.

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GA in Weeks	Number of fetuses	Mean weight of right lung	Mean weight of left lung	Mean weight of both lungs	Mean of fetal body weight	Ratio of Fetal lung weight & body weight
12	3	1.87	1.6	3.53	37.17	0.0945
14	3	3.6	3.33	6.93	111.33	0.0623
16	2	4.2	4	8.2	132.5	0.0619
17	4	5.05	4.7	9.75	180.5	0.0540
18	4	5.85	5.5	11.35	253.88	0.0449
19	1	5.2	4.8	10	250	0.04
20	4	7.9	7.4	14.8	328.75	0.0450
21	5	12.56	12.08	24.64	366	0.0673
22	3	13.87	13.13	27	451.67	0.0598
23	5	15.84	15.28	31.52	563	0.0559
25	1	15.6	15	30.6	414	0.0739
26	4	18.9	18.3	37.2	760	0.0489
27	4	19.7	19.1	38.8	890	0.0436
28	4	20	19.45	39.45	1070	0.0369
29	4	22.2	19.8	40.25	1235	0.0326
31	2	22.2	21.7	43.9	1782.5	0.0246
32	3	21.13	21.6	45.7	1873.33	0.0244
33	2	23.4	23	46.4	2150	0.0216
34	4	24.05	23.55	48.93	2290	0.0214
35	4	23.75	23.2	46.95	2507.5	0.0187
36	4	24.65	24.15	48.65	3012.5	0.0161
38	4	26.6	26.1	52.3	3063.75	0.0171
39	1	25.6	25	50.6	2500	0.0202
40	2	28.6	28.1	56.7	3650	0.0155

Table 1:The results of mean fetal body weight, fetal lung weights (right &left) and ratio of fetal lung weight & body weight as per gestational week

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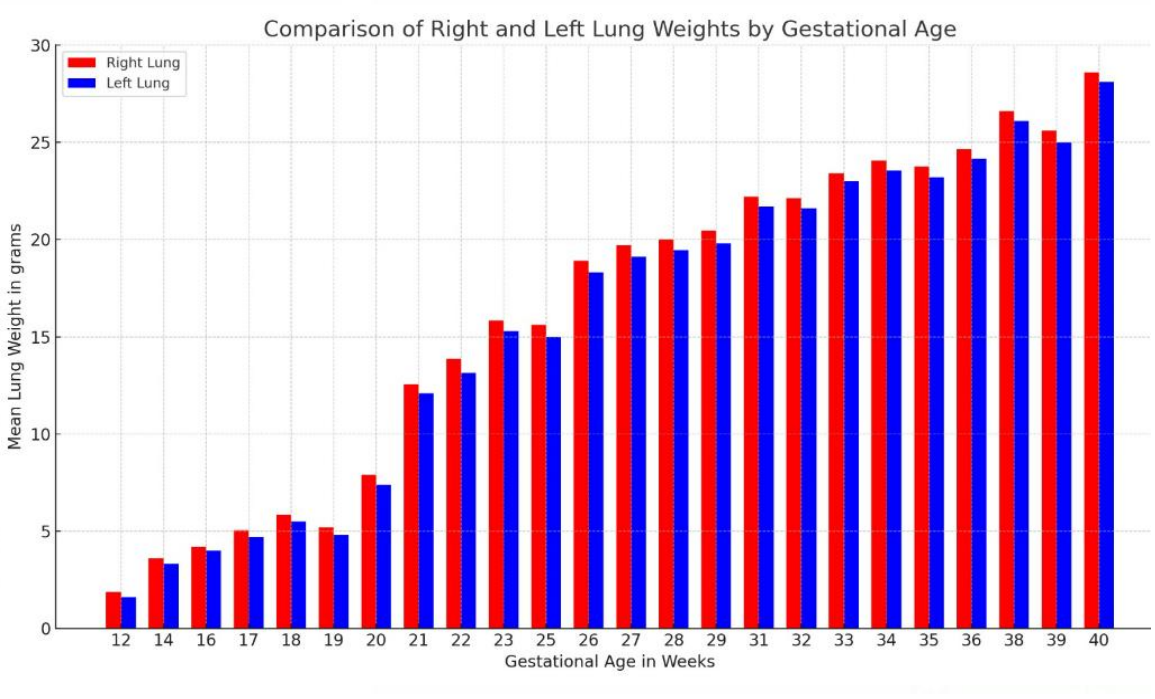

Figure 4 :Column chart showing comparison of right and left mean weights in grams against gestational age in weeks

Analysis of fetal lung weights against fetal body weight as per groups is shown in table-2**.**Beginning with Group I (12-16 weeks), mean lung weights were observed at 3.22 grams for the right lung and 2.98 grams for the left lung, with standard deviations indicating minimal variability. As gestation progresses, a consistent increase in mean lung weights is evident, culminating in Group VII (37-40 weeks) with mean weights of 26.94 grams for the right lung and 26.40 grams for the left lung. Notably, the standard deviation values slightly increase in later groups, reflecting greater individual variability in lung weight. This pattern underscores a predictable growth trajectory, albeit with individual differences emerging more prominently as development advances. The close alignment of mean weights between the right and left lungs across all groups highlights the symmetrical nature of lung growth throughout fetal development.Column chart showing mean weight of right and left lung in gram against gestational age as per groups is shown in [Fig-5].

Group	GA in weeks	No of fetuses	Mean weight of right lung	Mean weight of left lung	Mean weight of both lungs	Mean of fetal body weight	Ratio of Fetal lung weight & body weight
I	**12-16**	**8**	**3.22**	**2.98**	**6.20**	**0.073**	**0.0448**
II	**17-20**	**13**	**6**	**5.6**	**11.6**	**0.046**	**0.0462**
III	**21-24**	**13**	**14.09**	**13.5**	**27.59**	**0.061**	**0.0623**
IV	**25-28**	**13**	**18.55**	**17.96**	**36.51**	**0.051**	**0.0512**
V	**29-32**	**9**	**21.84**	**21.03**	**42.87**	**0.027**	**0.0275**

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VI	**33-36**	**14**	**23.96**	**23.47**	**47.43**	**0.02**	**0.0192**
VII	**37-40**	**7**	**26.94**	**26.4**	**53.34**	**0.018**	**0.1763**

Table 2: Group-wise distribution of mean fetal body weight, fetal lung weights (right &left) and ratio of fetal lung weight & body weight .

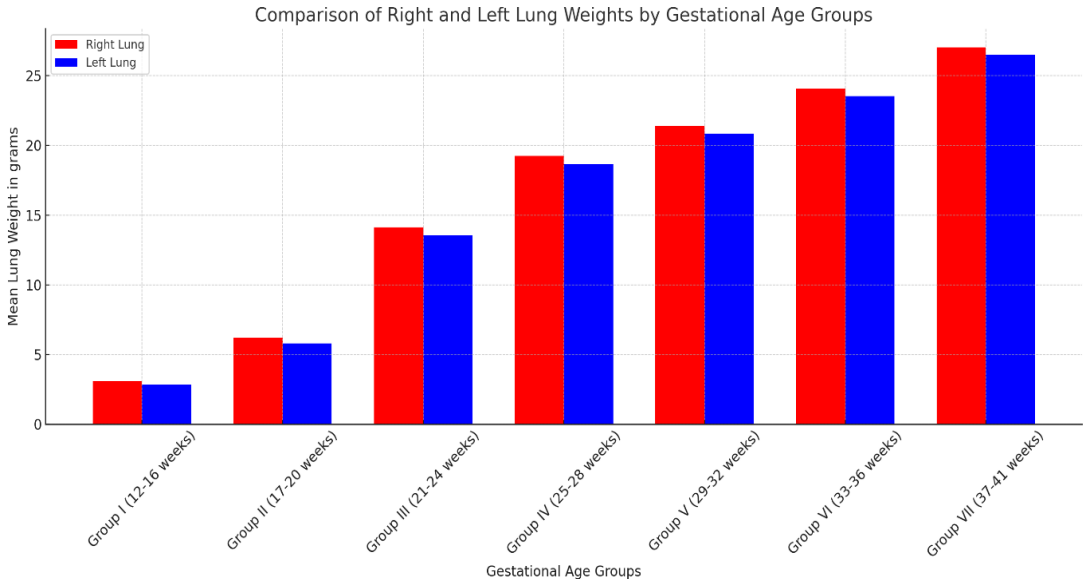

Figure 5:Column chart showing comparison of right and left mean weights in grams against gestational age in weeks as per groups

Scatter graph showing weight of foetuses against gestational age is shown in [Fig-6]. lung weight at 12th and 40th week were 37.17 gms and 3650 gms respectively.

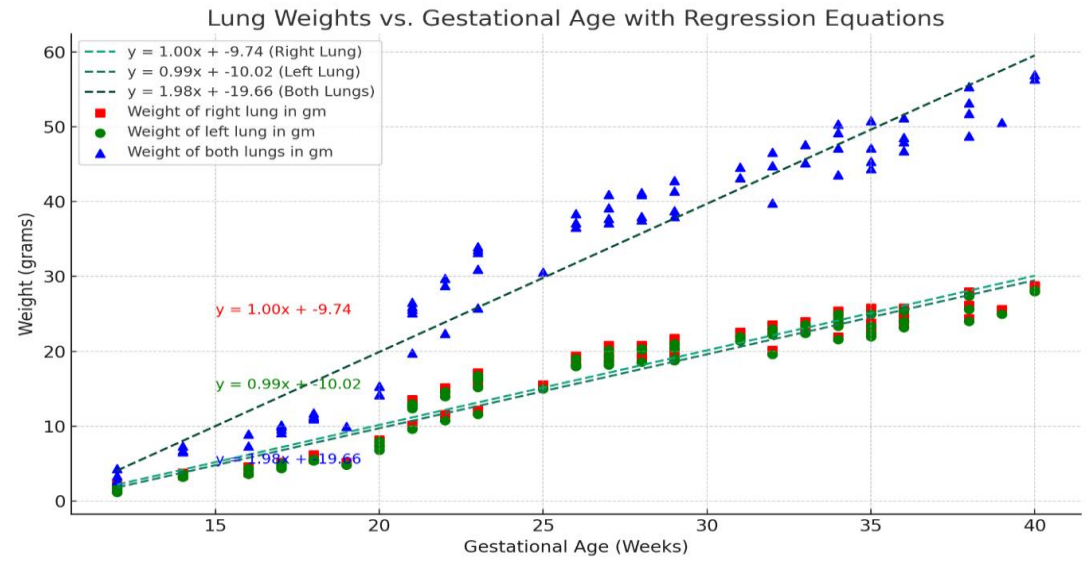

Figure 6: Scatter graph showing ratio of fetal lung and body weight against gestational age in weeks.*y* is the predicted lung weight in grams,*x* is the gestational age in weeks.

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The regression analysis of fetal lung weights against gestational age has yielded the following linear equations:

1. Right Lung: $y = 0.996x - 9.737$
2. Left Lung: $y = 0.988x - 10.023$
3. Both Lungs: $y = 1.979x - 19.665$

Growth Rate: The coefficients (slopes) of 0.996 for the right lung and 0.988 for the left lung indicate that both lungs are expected to increase in weight by approximately these values for each additional week of gestation. This demonstrates a nearly linear growth rate in the weight of the lungs throughout the gestational period studied.

Similarity Between Lungs: The similarity in the coefficients for the right and left lungs suggests that both lungs are growing at almost the same rate during fetal development.

Combined Lung Weight: The equation for the combined lung weight has a coefficient of 1.979, which is roughly the sum of the individual coefficients of the right and left lungs. This indicates that the model accurately reflects the total lung weight as the sum of both individual weights, as expected.

Scatter graph showing fetal lung and body weight [LW/BW] ratio against gestational age is shown in [Fig-7]: Mean LW/BW ranged between 0.0945-0.0619% between 12-16 weeks, and decreased to 0.0187 % by 35th week and 0.0155% at term.

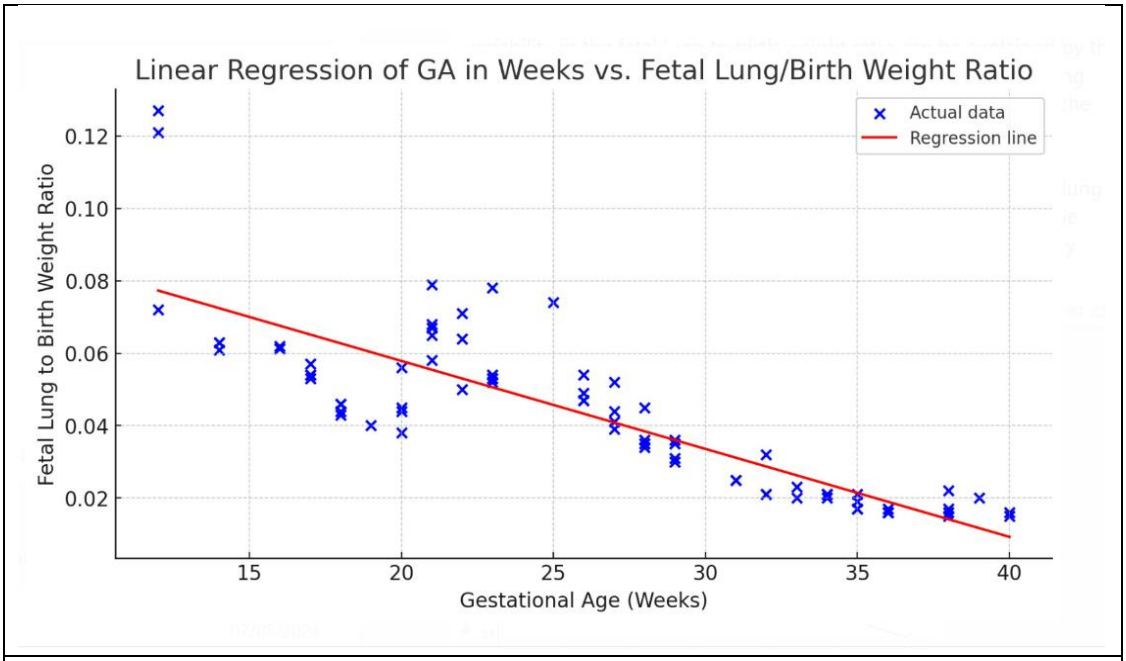

Figure 7 :Scatter graph showing ratio of fetal lung and body weight against gestational age in weeks.

Slope: The slope of the regression line is approximately −0.0024, indicating that for each additional week of gestational age, the fetal lung to birth weight ratio decreases by about 0.0024 units on average.The intercept of the regression line is approximately 0.106.

R2Value: The coefficient of determination, R2, is approximately 0.70. This indicates that about 70% of the variability in the fetal lung to birth weight ratio can be explained by the gestational age according to this model. This is a reasonably strong relationship, showing that gestational age is a good predictor of the lung to birth weight ratio in this data set.

DISCUSSION

In this study we assessed the the Correlation of the aborted human foetal lung to body weight ratio in relation with the gestational age.In general with advancing gestational age increase in organ weight as well as fetal body weight is a good indicator of foetal growth and well being.Similar findings were noted by Moore LK and Persaud TV.[9]

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In the present study the data suggest a steady increase in lung weights and body weight with advancing gestational age.[9] The body weight of foetuses showed gradual increase from 12th week to 40th week of gestation. The range of fetal weight in the study extended from a mere 22.0 grams at 12th week to 3750.0 grams at 40th week. The weight of left lung was seen less than the weight of right lung throughout the gestational age.These findings were comparable with findings of others researchers and Similar findings were noted in a study by hadlock FPet al[10] and doubilet PM et al[11] .

The coefficients (slopes) of 0.996 for the right lung and 0.988 for the left lung indicate that both lungs are expected to increase in weight by approximately these values for each additional week of gestation. The similarity in the coefficients for the right and left lungs suggests that both lungs are growing at almost the same rate during fetal development.These results were in well agreement with that of Rajeev Mukhia et al [12]and Monique E. De Paepe MD et al[13]

The results in this study indicate a statistically significant decrease in the fetal lung to birth weight ratio as gestation progresses from 12th week (0.0945) to 40th week (0.0155). This might reflect the relative growth rates of lung and overall body growth, where body growth may outpace lung development as gestation advances. These findings were comparable with the results of Tanimura T et al[14] and Rajeev Mukhia[15].

A study done by Rajeev Mukhia et al [12]and Mitropoulos G et al[16] reported that lung weight to body weight ratio was found almost constant after 31 weeks of gestation ,which was found to be conformity with results of the present study.

The findings of the present study were almost similar to other studies which was done by Shepard TH et al[17] except for few results in some weeks of gestation which may be deviated due to maternal Comorbidities,sample size ,environmental and genetic factors which may effect the fetal lung weight and body weight.[13,18]

In the present study maternal Comorbidities like severe anemia, negatively affected the anthropometric parameters of the fetuses.we observed that low birth weight of fetuses [IUGR- intra uterine growth retardation]born to mothers with severe anaemia.In these fetuses the ratio of lung weight to body weight [LW/BW] is lower than expected.By correcting maternal anemia ,improving maternal nutrition and early identification of pregnancies at risk we can reduce the number of IUGR/Small fir gestational age (SGA) births[19,20].

Conclusion

We conclude that by evaluating fetal lung weight , body weight ,LW/BW ratio and measurements against age matched known standards is an crucial part of perinatal pathology and also during autopsy to assess the lung growth ,particularly in preterm infants .

It also provides new insights for developing knowledge and understanding in both normal and pathological conditions of lung tissue to the anatomist and clinician for early recognition and interventions of pathological lung conditions during fetal anomaly scans.The findings could be used as reference values for normal lung development. Deviations from these trends could indicate potential growth anomalies, which may necessitate further medical evaluation.

Limitations: As with any model, these findings are subject to limitations. The linear model does not capture the more complex patterns of growth that may occur outside the range of gestational ages studied. Moreover, the model's predictions are based on the assumption that the observed linear trend continues outside the range of the data, which may not always be the case.

Author's contribution

Conceptualization, design of the study & supervision: Dr. N. Vishali and Dr. L. Peter.

Dr. Himabindhu: Methodology for autopsy & fetal anthropometry and writing-original draft:S.Savitha: conducted research, collected the data and analyzed the data

Dr.B.Swapna Kumari: interpreted the data, Writing-review, editing and approval of final manuscript by all authors.

Source of Funding: No funding to declare

Conflict of interests: None

Future Recommendation

The following staining methods were employed in this fetal lung tissue specimens for histological examination

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and characterization of the lung tissues at different weeks gestation.Hematoxylin and eosin staining were employed to demonstrate the microscopic structure of the lungs,Masson's trichrome staining was used to visualize and assess connective tissue deposition in the developing lung,Immunostaining with anti fibroblast growth factor-10 (FGF-10) antibodies and histomorphometry.

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