International Journal of Basic and Applied Medical Sciences ISSN: 2277-2103 (Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/jms.htm
2015 Vol. 5 (2) May-August, pp. 316-321/Kumari et al.
Research Article

OSSIFICATION CENTERS OF DISTAL FEMUR, PROXIMAL TIBIA AND PROXIMAL HUMERUS AS A TOOL FOR ESTIMATING GESTATIONAL AGE OF FETUSES IN THIRD TRIMESTER OF PREGNANCY IN WEST INDIAN POPULATION: AN ULTRASONOGRAPHIC STUDY

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ABSTRACT
The study was conducted to see if the identification of distal femoral, proximal tibial and proximal humeral epiphyseal ossification centers on ultrasonography can be a useful tool for estimating gestational age of fetus at the third trimester. These ossification centers were identified at knee joint and shoulder joint respectively and sizes were measured. Although there are several other parameters to determine the gestational age but studies on using ossification centers as a mean to find out the gestational age and vitality of fetus is not very common. Our study will definitely add a valuable contribution the existing literature.

Keywords: *DFE- Distal Femoral Epiphysis, PTE- Proximal Tibial Epiphysis, PHE- Proximal Humeral Epiphysis, MM- Millimeter, Gestational Age, Ossification Centers*

INTRODUCTION
The accurate dating of pregnancy is critically importantfor pregnancy management from the first trimester todelivery, and is particularly necessary for determining viabilityin premature labor and in post-dates deliveries (Kalish, 2005).
Prior tothe widespread use of ultrasound, caregivers relied on acombination of history and physical examination to clinicallydetermine gestational age. Ultrasound gave clinicians a methodto measure the fetus and therefore to estimate gestationalage. Much of our current clinical practice is based on studiesfrom the 1980s and 1990s.
As new information emerges infields, such as reproductive biology, perinatal epidemiology, and medical imaging, our current clinical practice is beingchallenged. “Certain” menstrual dating, for example, is lesscertain than previously thought (Butt and Lim, 2014). When ultrasound is performed with quality and precision, there is evidence to suggest that dating pregnancy usingultrasound measurements is clinically superior to usingmenstrual dating with or without ultrasound, and this hasbeen advocated and adopted in other jurisdictions (Bottemley, 2009; Gardosi, 1997-1998; Hughes, 2008; Solomon, 2013).
As per the need of hour, our clinicians have to see for alternative means to determine the gestational age and viability of the fetus. And the time of appearance of various epiphyseal ossification centers and their measurements play a key role for the purpose. There has been studies regarding use of Distal Femoral epiphysis as marker for estimating the gestational age but using Proximal tibial and proximal humeral epiphysis and their inter-relation is very rare. The present study will definitely provide an insight for the use of these ossification centers in clinical practice.
The main ossification centers appear ultrasonically as egg shaped echo rich areas. The ossification centers of Distal Femoral and Proximal tibial Epiphysis can be seen at the level of knee joint whereas the proximal humeral epiphysis is seen at shoulder joint. The aim of the study was to see the importance of

distal femoral, proximal tibial and proximal humeral ossification centers as a tool for estimating the gestational ages of fetuses in the third trimester.

MATERIALS AND METHODS

The study was done in 100 normal pregnant women with gestational age from 30 weeks to 40 weeks carrying singleton pregnancies, which had come for routine ultrasonographic checkup in Mahatma Gandhi Mission Medical College Hospital, Navi Mumbai.

The study was reviewed and approved by Ethical Committee of University and written informed consents were taken from all the participants. To be included in the study, women also had to be sure of their last menstrual period and to have had this date confirmed by ultrasonography during first trimester of pregnancy.

All the participants were distributed in six groups of 25 each. First group was of the participants with a fetus of 30-31 weeks of menstrual age, second with 32-33 weeks, third with 34-35 weeks, fourth with 36-37, fifth with 38-39 weeks and sixth was with 40 weeks of menstrual age.During their normal ultrasonographic check-up; the ossification centers were identified as an oval or globoid echo rich area at the knee joint for DFE and PTE and at shoulder joint for PHE by Expert Radiologist. Measurements of the epiphysis were taken from the outer to outer margins in an axial plane along the axial plane along the medio-lateral surface as shown in figures a, b, c and d.

Figure 1: (a) Ultrasonographic Image showing DFE measurementtaken from the outer to outer margins in an axial plane along the axial plane along the medio-lateral surface. (b) Ultrasonographic Image showing PTE measurementtaken from the outer to outer margins in an axial plane along the axial plane along the medio-lateral surface. (c) & (d)Ultrasonographic Image showing PHE measurementtaken from the outer to outer margins in an axial plane along the axial plane along the medio-lateral surface

Once the ossification centers were identified, three consecutive diameters of each epiphysis were taken and largest diameters were recorded for the study and further evaluation. For every group mean diameter of DFE, PTE and PHE were measured. Identification and measurements were done carefully as adjacent structures to the cartilaginous centers i.e. synovium or capsule may be misinterpreted as the epiphyseal centers.As the diameters has to be measured in round figure value i.e. 1,2,3 and so on; so the values after point which were below 0.5 were included in the lower number whicle more than 0.5 were included in the higher number.All the observations were noted, tabulated and statistical analysis was done.

RESULTS AND DISCUSSION

Minimum Estimated Age if all the three i.e. DFE, PTE, PHE were seen = 32.46 weeksMaximum Estimated Age if all the three i.e. DFE, PTE, PHE were seen =36.8 weeksMean Time of appearance of DFE = 32-33 weeksMean Time of appearance of PTE = 34-35 weeksMean Time of appearance of PHE = 35-36 weeks

Chart Showing Correlation of GA (Gestational Age in weeks) with DFE (Distal Femoral Epiphysis in mm)

DFE(mm) / GA(wks)	0	1	2	3	4	5	6	7	8	9		
30-31	23	2									25	
32-33		3	15	6	1						25	
34-35	1		2	3	1	18					25	
36-37					4	1	38				25	
38-39							4	165			25	
40								119		5	25	

Chart Showing Correlation of GA (Gestational Age in weeks) with PTE (Proximal Tibial Epiphysis in mm)

PTE(mm) / GA(wk	0	1	2	3	4	5	6	7	8	9		
30-31	25										25	
32-33	12	13									25	
34-35	1		4	14	6						25	
36-37				2	1	28	3				25	
38-39							5	155			25	
40							2	174		2	25	

Chart Showing Correlation of GA (Gestational Age in weeks) with PHE (Proximal Humeral Epiphysis in mm)

PHE(mm) / GA(wk	0	1	2	3	4	5	6	7	8	9		
30-31	25										25	
32-33	24	1									25	
34-35	4	2	01								25	
36-37		2	7	11	5						25	
38-39						6	14	5			25	
40								7	135		25	

Table showing menstrual age in relation to the mean size of DFE, PTE, and PHE in millimeter

Sr. No.	Menstrual age of fetus (weeks)	Number of Cases	Average measurement of Epiphysis (mm)		
			DFE	PTE	PHE
1.	30-31 weeks	25	0.08 mm	Not seen	Not seen
2.	32-33 weeks	25	2.2 mm	0.5 mm	0.04 mm
3.	34-35 weeks	25	3.9 mm	3 mm	0.9 mm
4.	36-37 weeks	25	5.2 mm	4.5 mm	2.8 mm
5.	38-39 weeks	25	7.04 mm	7 mm	6 mm
6.	40 weeks	25	7.8 mm	7.2 mm	8 mm
7.	Total	150			

From the results we had prepared reference charts for estimating the gestational age in third trimester using Distal Femoral, Proximal Tibial and Proximal Humeral Epiphysis; which were not observed earlier in West Indian Population. As per results of observed cases, the time of appearance of DFE was at 32-33 weeks and before that it was not seen. So we can conclude that during ultrasonography, if DFE has not appeared then the gestational age should be below 32 weeks. Similarly, for PTE if not seen, then the gestational age should be below 34 weeks and for PHE if not seen the gestational age should be below 35 weeks. These results can be used in combination with other anthropometric parameters of Ultrasonography (Birang, 2013).

In 1950's it was recognized that the identification of the fetal skeletal epiphyseal ossification centers were useful for the estimation of gestational age. But due to technical errors, the procedures were not followed. Along with advancement of radiology techniques and use of ultrasound, it was overcome. Most of the the traditional methods that we use today are from 1980's and 1990's.

Donne in a study with three ossification centersspecifies the use of visualization and measurements of these epiphyseal centers as a marker for finding the gestational age in Brazilian population. He found that DFE appeared in 6 of 36 (17 %) as early30 weeks while in our study it was not seen before 30 weeks of age, only in 2 of 25 cases (8%) it appeared at 31 weeks. DFE was detectable in 72% of the cases while in ours it was seen in 100% of the cases at 32 weeks.He used a normogram of fetal bone development using the sum of diameter of DFE, PTE and PHE. Gestational age correlated well with the diameters. Positive predictive values of fetus having gestational age of at least 37 weeks when sum of the three ossification centers was 7, 11 and 13 mm were 82 %, 94 %, and 100 % respectively (Donne, 2005).

In an Iranian population study of DFE, Birang S emphasized the use of DFE as a marker for determining gestational age. A reference chart was also prepared for DFE. He showed the presence of DFE at 29 weeks of gestation in 5 of 100 (5%) and at 30 weeks of gestation in 15 of 100 (15%)as compared to ours it was only 8% at 31 weeks (Birang, 2013).

Just as our study, a study in American population also showed the meantime of appearance of DFE 32-33 weeks (Mahony, 1985). If DFE was not visualized it was concluded to be of below 34 weeks as compared to our study if not seen it was below 32 weeks (Goldstein, 1988; Mahony, 2013).

WU reported that, 29 weeks of gestationfor first appearance of DFE in Chinese population and the presence of DFE was seen in 100 % cases at 34 week of gestation which in ours is 31 weeks for appearance and 35 week for 100% appearance of DFE (Wu, 1996).

Gentili P noted the presence of DFE and PHE ossification centers from 32 weeks and 36 weeks respectively. The size of DFE was greater than or equal to 6 mm in diameter at a gestational age between 31-38 weeks (Gentili, 1984).

Identification of certain US findings suggests that a fetushas reached the third trimester and may correlate withfetal lung maturity and gestational age. These parameters are the epiphyseal ossification centers of the distal femur, proximal tibia, and proximal humerus. The measurement of these ossification centers does not precisely correlate withgestational age; however, their presence may be helpful latein pregnancy when the gestational age is not known. The presence of distal femoral epiphysis has a positive predictive value of 96% forindicating a pregnancy of at least 32 weeks; the proximaltibial epiphysis has a positive

predictive value of 83% for indicating a pregnancy of at least 37 weeks, and the proximal humeral epiphysishas a positive predictive value of 100% for indicating a pregnancy of at least38 weeks (Donne *et al.*,).

The measurement of epiphyseal ossification centers of long bones as marker of gestational age using Radiography was first described about 50 years ago. These studies were based on findings of maternal abdominal x-rays carried out during pregnancy (Reece, 1984; Mahony, 1985; Gottlieb, 2008) and x-rays of neonatal extremities (Donne, 2005). However, the ill effects of radiation exposure to the fetus and neonatal, technical problems in visualization and large variability in figures obtained lead to discontinuation of this practice. However, ultrasonography has solved technical problems as well as the fear of radiation exposure (Donne, 2005). We can measure any epiphyseal center using ultrasonography as long as it is 1 mm in size (Mahony, 1985). Crown Rump Length measured in first trimester is the most accurate method to determine the gestational age. Initially all fetuses grow at the same rate, whereas as a result of different environmental and genetic factors, the variation in size and weight occurs as the gestational age progresses (Gottlieb, 2008). As the epiphyseal ossification centers appear in the last trimester, when all other traditional methods are least accurate, they prove to be useful in evaluating the gestational age and IUGR in pregnancy with unknown dates. Correlation has also been observed between ossification of fetal long bone as detected ultrasonographically and fetal lung maturity (Gentili, 2008).

Conclusion

In observed cases, the ossification centers appeared after 31st week gestation. The order of appearance is DFE, PTE and PHE as first, second and third respectively. At first the average size of Distal Femoral Epiphysis was more than Proximal Tibial and Proximal Humeral Epiphysis but on reaching at a menstrual age of 38-39 weeks, the size of epiphysis become almost same. This shows that the proximal humeral epiphysis is growing at a faster pace as compared to proximal tibial and distal femoral epiphysis. So, the size and appearance of these epiphyseal centers will be helpful to determine the gestational age and viability of the fetus in normal as well as medico legal cases. It can also be drawn from the conducted studies that the identification and measurement of these ossification centers may be less affected by fetal growth restriction or excessive growth than other anthropometric ultrasonographic measurements like Crown Rump Length, Abdominal Circumference, etc. However, sometimes Calcium and mineral deficiency might lead to delay in appearance of the same (Birang, 2013).

There is enormous scope for further research into the possible usefulness of ultrasonographic visualization and measurements of distal femoral, proximal tibial and proximal humeral as well as other epiphyseal ossification centers. Future studies may also focus on validation and degree of reliabilityof these charts with its advantages and disadvantages in relation to the other regional and racial populations.

ACKNOWLEDGEMENT

Author wants to thank the staff of Ultrasonography Unit, M.G.M. Medical College Hospital for their Co-operation**.**

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