

International Journal of Radiology and Diagnostic Imaging



E-ISSN: 2664-4444
P-ISSN: 2664-4436
IJRDI 2020; 3(1): 49-58
Received: 24-11-2019
Accepted: 28-12-2019

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Prenatal assessment of fetal lung to liver signal intensity ratio using magnetic resonance imaging to predict neonatal respiratory outcome

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DOI: <http://dx.doi.org/10.33545/26644436.2020.v3.i1a.58>

Abstract

Introduction: Fetal and maternal health problems lead to increase in incidence of preterm birth that has become a major concern in obstetric practice. Perinatal survival depends crucially on a sufficiently sized and a functionally developed cardiopulmonary system. So it is extremely important to diagnose lung maturity before birth because of the increase in the indications for early induction of labour. In these conditions, assessing the lung maturity will decide timing for inducing labour. Fetal MRI is a recently developing field that provides adequate information regarding the size, structure and biochemical maturity of developing Fetal lung that overcomes the adverse effects of amniocentesis. Therefore a ratio is considered for comparing the signal intensity of the Fetal lungs with that of another structure at a comparable depth. The ideal criteria for the reference structures are sufficient size, close proximity to the lung, homogeneity and stability through the pregnancy.

Aim: Our aim was to establish a linear relationship between the estimated gestational age and the Lung- Liver Signal Intensity Ratio (LLSIR) values and to ultimately predict the lung maturity from this relationship.

Materials and Methods: The patients for this study were selected from the antenatal outpatient department of a large medical college hospital in Chennai, India. The study population consisted of a total of 50 patients who were referred from the antenatal OPD for MRI for various other indications. The liver and lung images were taken in the same imaging plane for the analysis either in the coronal or sagittal view.

Results: Magnetic resonance imaging of 50 cases were carried out during 19th and 40th week of gestation in antenatal women with age group from 23 to 31 years. LLSIR was calculated by taking the ratio of lung and liver signal intensity. The range of LLSIR is 1.54 to 4.03 (2.808+0.739, mean+SD). There was no significant correlation between the liver intensity and EGA. The range of liver intensity was from 175 to 707 (425.08+115.22, mean+SD). The Pearson correlation coefficient between liver intensity and EGA was 0.232 ($p < 0.053$) that showed no correlation between liver intensity and EGA. Linear regression analysis does not show a statistically significant association between liver intensity and EGA (r^2 0.034, $p < 0.105$).

Conclusion: We conclude that the lung to liver signal intensity ratio is steadily increasing with increasing gestational age as confirmed in other studies. As fetal lung maturity increases with increase in gestational age, lung to liver signal intensity ratio can be used to assess the respiratory outcome of the neonates.

Keywords: Perinatal mortality, fetal lung maturity, amniocentesis, fetal MRI and liver lung signal intensity ratio

Introduction

Fetal and maternal health problems lead to increase in incidence of preterm birth that has become a major concern in obstetric practice. Incidence of preterm labour is 23.3% and of preterm birth is 10-69% in India [1]. It is rising all over the world, more in the developing countries because of the increased frequency of multiple births, assisted reproductive techniques, increasing psychological stress and medically induced prematurity. Perinatal survival depends crucially on a sufficiently sized and a functionally developed cardiopulmonary system. The important determinants of survival after birth are development of lungs with complete structural and biochemical maturity in utero. Since most of the complex processes influencing the growth of lungs occur in the intrauterine period, it can be clinically applied for the assessment of lung functions even before birth by means of

biochemical analysis and imaging techniques [2]. Since the lung is the most important organ to survive in the extra uterine environment, immediate intensive care is required for neonates with immature lungs. So it is extremely important to diagnose lung maturity before birth because of the increase in the indications for early induction of labour. In these conditions, assessing the lung maturity will decide timing for inducing labour. Maturity is usually assessed by LS (Lecithin/Sphingomyelin) ratio and specific phosphatidylcholine (SPC) which requires amniocentesis. As amniocentesis is an invasive procedure, it leads to number of maternal and fetal complications that preclude its usage in many conditions. There is reported pregnancy loss rate of 0.6% within 14 days after amniocentesis [3]. This ratio increases to 0.9% for pregnancies that have not reached 24 weeks, and 1.9% for all pregnancies [4].

Fetal MRI is a recently developing field that provides adequate information regarding the size, structure and biochemical maturity of developing fetal lung that overcomes the adverse effects of amniocentesis. Because lung fluid is secreted from the epithelial cells of the fetal lung, the production starts increasing in the later weeks of gestation. The quantity of lung fluid increases progressively with fetal growth, and fetal lung becomes organ rich in fluid content [5]. Therefore, high signal intensity indicates a large amount of fetal lung fluid in the airways and alveoli, indicating lung maturation. In contrast, low intensity suggests a deficiency of lung fluid and suggests pulmonary immaturity. Using this phenomenon, MRI is used to predict fetal lung maturity [6]. Assessment of fetal lung development based on its absolute SI of the normal lungs found that the SI increases on T2-weighted images and decreases on T1-weighted images throughout gestation. The absolute SI measurements, however, depend on the distance between the organ and the coil and are therefore not consistent between patients or between types of MRI machines.

Therefore a ratio is considered for comparing the signal intensity of the fetal lungs with that of another structure at a comparable depth. The structures considered include CSF, fetal liver, and amniotic fluid. It is assumed that these structures are adjacent to the fetal lungs and would not change considerably with increasing gestational age. The ideal criteria for the reference structures are sufficient size, close proximity to the lung, homogeneity and stability through the pregnancy. Although fetal liver signal intensity may change through pregnancy [7], the liver satisfies almost all these conditions.

Therefore we conducted this study by taking the lung to liver signal intensity ratio of foetuses in pregnant women and compared them with their respective estimated gestational ages. Our aim was to establish a linear relationship between the estimated gestational age and the LLSIR values and to ultimately predict the lung maturity from this relationship.

Materials and Methods

The patients for this study were selected from the antenatal outpatient department of a large medical college hospital in Chennai, India. The study was spread over a period of 24 months from August 2014 to July 2016. The study population consisted of a total of 50 patients who were referred from the antenatal OPD for MRI for various other indications like abdominal pain, suspected appendicitis, suspected renal colic and suspected congenital anomalies in

ultrasound. Pregnant women with GA of 18 to 40 weeks, older than 18 years, pregnant women and those capable of signing an informed consent are included in our study. The exclusion criteria for this study were Foetuses with suspected anomalies of lung and liver. Pregnant women in 1st trimester, Patients who had undergone corticosteroid treatment before as it will affect the fetal lung maturity, Women with multiple gestations, and Women with contraindications for MR examination such as those having metal implants, pacemakers, or those with claustrophobia. Participants of the study were made to first undergo antenatal ultrasonogram. The fetal estimated GA was assessed by using ultrasonogram at the time of study and also from 1st trimester USG and last menstrual period whichever was available and compared with MRI findings. Ultrasound was done using Philips HD 11XE or GE LOGIC S7 Expert machines and the imaging findings were recorded and kept. Then after obtaining informed consent patient was subjected to MR examination. The pregnant women will be followed up and delivery will be tracked wherever possible. The neonatal well-being will be assessed from APGAR score. All MRI examinations were done with 1.5T MRI system (Multiva, Philips Healthcare, Holland). MRI examination were done in a single shot fast spin echo sequence of the foetal chest and abdomen (TR/TE = 3000/110; FLIP angle =90; Matrix = 324x256; number of signals acquired = 2; FOV = 25x25cms; Section thickness = 3mm; Gap 4mm) in coronal, axial and sagittal planes. Additional sequences if required were obtained. The liver and lung images were taken in the same imaging plane for the analysis either in the coronal or sagittal view. The ROI of liver and lung were taken to be visibly free of intra parenchymal vessels, adjacent structures and the organ border. For each organ examined three values (from different images) were taken and an average of the three was considered. The area of study ranged from 0.3 to 1.3 sq.cms. The ROI was placed at a similar distance from the surface receiving coil.

The ROI was kept away from the heart to reduce motion artefacts.

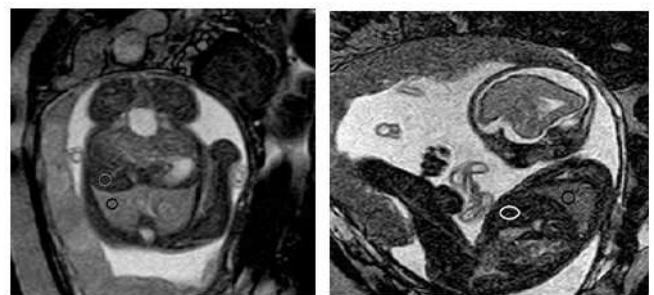


Fig 1: Figure showing the ROI being kept in the region of the fetal lungs (black ellipse) and fetal liver (white ellipse).

Statistical analysis

The study was conducted to predict the fetal lung maturity prenatally by assessment of lung to liver signal intensity ratio in antenatal women by single shot fast spin echo sequence in MRI and to determine its association with fetal gestational age.

- Statistical analysis was performed using SPSS 20.0.
- Qualitative data were tabulated in frequencies and percentages.
- Quantitative data were given in mean and standard

deviation.

- Linear regression analysis was used in analysing the relation between GA and LLSIR, GA and lung intensity, GA and liver intensity.
- Analysis of variance and Pearson correlation coefficient were also used to evaluate the data.
- $P < 0.05$ was considered as the limit for statistical significance

Observation and Results

Table 1: Age distribution

| AGE | Frequency | Percent |
|-------|-----------|---------|
| 20-25 | 34 | 68 |
| 26-30 | 15 | 30 |
| 31-35 | 1 | 2 |
| Total | 50 | 100.0 |

Among 50 subjects, 34 antenatal women were in age group 20-25, 15 in age group 26-30, 1 in the age group 31-35. The mean age of pregnant women in our study group was 24.62 and standard deviation was 3.232.

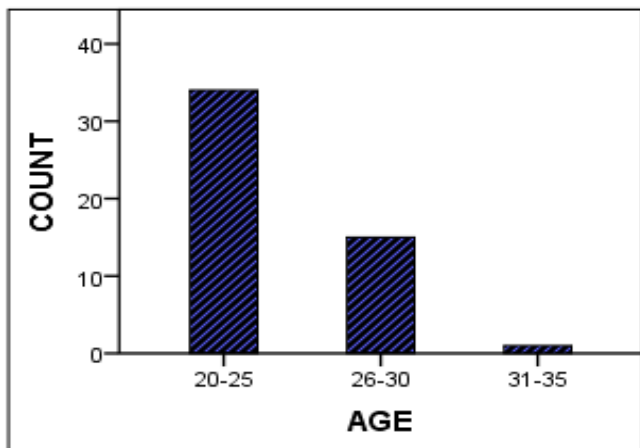


Fig 2: Distribution of Age

The ultrasound parameters which were used to calculate the gestational age are tabulated below as mean \pm standard deviation.

Table 2: Gestational age distribution

| | N | Mean | Std. Deviation |
|--------------|----|---------|----------------|
| LIQOUR | 50 | 14.64 | 3.01 |
| FHR | 50 | 148.02 | 8.28 |
| BPD | 50 | 7.41 | 1.45 |
| HC | 50 | 27.16 | 4.89 |
| AC | 50 | 25.66 | 5.68 |
| FEMUR LENGTH | 50 | 5.65 | 1.26 |
| WEIGHT | 50 | 1712.86 | 971.68 |

| | Frequency | Percent |
|-------|-----------|---------|
| Valid | <20 | 1.9 |
| | 20-25 | 26.9 |
| | 26-30 | 17.3 |
| | 31-35 | 32.7 |
| | 36-40 | 17.3 |
| | Total | 50 |

Among 50 subjects 1 had GA corresponding to <20 weeks,

14 had GA between 20 -25 weeks, 9 had GA between 26-30 weeks, 17 had GA between 31-35 weeks, 9 had GA between 36-40 weeks.

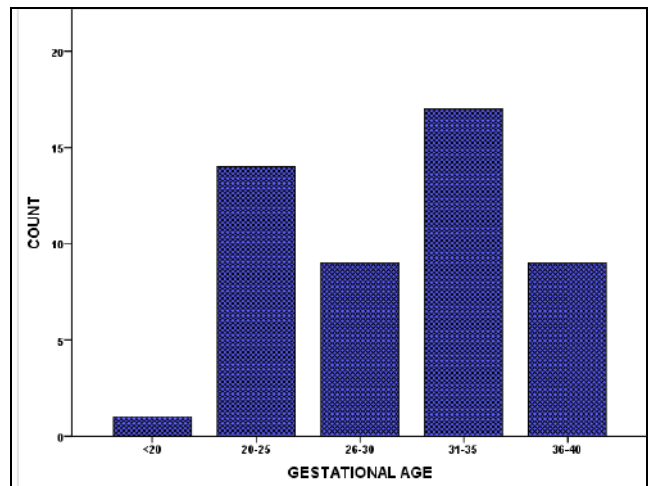


Fig 3: Gestational age Distribution

Report

Table 3: Weight

| GA | Mean | N | Std. Deviation |
|-------|---------|----|----------------|
| <20 | 311.00 | 1 | . |
| 20-25 | 623.21 | 14 | 142.93 |
| 26-30 | 1204.78 | 9 | 272.92 |
| 31-35 | 2209.35 | 17 | 327.03 |
| 36-40 | 3133.89 | 9 | 227.93 |

The mean weight is increasing with increase in GA. In pregnant women with GA of <20 weeks it is 311, in 20-25 weeks it is 623.21 ± 142.93 , in 26-30 weeks it is 1204.78 ± 272.92 , in 31-35 weeks it is 2209.35 ± 327.03 , in 36-40 weeks it is 3133.89 ± 227.93 .

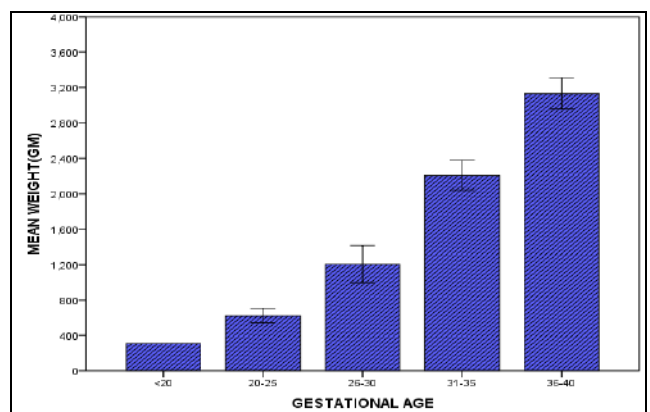


Fig 4: Weight distribution

Table 4: Liver Intensity

| GA | Mean | N | Std. Deviation |
|-------|--------|----|----------------|
| <20 | 363.00 | 1 | . |
| 20-25 | 481.04 | 14 | 135.71 |
| 26-30 | 434.88 | 9 | 117.90 |
| 31-35 | 393.14 | 17 | 111.62 |
| 36-40 | 412.11 | 9 | 64.82 |

In pregnant women with GA of <20 weeks it is 363.00, in 20-25 weeks it is 481.04 ± 135.71 , in 26-30 weeks it is

434.88 ± 117.90, in 31-35 weeks it is 393.14 ± 111.62, in 36-40 weeks it is 412.08 ± 115.22. The mean ± SD of liver

intensity of the subjects in our study is 428.08 ± 115.22.

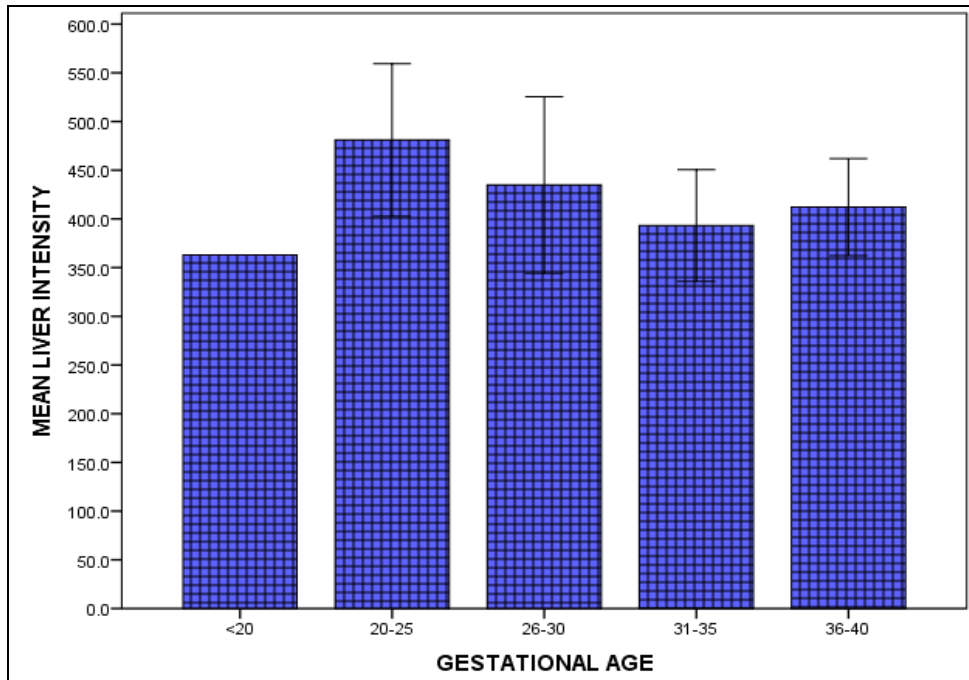


Fig 5: Liver intensity vs gestational age

Table 5: Lung Intensity

| GA | Mean | N | SD |
|-------|---------|----|--------|
| <20 | 750.00 | 1 | . |
| 20-25 | 953.63 | 14 | 214.84 |
| 26-30 | 1072.88 | 9 | 296.93 |
| 31-35 | 1219.13 | 17 | 305.21 |
| 36-40 | 1556.44 | 9 | 217.12 |

The mean LLSIR is significantly increasing with increase in GA. In pregnant women with GA of <20 weeks it is 750, in 20-25 weeks it is 953.63 ± 214.84, in 26-30 weeks it is 1072.88 ± 296.93, in 31-35 weeks it is 1219.13 ± 305.21, in 36-40 weeks it is 1556.44 ± 334.26. The mean ± SD of lung intensity in our study is 1169.80 ± 334.26.

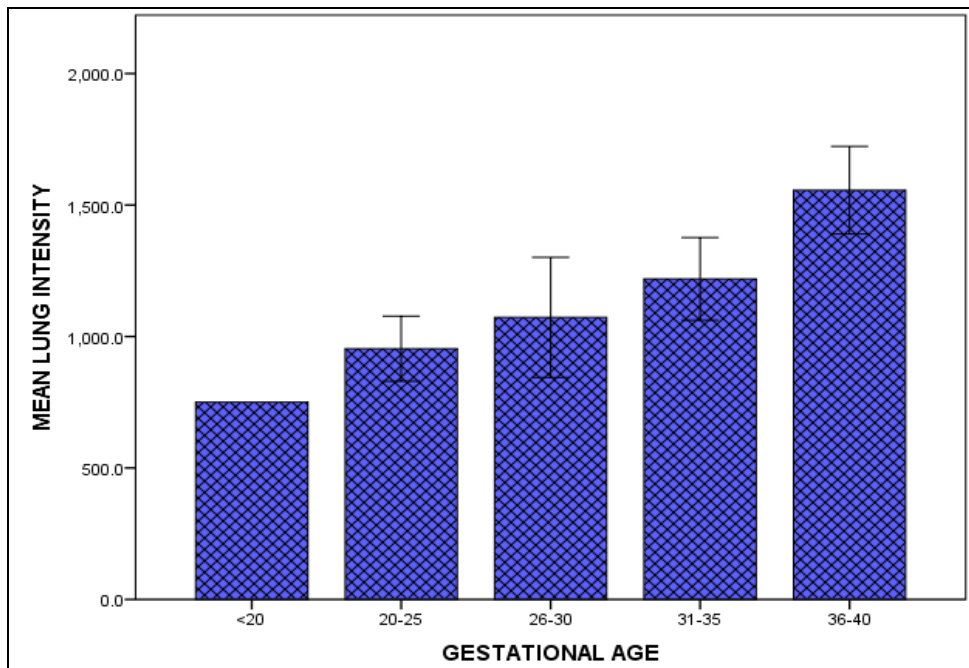


Fig 6: Lung intensity vs gestational age

Lung to Liver Signal Intensity Ratio

The mean ± SD LLSIR in our study is 2.808 ± 0.739

Table 6: Gestational Age and LLSIR

| | N | Mean | Std. Deviation | 95% Confidence Interval for Mean | | Minimum | Maximum |
|-------|----|------|----------------|----------------------------------|-------------|---------|---------|
| | | | | Lower Bound | Upper Bound | | |
| <20 | 1 | 2.01 | . | . | . | 2.01 | 2.01 |
| 20-25 | 14 | 2.02 | .26 | 1.87 | 2.17 | 1.54 | 2.50 |
| 26-30 | 9 | 2.47 | .31 | 2.22 | 2.71 | 1.89 | 3.07 |
| 31-35 | 17 | 3.16 | .46 | 2.91 | 3.40 | 1.86 | 4.10 |
| 36-40 | 9 | 3.78 | .28 | 3.56 | 4.00 | 3.24 | 4.20 |

The mean LLSIR is increasing with increase in GA. In pregnant women with GA of <20 weeks it is 2.01 , in 20-25 weeks it is 2.02 ± 0.26 in 26-30 weeks it is 2.47 ± 0.31 in 31-35 weeks it is 3.16 ± 0.46 in 36-40 weeks it is 3.78 ± 0.28

Table 7: Oneway analysis of LLSIR

| | Sum of Squares | df | Mean Square | F | Sig. |
|----------------|----------------|----|-------------|--------|------|
| Between Groups | 20.990 | 4 | 5.247 | 40.493 | .000 |
| Within Groups | 5.831 | 45 | .130 | | |
| Total | 26.821 | 49 | | | |

Oneway analysis shows that there is a statistically significant association between LLSIR and EGA ($p < 0.0001$)

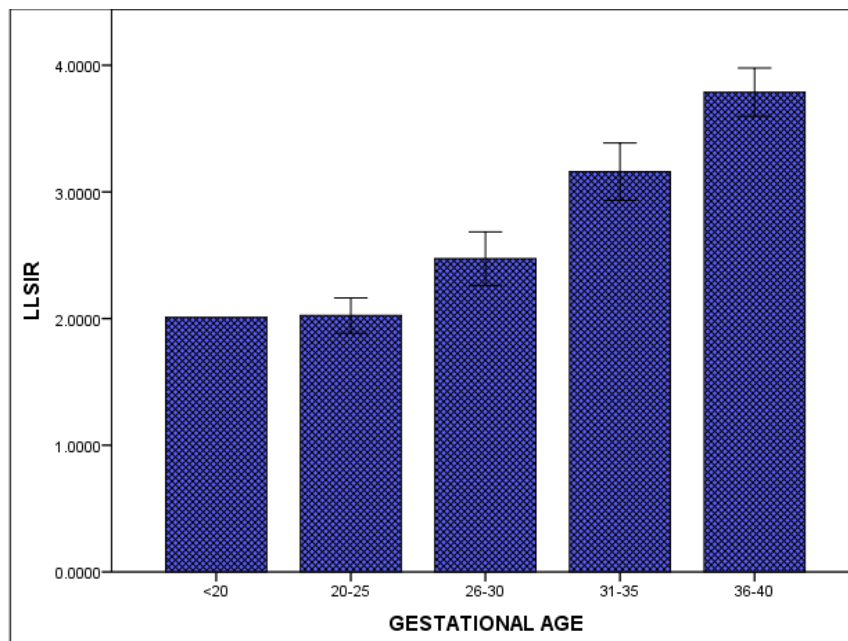


Fig 7: LLSIR Vs Gestational Age

Table 8: Correlation between LLSIR and GA

| Correlations | | | |
|--------------|---------------------|--------|--------|
| | | GA | LLSIR |
| GA | Pearson Correlation | 1 | .891** |
| | Sig. (2-tailed) | | .000 |
| | N | 50 | 50 |
| LLSIR | Pearson Correlation | .891** | 1 |
| | Sig. (2-tailed) | .000 | |
| | N | 50 | 50 |

** . Correlation is significant at the 0.01 level (2-tailed).

Pearson correlation coefficient of 0.891 indicates that there is variation around the line of best fit. Pearson's correlation determines the degree to which a relationship is linear. There is a linear component of association between two continuous variables...

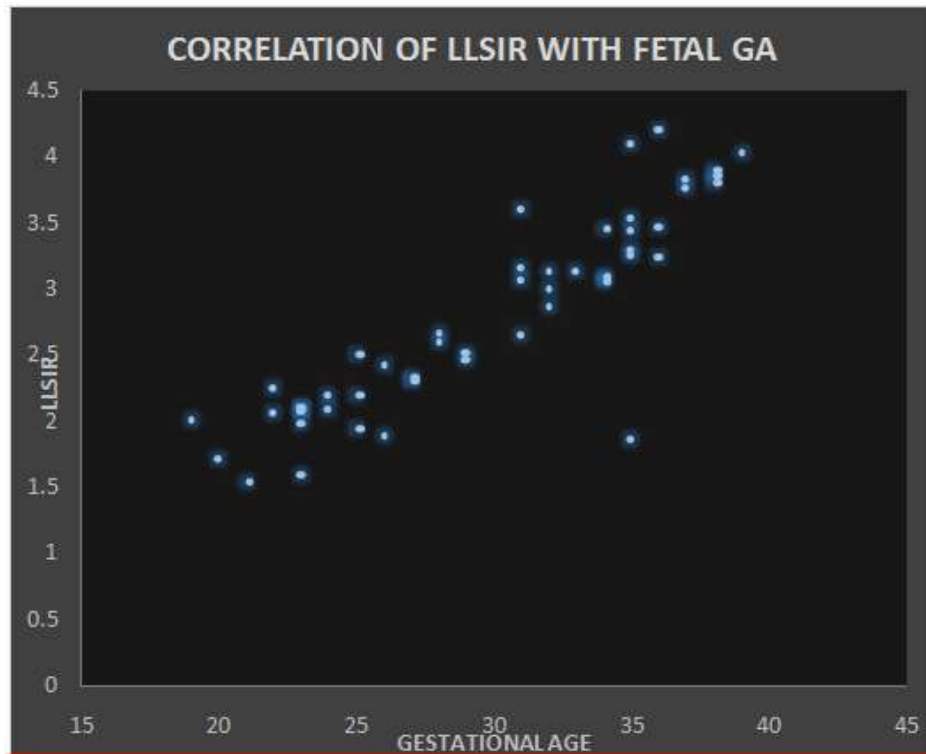


Fig 8: LLSIR Vs Fetal GA

Table 9: Linear Regression Analysis

| Model | R | R Square | Adjusted R Square | Std. Error of the Estimate |
|-------|-------------------|----------|-------------------|----------------------------|
| 1 | .891 ^a | .794 | .789 | .3395496 |

a. Predictors :GA

b. Dependent Variable: LLSIR

This table provides the *R* and *R*² values. The *R* value represents the simple correlation and is 0.891 (the "R" Column), which indicates a high degree of correlation. The *R*² value (the "R Square" column) indicates how much of the total variation in the LLSIR, (dependent variable), can be explained by the GA (independent variable) . In this case, it is 0.789, which is very large.

| Model | Sum of Squares | df | Mean Square | F | Sig. | |
|-------|----------------|--------|-------------|--------|---------|-------------------|
| 1 | Regression | 21.287 | 1 | 21.287 | 184.634 | .000 ^b |
| | Residual | 5.534 | 48 | .115 | | |
| | Total | 26.821 | 49 | | | |

a. Dependent Variable: LLSIR

b. Predictors: (Constant), GA

This table indicates that the regression model predicts the LLSIR i.e. dependent variable significantly well. From the "Regression" row and the "Sig." column there is statistical significance of the regression model Here, $p < 0.0005$,

which is less than 0.05, and indicates that, overall, the regression model statistically significantly predicts the outcome variable.

Table 10: Coefficients

| Model | Unstandardized Coefficients | | Standardized Coefficients | t | Sig. | 95.0% Confidence Interval for B | | |
|-------|-----------------------------|------------|---------------------------|------|--------|---------------------------------|-------------|-------|
| | B | Std. Error | Beta | | | Lower Bound | Upper Bound | |
| 1 | (Constant) | -.643 | .259 | | -2.488 | .016 | -1.163 | -.123 |
| | GA | .115 | .008 | .891 | 13.588 | .000 | .098 | .132 |

a. Dependent Variable: LLSIR

The Coefficients table provides us with the necessary information to predict LLSIR from GA. The values in the B column gives us constant values of the equation from which LLSIR can be predicted from the gestational age. The best

fit for LLSIR of normal lung was represented by the regression line $Y = 0.1154X + 0.6431$ ($r^2 = 0.7937$; $p < 0.001$), in which Y is LLSIR and X is gestational age in weeks.

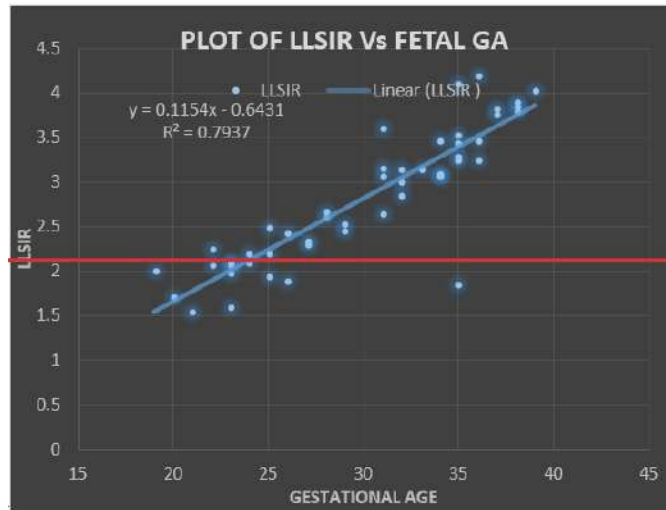


Fig 9: Coefficients of LLSIR Vs Fetal GA

Table 11: Correlation between lung intensity and GA

| | | Lung intensity | GA |
|---------------------|----------------|----------------|-------|
| Pearson Correlation | Lung intensity | 1.000 | .624 |
| | GA Bucket | .624 | 1.000 |
| Sig. (1-tailed) | Lung intensity | . | .000 |
| | GA Bucket | .000 | . |
| N | Lung intensity | 50 | 50 |
| | GA Bucket | 50 | 50 |

| **. Correlation is significant at the 0.01 level (2-tailed). | | | | | |
|--|-------------------|----------|-------------------|----------------------------|---------------|
| Pearson correlation coefficient of 0.624. This indicate that there is variation around the line of best fit ($p < 0.0001$) | | | | | |
| Model Summary | | | | | |
| Model | R | R Square | Adjusted R Square | Std. Error of the Estimate | Sig. F Change |
| 1 | .624 ^a | .390 | .377 | 263.8518 | .000 |

a. Predictors: (Constant), GA BUCKET

This table provides the R and R^2 values. The R value represents the simple correlation and is 0.624 (the "R" Column), which indicates a moderate degree of correlation. The R^2 value is 0.377 (the "R Square" column) indicates

how much of the total variation in the lung intensity, (dependent variable), can be explained by the GA (independent variable). In this case, it is 0.377, it is average.

Table 12: Comparison of Coefficients

| Model | | Unstandardized Coefficients | | Standardized Coefficients | t | Sig. |
|-------|------------|-----------------------------|------------|---------------------------|-------|------|
| | | B | Std. Error | Beta | | |
| 1 | (Constant) | 368.787 | 149.441 | | 2.468 | .017 |
| | GA BUCKET | 182.881 | 33.038 | .624 | 5.535 | .000 |

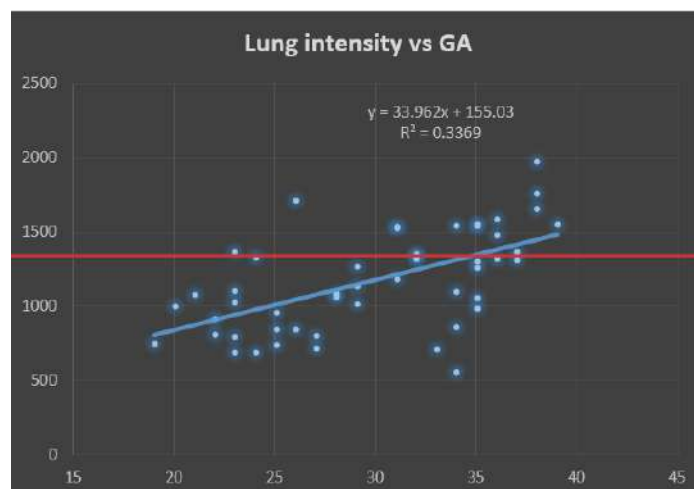


Fig 10: Lung Intensity Vs GA

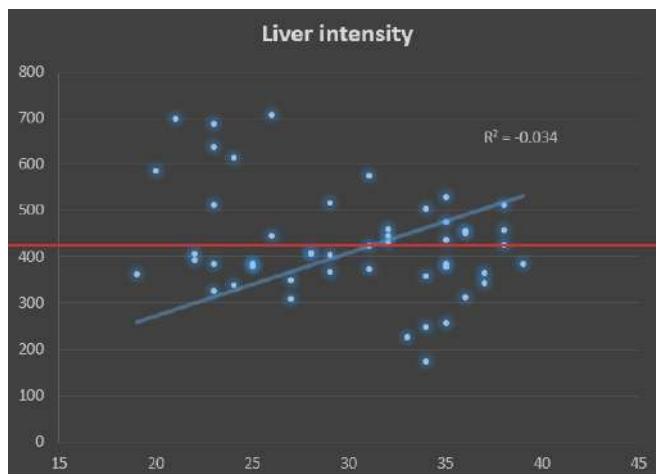
Table 13: Correlation between liver intensity and GA

| | | Liver intensity | GA Bucket |
|---------------------|-----------------|-----------------|-----------|
| Pearson Correlation | Liver intensity | 1.000 | -.232 |
| | GA Bucket | -.232 | 1.000 |
| Sig. (1-tailed) | Liver intensity | . | .053 |
| | GA Bucket | .053 | . |
| N | Liver intensity | 50 | 50 |
| | GA Bucket | 50 | 50 |

Pearson correlation coefficient of 0.232. This indicate that there is no correlation between liver intensity and G

| Model | R | R Square | Adjusted R Square | Std. Error of the Estimate | Sig. F Change |
|--------------------------------------|-------------------|----------|-------------------|----------------------------|---------------|
| 1 | .232 ^a | .054 | .034 | 113.2537 | .105 |
| a. Predictors: (Constant), GA Bucket | | | | | |

This table provides the R and R² values. The R value represents the simple correlation and is 0.232 (the "R" Column), which indicates that there is no correlation. The R² value is 0.054 (the "R Square" column). In this case, it is 0.034, which shows there is no significant change in liver intensity with EGA (p<0.105).



Results

Magnetic resonance imaging of 50 cases were carried out during 19th and 40th week of gestation (29.92+5.714, mean+SD) in antenatal women with age group from 23 to 31 years. (24.62+2.23, mean+SD).

LLSIR was calculated by taking the ratio of lung and liver signal intensity.

The range of LLSIR is 1.54 to 4.03 (2.808+0.739, mean+SD). The Pearson’s correlation coefficient between LLSIR and EGA was 0.891(p<0.0001) that showed a high degree of correlation between LLSIR and EGA. Linear regression analysis showed a statistically significant association between LLSIR and EGA (p <0.001). The best fit for LLSIR of normal lung was represented by the regression line $Y = 0.1154X + 0.6431$ ($r^2 = 0.7937$; p<0.001), in which Y is LLSIR and X is gestational age in weeks. This ratio increased in a linear manner as EGA progressed.

Correlation and linear regression analysis was also done between lung intensity and GA. The range of lung intensity is from 750 to 1966 (1169.80+334.26). The Pearson

correlation coefficient between lung intensity and EGA was 0.624(p<0.001) that showed a degree of correlation between lung intensity and EGA. Linear regression analysis showed a statistically significant association between lung intensity and EGA (r^2 0.377, p <0.001).

Still the square of ‘r’ value for lung intensity (0.377) is comparatively much less when compared to the square of ‘r’ value for LLSIR (0.7937) by linear regression analysis suggesting the superiority of LLSIR over lung signal intensity alone.

There was no significant correlation between the liver intensity and EGA. The range of liver intensity was from 175 to 707 (425.08+115.22, mean+SD). The Pearson correlation coefficient between liver intensity and EGA was 0.232(p<0.053) that showed no correlation between liver intensity and EGA. Linear regression analysis does not show a statistically significant association between liver intensity and EGA (r^2 0.034, p<0.105).

Discussion

The objective of our study was to establish a linear relationship between LLSIR and increasing gestational age and thus predict the progression of lung maturity as the gestational age increases. Therefore we could assess whether MRI can be used in predicting neonatal respiratory outcome which will be useful in reducing perinatal mortality.

In our study we took 50 pregnant women with gestational ages between 19 and 39 weeks who had come for MRI for various other indications. The age of pregnant women in our study group ranged from 20 to 31 years with a mean of 24.62.

Relevant history and previous records (wherever available) were collected from them. They were subjected to antenatal ultrasonogram at the time of study and gestational ages were calculated from the USG findings and also from the LMP dates. USG findings were documented.

Then they were subjected to MR examination. The liver and lung images were taken in the same imaging plane for the analysis either in the coronal or sagittal view. For each organ examined three values (from different images) were taken and an average of the three was considered. Lung to liver signal intensity ratio was calculated by taking the ratio of lung and liver signal intensities.

The range of lung to liver signal intensity ratio varied from 1.54 to 4.03. The Pearson’s correlation coefficient of 0.891(p<0.0001) showed a high degree of correlation between the lung to liver signal intensity ratio and the estimated gestational age. Linear regression analysis showed a statistically significant association between lung to liver signal intensity ratio and estimated gestational age. This ratio increased in a linear manner as EGA progressed. “r²” coefficient of determination is a statistical measure of how well the regression line approximates the real data points. An r² of 1 indicates that the regression line perfectly fits the data (i.e., 100% correlation). Therefore r² value of .7937(i.e., 79.37%) indicates a strong association between the variables. This is in accordance with the studies published by Moshiri *et al.* , Lee J. Brewerton *et al.* and Yasuko Oka *et al.* who obtained similar results with “P” value of less than 0.001 (p<0.001) indicating a significant relationship between the variables.

Correlation and linear regression analysis was also done between lung intensity and GA. The Pearson correlation

coefficient between lung intensity and estimated gestational age was 0.624 ($p < 0.001$) that showed correlation between lung intensity and estimated gestational age. Linear regression analysis showed a statistically significant association between lung intensity and estimated gestational age.

This is in accordance with the studies by Ikeda *et al.* [8] and Levine *et al.* [9] who found that absolute SI of the normal lungs increases on T2-weighted images and decreases on T1-weighted images throughout gestation. Cannie *et al.* [10] also found that the absolute T2 SI of the normally developing fetal lung increases with advancing gestational age. But the 'r²' value for lung intensity (0.377) is comparatively much less when compared to the square of 'r²' value for lung to liver signal intensity ratio (0.7937) by linear regression analysis suggesting the superiority of lung to liver signal intensity ratio over lung signal intensity alone.

In our study there was no significant correlation between the liver intensity and the estimated gestational age. But this is contradicting the study done by Duncan *et al.* [11] and Keller *et al.* [12] who found that the absolute T2 SI of the fetal liver increases with advancing gestational age. But our study result is similar to the study done by Kuwashima S *et al.* [13] who demonstrated that liver would not change considerably with gestational age.

In obstetrics literature, 36 weeks [14-17] is considered a cut off for normal lung development, above which corticosteroid therapy is not mandated. So with a best fit equation of $Y = 0.115X - 0.643$ in the regression analysis, keeping the gestational age at 36 weeks, we arrive at a lung to liver signal intensity ratio value of 3.497. This value can be used as a cut off for distinguishing mature from immature fetal lungs.

Therefore in our study we conclude that the lung to liver signal intensity ratio is steadily increasing with increasing gestational age as confirmed in other studies. As fetal lung maturity increases with increase in gestational age, lung to liver signal intensity ratio can be used to assess the respiratory outcome of the neonates.

We followed up 9 pregnant women with gestational ages between 36-39 weeks (mean LLSIR is 3.788) after their labour and the APGAR of their foetuses were assessed. The APGAR score was between 8 and 10 in the foetuses followed up which indicates a good respiratory outcome.

Of the total cases, 12 women could not be followed up because their deliveries happened outside our institution and also could not be contacted through phone to determine the normalcy of the foetus.

29 patients were in the GA of 19 to 36 weeks. Because the time lag between the study and the time of their deliveries was large, the lung maturity at the time of study would vary considerably with lung maturity at the time of their deliveries. Therefore the APGAR scores of their foetuses could not be taken for comparison with the obtained lung to liver signal intensity ratio values. These women (with GA of 19 to 36 weeks) were included in our study to demonstrate the progressive increase of lung to liver signal intensity ratio with increasing gestational age.

Limitations

One of the limitations of the study was that the same foetuses were not imaged at different stages of gestation to prove changes in LLSIR.

We did not have histologic correlation to absolutely prove the stage of lung-tissue maturity.

Because many variables affect pregnancy outcome, direct correlation between the MRI findings and pregnancy outcome would have been possible only if a large time lapse between MRI and delivery was not present.

Summary and Conclusion

Preterm labour is a major cause of neonatal mortality and morbidity. In determining the timing of elective preterm deliveries fetal lung maturity assessment is the most important factor. The current practise for evaluating the lung maturity is the determination of biochemical parameters like LS ratio which requires amniocentesis. Amniocentesis, being an invasive procedure, has various maternal and fetal complications including fetal miscarriage.

Therefore a non-invasive method to assess the foetal lung maturity will have major clinical implications and will also be useful in prenatal counselling and optimising the patient care.

The analysis of our study showed a statistically significant linear relationship between the lung to liver signal intensity ratio and the estimated gestational age. This relation can be used in assessing the fetal lung maturity and ultimately predict the neonatal respiratory outcome.

Our study was unique from other studies investigating lung to liver signal intensity ratio in that ours was a prospective study while others were mostly retrospective.

In using fetal MRI for clinical practice, the availability and the cost of MRI can be a limiting factor, especially in developing countries like India.

Our study has the potential to replace amniocentesis as the primary diagnostic test for the assessment of fetal lung maturity since it is non-invasive and fast. This method also has the advantage of non-invasive monitoring of foetuses at serial examinations over time, especially if corticosteroid therapy is initiated before delivery to promote fetal lung maturity.

Further studies are needed to establish the changes in the signal intensities of various other sequences and for the development of a normogram that can be used as a reference standard for the assessment of fetal lung maturity.

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