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Epiphyseal Ossification Centers as Predictor of Fetal Lung Maturity by Ultrasound

Obstetrics & Gynecology

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ABSTRACT

Background: Prediction of lung maturity is important in high-risk pregnancy management. The strongest predictor of lung maturity is gestational age. As a result, infants delivered at fewer than 39 weeks have much greater rates of neonatal morbidity than infants delivered at 39 weeks or longer gestation.

Aim of the work: To evaluate the distal femoral, proximal tibial, as well as proximal humeral ossification centres as predictive tools of the maturity of the fetal lung.

Patients and methods: A sample of 100 pregnant women will be studied in an observational prospective study at the Obstetrics and Gynecology department, Al-Azhar University Hospitals, Sayed Jalal and Damanhour National Medical Institute.

Results: The sensitivity, specificity and accuracy of epiphyseal ossification femoral in predict respiratory distress were 96.0%, 92.0% and 94.0% respectively at cut off value 3, the Epiphyseal Ossification tibia show in predict respiratory distress was 94.0%, 90.0% and 92.0% respectively at cut off value 7. The Epiphyseal Ossification humeral show in predict respiratory distress was 80.0%, 77.0% and 79.0% respectively at cut off value 3.0. Finally the Epiphyseal Ossification Femoral + tibia show sensitivity, specificity and accuracy 100.0% at cut off value 16.0.

Conclusion: The ossification centres of the distal femoral, proximal tibial, as well as proximal humeral bones have a good predictive value for the maturity of the fetal lung.

Keywords: *EpiphyseaL; Ossification Centers; Fetal Lung Maturity; Ultrasound.*

INTRODUCTION

Lung immaturity is the leading cause of neonatal death and morbidity in preterm and early-term foetuses. Respiratory distress syndrome (RDS) seems to be a common trigger of neonatal death and morbidity in which the lungs are unable to produce enough oxygen. [1]

Prediction of lung maturity is important in high-risk pregnancy management. The strongest predictor of lung maturity is gestational age. As a result, infants delivered at fewer than 39 weeks have much greater rates of neonatal morbidity than infants delivered at 39 weeks or longer gestation.[2]

There are various methods of determination of fetal lung maturity, such as clinical approaches like menstruation history and last menstrual period (LMP), per abdomen inspection, and time of quickening. [3]

In our country, health education is poor. Majority of females are quite careless about their menstrual history. So, we cannot determine the exact gestational age to assess the maturity clinically.

In circumstances like as polyhydrominos, multiple gestation, or IUGR, per abdominal exams can potentially produce false findings. So, to avoid the drawbacks of clinical methods, additional help of ancillary methods like amniocentesis, radiography and ultrasonography is required to assess the fetal maturity. Amniocentesis is an invasive technique and use of X-rays is hazardous to fetus.[4]

Ultrasonographic markers of the maturity of the fetal lung could be used to determine foetal lung maturity indirectly. Over the last 30 years, noninvasive ultrasonography approaches for predicting lung maturity have been extensively investigated. [5]

Previous research comparing fetal lung echogenicity to that of the placenta, fetal gut, and liver revealed ultrasonographic alterations related to the maturity of the foetal lung.[6]

Free-floating particles in amniotic fluid were employed in other research to assess foetal lung maturation by ultrasonography. [7]

Long-bone epiphyseal ossification centres could be accurately detected and measured sonographically, which may be a useful marker of fetal lung maturity. [8]

It was 50 years ago that radiography was first used to measure the epiphyseal ossification centres of long bones as indicators of gestational age. The results of maternal abdomen x-rays taken throughout pregnancy, as well as x-rays of neonatal limbs, were used in these studies. Nevertheless, the danger of subjecting the fetus to radiation, as well as the considerable variation in the data obtained, contributed to the discontinuance of this approach for determining gestational age. [9]

The development of ultrasonography alleviated the majority of the technical challenges associated with radiography, as well as the concern of fetal radiation. Moreover, as long as the diameter seems to be at minimum 1 mm, ultrasound may identify every ossification centre significantly early. Ultrasonically, the primary ossification centres emerge as egg-shaped echo-rich zones. At the knee joint, the ossification centres of the distal femoral and proximal tibial epiphyses may be observed, while the proximal humeral epiphysis can be observed at the shoulder joint. [10]

The aim of this thesis was to evaluate the distal femoral, proximal tibial, as well as proximal humeral ossification centres as predictive tools of fetal lung maturity.

PATIENTS AND METHODS

A sample of 100 pregnant women will be studied in an observational prospective study at the Obstetrics and Gynecology department, Al-Azhar University Hospitals, Sayed Jalal and Damanhour National Medical Institute.

Inclusion criteria:

The study will include women who fulfil the following criteria:

Age: 18-40

Singleton pregnancies at 35 – 40 weeks

Delivering within 72 hours from scan

Exclusion criteria:

Multiple gestations.

Uncertain gestational age.

Cases with major congenital anomalies, hydrops fetalis, premature rupture of membranes, umbilical cord prolapse and placental abruption.

Polyhydramnios and oligohydramnios .

Large for gestational age, small for gestational age, or presence of meconium stained amniotic fluid.

Methods:

History will be taken including:

Personal history .

Menstrual history.

Obstetric history.

Present history included:

Gynecological symptoms which may suggest sexually transmitted diseases as vaginal discharge, pelvic discomfort, purities, dysparunia or post coital bleeding.

Urinary symptoms which suggest urinary tract infection as dysuria, frequency or urgency.

Past history included history of medical diseases (diabetes mellitus, hypertension, heart disease, chest disease, and rheumatic disease), any previous operations and sensitivity to any drugs.

Examination including:

General examination included general condition, height, weight, gait and vital signs (temperature, blood pressure, pulse rate, and respiration rate).

Abdominal examination included:

Inspection (size, shape, scars, striae gravidarum and the presence of hernia).

Palpation (fundal level, the rest of abdomen to detect any abnormality and for presence of contractions).

Auscultation of fetal heart sounds.

Vaginal examination: If it is indicated.

Investigations:

Routine investigations include complete blood count, blood group, Rh. group, urine analysis, fasting blood sugar and blood sugar two hours after eating.

Ultrasounds scan to assess the gestational age and to detect any abnormality.

Interventions:

Obestetric U.S. to measure fetal maturity and confirm the gestational age by measuring (BPD, FL,AC) The ultrasound was performed using VINNO X2 ultrasound machine trans-abdominal 4.5 MHZ probe to measure :

We will assess the fetal condition, gestational age, the presence of any fetal or uterine anomalies, the placenta and the amniotic fluid.

Ultrasonically, the primary ossification centres emerge as egg-shaped echo-rich zones. At the knee joint, the ossification centres of the distal femoral and proximal tibial epiphyses may be observed, while the proximal humeral epiphysis can be observed at the shoulder joint.

Measurements of the epiphysis will be obtained in an axial plane along the medio-lateral surface, from the outer to outer margins.

Each measure will be made from a separate scan image. At least three measurements will be taken and the mean value of the three measures will be considered as the current diameter.

Primary out come

The primary outcome was the mode of delivery and evaluate the distal femoral, proximal tibial as well as proximal humeral ossification centers as predictive tools of fetal lung maturity.

RESULTS

The maternal age ranged from 20-31 with mean value 25.38±3.311, while BMI ranged from 23.2-38.7 with mean value 30.983±4.578.

The gestational age ranged from 35-40 with mean value 37.79±1.701. Gravidity ranged from 1-5 with mean value 3.07±1.465. Number of living children ranged from 0-4 with mean value 1.9±1.467. Cases without previous abortion were 92(92%) and cases with previous abortion were 8(8%).

The previous operation was higher 11(11%) followed D.M 10(10%), hypertension 6(6%), heart disease 4(4%) and rheumatic disease 2(2%).

The gestational age ranged from 34.97-40.81 with mean value 38.20±1.762. Epiphyseal ossification femoral ranged from 2.1-9 with mean value 6.20±1.846. Epiphyseal ossification tibia ranged from 4.5-9.8 with mean value 7.67±1.270. Epiphyseal ossification humeral ranged 2.22-6.49 with mean value 4.19±1.161.

The mode of delivery showed that the normal vaginal delivery were 32(32%) and cases with C.S. were 68(68%).

The outcome fetes distribution regarding sex was 53 (53%) were male, while females were 47(47%).

The APGAR score at 1 min showed that score 5.00 and 7.00 was the same with 29(29%), followed by score 6.00 was 27(27%) and score 8.00 was 15(15%). While at 5 min showed that score 9.00 was 30(30%) followed by score 8.00 and score 10.00 was the same 23(23%), score 7.00 was 15(15%), score 5.00 was 3(3%).

The incidence of respiratory distress syndrome were 9(9%) and cases without respiratory distress syndrome were 91(91%). The incidence of cases with ICU admission syndrome were 9(9%) and cases without ICU admission were 91(91%).

	Neonatal Respiratory distress syndrome		Total	T P
	No "n=91"	Yes "n=9"		
Distal Epiphyseal Ossification	3.90-9.00	2.10-3.60	2.10-9.00	53.946
Femoral	6.55	2.72	6.20	0.001*
Range	1.55	0.44	1.85	
Mean				
S.D.				
Epiphyseal Ossification tibia	6.00-9.80	4.50-7.00	4.50-9.80	39.893
Range	7.89	5.51	7.67	0.001*
Mean	1.10	0.82	1.27	
S.D.				
Epiphyseal Ossification humeral	2.50-6.50	2.20-3.50	2.20-6.50	20.534
Range	4.35	2.67	4.20	0.001*
Mean	1.10	0.37	1.16	
S.D.				

T= student t-test

Table 1: Relation between Epiphyseal Ossification and neonatal Respiratory distress syndrome.

Table (1) showed the relation between mean Epiphyseal ossification centres and neonatal respiratory distress syndrome, it was found that the mean Epiphyseal Ossification centres was significantly low in neonatal with respiratory distress syndrome ($p < 0.05$).

	ICU admission		Total	T P
	No "n=91"	Yes "n=9"		
Distal Epiphyseal Ossification	2.70-9.00	2.10-4.10	2.10-9.00	41.298
Femoral	6.52	3.02	6.20	0.001*
Range	1.61	0.75	1.85	
Mean				
S.D.				
Epiphyseal Ossification tibia	4.80-9.80	4.50-6.30	4.50-9.80	36.037
Range	7.88	5.59	7.67	0.001*
Mean	1.12	0.68	1.27	
S.D.				
Epiphyseal Ossification humeral	2.50-6.50	2.20-3.00	2.20-6.50	22.015
Range	4.35	2.62	4.20	0.001*
Mean	1.10	0.26	1.16	
S.D.				

Table 2: Relation between Epiphyseal Ossification and ICU admission

Table (2), showed the relation between Mean Epiphyseal Ossification Centres and ICU admission, it was found that the neonatal ICU admission show a low epiphyseal ossification centers ($p < 0.05$).

	Neonatal Respiratory distress syndrome		Total	T P
	No "n=91"	Yes "n=9"		
Down score	0-0	1-2	0.00-2.00	1630.7
Range	0	1.78	0.160	0.001*
Mean	0	0.44	0.526	
S.D.				

Table (3): relations between neonatal respiratory distress and down score.

Table (3) displays that there have been statistically significant differences between neonatal respiratory distress and down score ($P < 0.05$)

	Icu admission		Total	T P
	No "n=91"	Yes "n=9"		
Down score	0.00-2.00	0.00-2.00	0.00-2.00	143.75
Range	0.03	1.44	0.16	0.001*
Mean	0.23	0.88	0.53	
S.D.				

Table 4: relations between neonatal IC admission and down score.

Table (4) displays that there have been statistically significant differences between neonatal IC admission and down score (P < 0.05)

		Distal Epiphyseal Ossification Femoral	Epiphyseal Ossification tibia	Epiphyseal Ossification humeral	Neonatal APGAR score 1 min	APGAR score 5 min
Neontal APGAR score	Pearson Correlation	.099	.108	.092		
1 min	Sig. (2-tailed)	.328	.285	.360		
APGAR socre 5 min	Pearson Correlation	.209*	.215*	.202*	.226*	
	Sig. (2-tailed)	.037	.032	.044	.024	
Down score	Pearson Correlation	-.307**	-.316**	-.307**	-.234*	-.443**
	Sig. (2-tailed)	.002	.001	.002	.019	.000

Table 5: Correlations between epiphyseal ossification and both down score and APGAR score at 1 and 5 minutes.

Table (5) displays that there have been statistically significant differences between epiphyseal ossification and both down score and APGAR score at 1 and 5 minutes (P < 0.05) while regarding to neonatal APGAR score 1 min, there have been no statistically significant differences (P > 0.05)

G.A.	Distal Epiphyseal Ossification Femoral	Epiphyseal Ossification tibia	Epiphyseal Ossification humeral
35	3.58±0.74	5.89±0.50	2.69±0.25
36	4.25±0.83	6.27±0.59	3.04±0.23
37	5.35±0.76	7.02±0.60	3.49±0.12
38	6.49±0.32	7.89±0.20	4.19±0.34
39	7.29±1.21	8.45±0.40	4.82±0.55
40	8.48±0.30	9.28±0.29	5.85±0.42
Total	6.20±1.85	7.67±1.27	4.20±1.16
ANOVA	105.25	150.02	190.93
p	0.001*	0.001*	0.001*

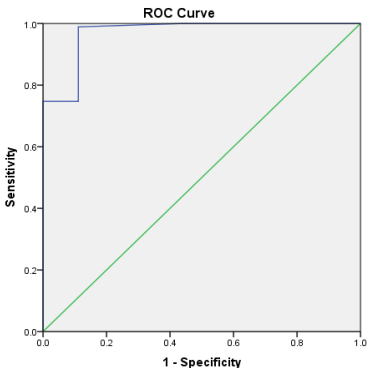
Table 6: Relation between distal Epiphyseal Ossification Femoral, tibia and humeral and gestational age.

Table (6) displays that there has been a statistically significant relationship between epiphyseal ossification femoral and gestational age.

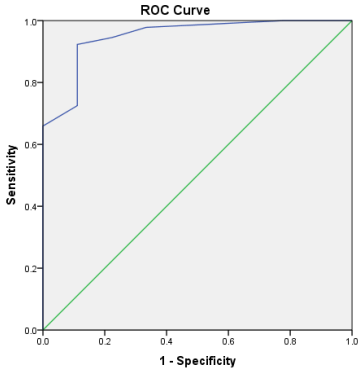
Variable	Area under the curve	Cut off value	P value	Asymptotic 95% C.I. Lower Bound	Asymptotic 95% C.I. Upper Bound	Sensitivity	Specificity	Accuracy
Epiphyseal Ossification Femoral	.970	8	0.0001*	.916	1.000	96.0	92.0	94.0
Epiphyseal Ossification tibia	0.949	8	0.0001*	.884	1.000	94.0	90.0	92.0
Epiphyseal Ossification humeral	0.819	3	0.002*	.683	0.955	80.0	77.0	79.0
Epiphyseal Ossification Femoral + tibia	1.00	16	0.0001*	1.00	1.00	100.0	100.0	100.0p

Table 7: Sensitivity, specificity and accuracy of the Epiphyseal Ossification Femoral, tibia, humeral and Femoral + tibia in predict the respiratory distress.

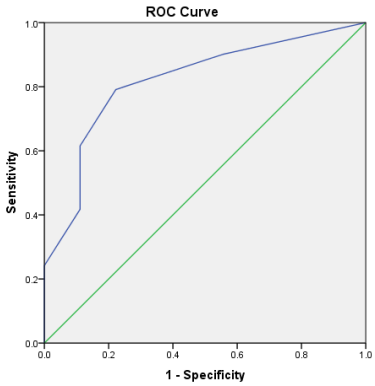
Table (7) displays the sensitivity, specificity, and accuracy of different measurements of ossification femoral.

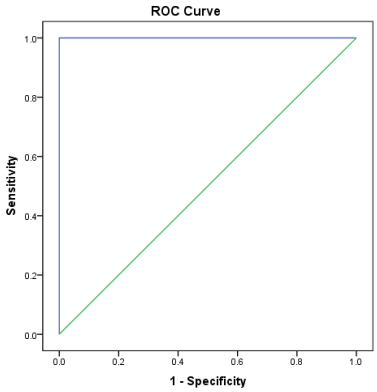


Epiphyseal Ossification Femoral



Epiphyseal Ossification tibia





Epiphyseal Ossification humeral Femoral + tibia

Fig. 1: ROC curve to predict the sensitivity, specificity and accuracy of the Epiphyseal Ossification Femoral, tibia, humeral and Femoral + tibia in predict the respiratory distress.

DISCUSSION

The mean age of mother in our study was 25.38±3.31 years, the mean BMI was 30.98±4.57. The mean gestational age by U/S was 37.79±1.70 weeks, the mean epiphyseal ossification femoral was ranged from 2.1-9.0 with a mean of 6.20±1.84, the epiphyseal ossification tibia was ranged from 4.5-9.8 with a mean of 7.67±1.27, and epiphyseal ossification humeral was ranged from 2.22-6.49 with a mean of 2.22±6.49.

At 32 weeks, ultrasonography was able to detect DFE in 71% of the participants. DFE was not yet evident by ultrasonography in 72% of our 32-week study. In his research, DFE was found in 100% of fetuses at 37 weeks of gestation, precisely as it was in ours.

According to the findings of this study, the DFE is not visible before 28 weeks of pregnancy in the American population, and the average age at which the DFE appears is 32–33 weeks of pregnancy 4. If a DFE is not visible, the foetus is most probably below 34 weeks of gestation, as the DFE is seen in 94% of foetuses at 34 weeks of gestation. [11]

Furthermore, in 84% of foetuses, a DFE of 3 millimetres or larger is linked to a gestational age of greater than 37 weeks. This study's mean gestational age was 36.71, which is comparable. [12]

WU et al. also found that the first occurrence of DFE in Chinese women occurs at 29 weeks of pregnancy. Nevertheless, at the conclusion of 34 weeks, the DFE has been detected in 100% of foetuses, compared to 37 weeks in this research. [13]

Gentili et al. observed that the foetal ossific centres become apparent sonographically at various gestational ages; they are not visible before 24 weeks; the calcaneal ossification centre is visible at 24 weeks; the talar ossification centre is discernible from 26 weeks; the distal femoral epiphyseal ossification centre is visible from 32 weeks; as well as the proximal tibial epiphyseal ossification center from 36 weeks. [14]

The use of radiography to evaluate the epiphyseal ossification centres of long bones as indicators of gestational age was originally documented fifty years ago. The results of maternal abdomen x-rays taken during gestation, as well as x-rays of neonatal limbs, have been used in these studies. [15]

Nevertheless, the danger of subjecting the foetus to radiation, the technical difficulty in identifying the epiphyses ossification centres, and the high variability in the figures produced resulted in the abandonment of this approach for determining gestational age. The development of ultrasonography, on the other hand, alleviated the majority of the technical issues associated with radiography and reduced the concern of fetal radiation. [16]

Ultrasound can detect every epiphysis ossification centre at a far earlier phase if the diameter has been at a minimum of 1 mm. [17]

Women with singleton pregnancies of 30–40 weeks of gestation have been enrolled in prospective research by (Donne et al., 2005), who had similar results. The proximal tibial, distal femoral, as well as proximal humeral ossification centres have been found and measured. [16]

A nomogram of fetal bone growth has been generated with the total of the 3 diameters. The diameters of the DFE and PTE centres were strongly associated with gestational age, but the total of the 3 ossification centres has been even better. When the aggregate of the 3 centres became 7, 11, and 13 mm, the positive predictive values for a foetus with a gestational age of at least 37 weeks became 82%, 94%, and 100%, respectively.

In our study, it was found that 9 cases had neonatal respiratory distress syndrome, and it was found that the mean Epiphyseal Ossification Centers was significantly low in neonatal with respiratory distress syndrome ($p < 0.05$).

Also in this study it was found that 9 cases admitted to ICU, and the neonatal ICU admission show a low epiphyseal ossification centers ($p < 0.05$). It was found that there was a positive significant correlation between mean epiphyseal ossification centers and the APGAR score at 5 minutes. It has also been found that there was a significant correlation with the Down score.

One of the most crucial tasks in deciding whether or not to deliver a foetus is to assess the foetal lung maturation. As far as is feasible, the goal ought to be to protect the foetus against hazards like RDS sequelae, necrotizing enterocolitis, intraventricular bleeding, patent ductus arteriozus, and neonatal sepsis. However, the clinical status of the mom and

the foetus, however, is the most important factor in determining when to give birth. [18]

In their research, Saba et al. (2014) determined that the ultrasonography appearance and size of the epiphyseal ossification centres of the femur, tibia, and humerus could be beneficial in predicting gestational age (GA) in the third trimester of gestation, a period when standard foetal biometrics estimations of GA are least reliable. The existence or lack of the distal femur epiphysis (DFE) seems to indicate GA<33 wks or >33 wks using this approach. [19]

The appearance of proximal tibia epiphyseal (PTE) ossification on ultrasonography is a strong predictor of GA (36) wks, whilst the emergence of proximal humerus epiphyseal (PHE) ossification almost verifies the foetus' maturity.

Saba et al., (2014) found that the proximal humeral epiphysis (PHE) was not observed before week 36 and has been found in a modest percentage of fetuses at 14 % at the 36th week of GA, increasing to 25% at the 37th, 66% at the 38th, and 100% at the 39th and 40th weeks, respectively. And the visualization of proximal humeral epiphysis also implies that fetus has attained maturity. [19]

Similar findings are found in Mahony BS, Callen PW et al.'s (2009) study, which discovered that all foetuses with a visible proximal humeral epiphysis (PHE) exhibited a mature amniocentesis that was a better indication of the maturity of the fetal lung depending on the ratio of L/S and phosphatidyl glycerol in the amniotic fluid. [20]

Similar findings are also found in Kumari et al, (2015) who found that during ultrasonography for proximal humeral epiphysis not seen with the GA below 35 weeks. [21]

And also, similar results are in line with our results in Abd EL-Fattah et al. (2018), who indicated that verification of fetal maturity can also be acquired by evaluating the ossification centres. At a gestational age of 32–33 weeks, the distal femoral epiphysis emerges. [22]

Its size increases linearly with gestational age. A mature amniocentesis lung profile has been linked to ultrasound identification of the proximal humeral epiphysis.

Following the 31st week of pregnancy, the ossification centres appear. The first, second, and third appearances are DFE, PTE, and PHE, in that order. Firstly, the mean size of the distal femoral epiphysis was greater than the proximal tibial and proximal humeral epiphyses, though by the time the woman reaches menstruation age, 38-39 weeks, the epiphysis sizes are about equal.

This indicates that the proximal humeral epiphysis grows more quickly than the proximal tibial and distal femoral epiphyses. In both normal and medicolegal instances, the size and appearance of such epiphyseal centres would be useful in determining the GA and the foetus' viability.

According to the results of the studies, the detection and measuring of such ossification centres would be less influenced by foetal growth restriction or excess growth compared to other anthropometric ultrasonographic measures such as crown rump length, abdominal circumference, and so on. [21]

CONCLUSION

It was concluded that the distal femoral, proximal tibial, as well as proximal humeral ossification centers have a good predictive value for the maturity of the fetal maturity.

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