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Ultrasonographic Measurement of Femur Length as a Predictor of Menstrual Age and Study Their Relationship in Foetuses of Manipur.

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Abstract: *The study aims at ultrasonographic measurement of foetal femur length as a predictor of menstrual age in second and third trimesters and to study their relations by constructing regression equations. It was a prospective cross sectional study done on 304 antenatal Meitei women who were the plain inhabitants of Manipur. They were of 18 to 35 years of age and 13 to 40 weeks of gestation with known date of last day of normal menstrual period of regular 28 days cycle, attending routine Obstetrics and Gynaecology Department and Radiology Department, RIMS, Lamphelpat, Manipur. The study revealed foetal femur length as a good predictor of menstrual age in second and third trimester with correlation co-efficient R2=0.973 and p<0.001. The study established the linear relationship of the femur length in centimetres with the advancing menstrual age in weeks. It was observed that the length of foetal femur gradually increased from 13+0 to 40+6 weeks of gestation with the mean femur lengths range from 1.2cm to 7.4cm. Normograms of length of foetal femur and menstrual age could be constructed from the study for that particular ethnic group of that particular geographical region of North-Eastern India.*

Keywords: *Fetal femur length (FL), Menstrual age (MA), Regression equation, Last menstrual period (LMP)*

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I. Introduction

Foetal age actually begins at conception, and an equivalent term is conceptional age.[1] The menstrual age is calculated from the conceptional age, based on the assumption of mid-cycle ovulation i.e., menstrual age = conceptional age + 14 days.[1] In clinical obstetric practice, obstetricians use the term gestational age. interchangeably with menstrual age, although gestational age should be equivalent to conceptional age. Gestational age is approximately 280 days, or 40 weeks, elapse on average between the first day of the Last Menstrual Period and the birth. A quick estimate of a pregnancy due date based on menstrual date can be made by adding 7 days to the 9 calendar months from 1st day LMP by Naegele's rule.[2] Foetal period is the time from the beginning of ninth week of intrauterine life to birth.[3]

1.1 Importance of accurate pregnancy dating: The accurate knowledge of Gestational age is important to the obstetrician because it affects clinical management in a number of important ways. First, knowledge of GA is used in early pregnancy for scheduling of invasive procedures such as chorionic villous sampling and amniocentesis, and in the interpretation of biochemical test such as expanded maternal serum biomarker screening, quad screening, for risk assessment for neural tube defects and chromosomal anomalies like trisomy21 and 18, in which the normal range of values changes overtime. Quad test screens for maternal serum levels of Alpha-fetoprotein, Human chorionic gonadotrophin, Un-conjugated estriol, and Inhibin-A which are done most accurately between 16 to 18 weeks of GA. Second, knowledge of GA allows the obstetrician to anticipate normal spontaneous delivery or to plan elective induction or caesarean delivery within the time frame of a term pregnancy from 37 to 42 weeks and to institute measures that will optimize fatal outcome when labour ensues before 37 weeks or fails to ensue after 42 weeks. Thus, differentiation between term and preterm, and characterization of a foetus as postdate depend on GA. Third, it is important in evaluating foetal growth because the normal range for the size of any foetal parameter changes with advancing age. Fourth, IUGR can be confidently diagnosed only if the Gestational age is verified at an early stage. Fifth, knowledge of GA is critical in distinguishing normal from pathological foetal development. Midgut herniation is normal up-to 11 to 12

weeks of gestation but signifies omphalocele thereafter. Sixth, estimation of foetal weight alone or in relation to GA may influence obstetrics management decisions concerning the timing and route of delivery. Thus, all important clinical decisions require knowledge of menstrual age.[1,4,5]

II. Materials and Methods

This was a prospective cross-sectional study carried out at the Departments of Anatomy & Obstetrics and Gynaecology, RIMS, Imphal, between Aug.2016 to Sept.2018. The study was approved by the Research Ethics Board of RIMS, Imphal, Manipur and before inclusion of the patients, informed consents from the respective individuals were taken after fully explaining the purpose of the research work. Full confidentiality of the individual was maintained.

A total number of 304 Antenatal women of Meitei population who are the plain inhabitants of Manipur, 18-35 years of age and parity range of 1-3 with normal pregnancy in between 13^0 to 40^{+6} weeks of gestation who fulfil all the inclusion and exclusion criteria, attending the Obstetrics and Gynaecology OPD and referring for routine ultrasonography in Radiology OPD, RIMS, Imphal, after a complete antenatal check-up by obstetrician and maternal laboratory investigations such as complete blood count, venereal disease research laboratory test, blood urea and sugar, HIV test, urine routine and microscopic test, were selected for the study. Pregnant women fulfilling the study criteria admitted in the antenatal and postnatal wards of Obstetrics and Gynaecology Department, having normal US reports were also selected. Each of those selected pregnant women was included only once in the study.

The following criteria were considered in candidate selection. Inclusion Criteria: Patient with singleton pregnancy and with known date of first day of last normal menstrual period and regular 28 days cycle with no exposure to Oral contraceptive pills in previous 3 months, and with no unusual bleeding; both parents ethnically Meitei. Exclusion Criteria: Multiple pregnancy like twins**;** pregnancy with congenital malformation, IUGR, PIH, eclampsia, family h/o congenital dwarfism; pregnancy with maternal diseases like gestational diabetes, asthma, chronic hypertension, heart disease, anaemia, hypothyroidism etc. which may concomitantly affect normal foetal growth; patients who are smokers and alcoholic.

2.1 Data acquisition: Obstetric ultrasonography was carried out on the patients using SAMSUNG HS70A real-time ultrasound machine, equipped with 3.5 MHz curvilinear transducer probe and an electronic calliper system. All those measurements were done in centimetre.

2.2 Foetal biometrics: The Femur Length was measured after proper alignment of the transducer to the long axis of the ossified diaphysis as shown in Fig.1 according to original technique described O'brien et al [6]. This could be ensured by demonstrating that both the femoral head or greater trochanter and the femoral condyle were simultaneously in the plane of section. The cursors should be positioned at the junction of the bone with the cartilage. The cartilaginous epiphysis was not included in the measurement. In the third trimester, particular care was taken not to include the epiphysis in the measurement. The distal femoral epiphyses are visible after 32 weeks. The proximal tibial epiphysis becomes visible at around 35 weeks.

2.3 Statistical analysis: The data were entered and analysed in a computer, using MS Excel 07 and Statistical Package for Social Sciences version 21. The descriptive statistics like mean, standard deviation, percentage were performed for the measurements of femur lengths at weekly intervals. Regression analyses and Regression equations for menstrual age and femur length were established. The P value < 0.05 was taken as significant.

III. Observations

3.1 Relationship between the menstrual age and the length of foetal femur: The results of measurements of the foetal femur length at each week of menstrual age from 13- 40 weeks were shown in Table 1. For the purpose of statistical study, adjustment had been made to get the Menstrual age in complete figures as "13weeks = 13weeks + 0day to 13weeks + 6 days" (1) and so on. It was observed that the length of foetal femur increased from 1.2 cm at 13 weeks to 7.4 cm at 40 weeks of gestation. The length of femur in foetuses of subjects from 13 to 40 weeks of gestation was plotted with menstrual age and it was observed that there is a linear relationship between the length of femur in cm and the menstrual age in weeks as shown in Fig. 2. The mean values of length of femur in cm plotted against advancing menstrual age from 13 to 40 weeks showed a perfect increasing linear trend with increasing menstrual age as in Fig. 3. From the results of Table 2, it could be seen that a significant and positive relationship was observed between menstrual age and the length of femur where $R=0.9893$ & $p<0.05$. It means that the menstrual age and the length of femur are dependent on each other. The length of foetal femur in cm increases with increasing menstrual age in weeks.

3.2 Regression analysis of relationship between the menstrual age and the length of foetal femur: The Simple Linear Regression Analysis was done to assess the dependent variable, Menstrual Age MA by another

independent variable Femur Length in total of 304 cases as shown in Table 3. The Table showed that foetal femur length was a good predictor of menstrual age with $p<0.001$. In this, 97% of the variability in menstrual age could be predicted by the femur length fitted in the model with $R^2= 0.973$ & $p<0.001$. The Regression Co-efficient constant was 7.86 and Regression Co-efficient for FL was 4.03. The data showed that the length of foetal femur is directly related to menstrual age, with simple linear regression modelling as shown in fig.4, yielding the equation in the form of y= a + b1x1 where 'y' is the dependent variable, 'a' is the regression coefficient constant, b1 is regression coefficient for independent variable and x1 is the independent variable itself i.e. MA= a + b1×FL where MA is the menstrual age in weeks and FL is the length of femur in cm.. Therefore, "MA = 7.86+4.03×FL" (2) Hence, the menstrual age can be predicted from the formula. Also, a simple linear regression equation "Y = -1.77 + 0.24 × MA" (3) where Y = femur length in cm. as the dependent variable and MA = Menstrual age in weeks as the independent variable, was derived as shown in Table 4 and femur length can be predicted from the formula.

IV. Figures and Tables

Fig. 1: Distance between the two asterisks is measured as femur length

Menstrual age (wks)	Number of cases	% of cases	Mean Femur Length (cm)	±SD
13	4	1.3	1.2	0.14
14	10	3.3	1.4	0.27
15	14	4.6	1.7	0.28
16	10	3.3	2.1	0.24
17	12	3.9	2.3	0.21
18	11	3.6	2.6	0.28
19	14	4.6	2.8	0.20
20	12	3.3	3.2	0.34
21	17	5.6	3.8	0.20
22	12	3.9	3.9	0.33
23	17	5.5	4.4	0.33
24	8	2.6	4.7	0.36
25	5	1.6	4.8	0.17
26	7	2.3	5.0	0.36
27	9	2.9	5.3	0.18
28	8	2.6	5.5	0.13
29	8	2.6	5.7	0.15
30	11	3.6	5.9	0.16
31	9	2.9	6.1	0.32
32	10	3.3	6.2	0.33
33	9	2.9	6.4	0.28
34	9	2.9	6.6	0.17
35	8	2.6	6.8	0.19
36	25	8.2	6.9	0.27
37	12	3.9	6.9	1.06
38	15	4.9	7.2	0.21
39	13	4.3	7.3	0.26
40	5	1.6	7.4	0.13

Table 1: Effect of advancing menstrual age on the lengths of foetal femur.

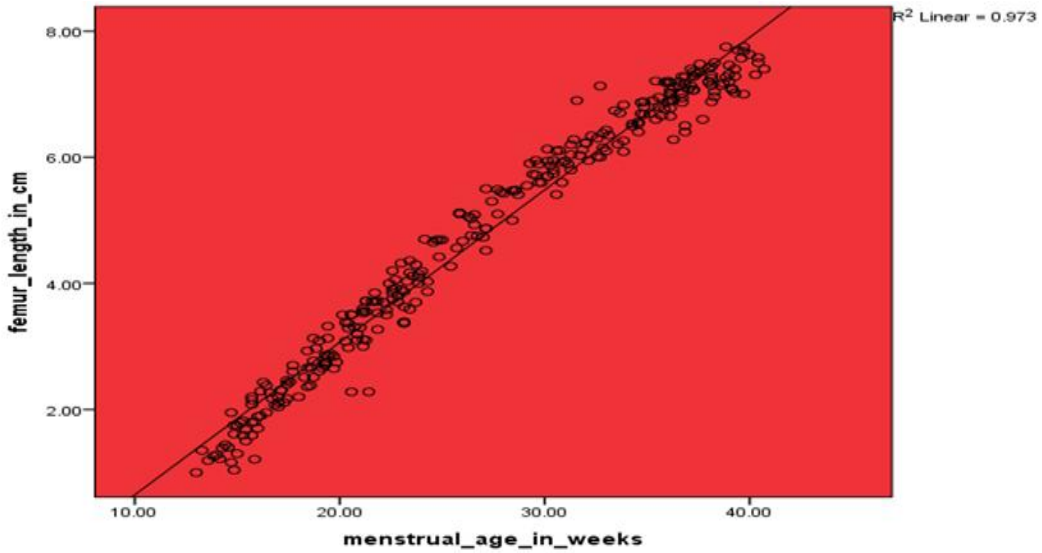

Fig. 2: Graph showing linear relationship between the length of femur in cm and the menstrual age in weeks of all cases N=304

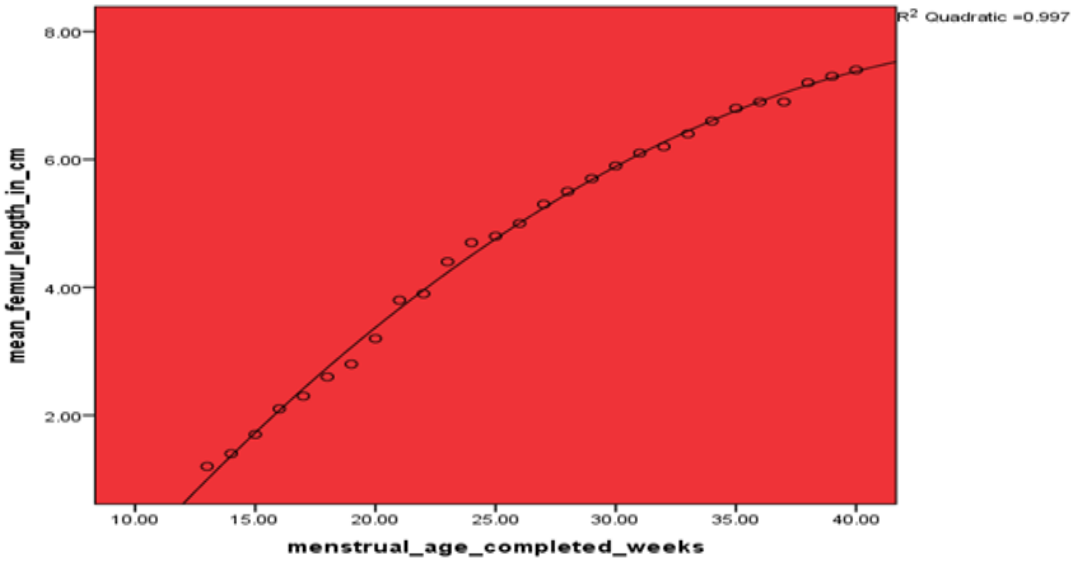

Fig.3: Graph showing relationship of the foetal mean femur length in cm to advancing menstrualage from 13 to 40 weeks.

Table 2: Correlation co-efficient (R) between the menstrual age in weeks withthe length of foetal femur in cm by karl pearson's correlation method.

		menstrual_age_in_weeks	femur_length_in_cm
menstrual_age_in_weeks	Pearson Correlation	1	.986**
	Sig. (2-tailed)		.000
	N	304	304
femur_length_in_cm	Pearson Correlation	.986**	1
	Sig. (2-tailed)	.000	
	N	304	304

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

Table 3: Simple linear regression analysis of the menstrual age by the lengthof foetal femur in cm. in total samples N=304

Independent variable	Regression coefficient	SE of regression coefficient	t-value	p-value	F-value	Regression equation
constant	7.86	.199	39.386	.000	10935.43	"MA=7.86+4.03 ×FL"(R^2=0.973,P <0.001)
FL	4.03	.038	104.573	.000		

Table 4: Simple linear regression analysis of the length of foetal femur in cm bythe menstrual age in weeks in total samples N=304

Independent variable	Regression coefficient	SE of regression coefficient	t-value	p-value	F-value	Regression equation
constant	-1.77	.065	-27.057	0.000	10935.43	FL=-1.77+0.24×MA (R^2=0.973,p<0.001)
MA	0.24	.002	104.573	0.000		

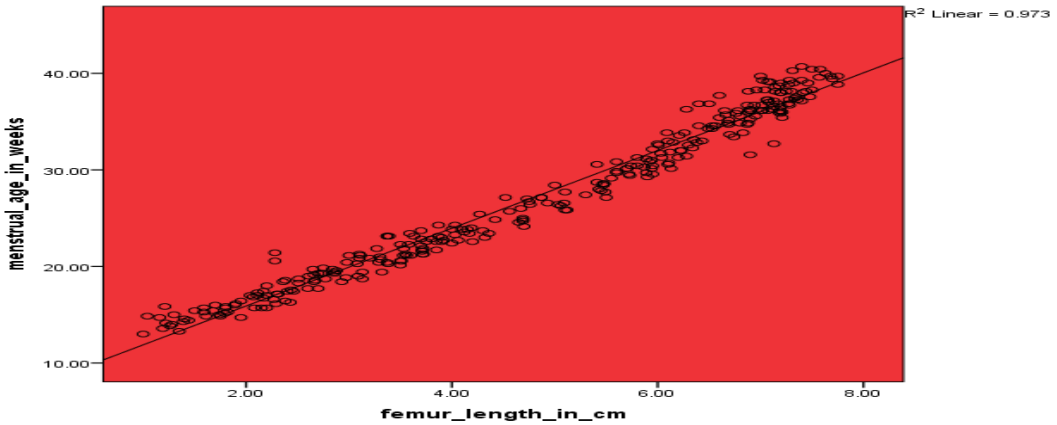

Fig.4: Graph showing simple linear relationship of menstrual age in week as dependent variable to femur length in cm as independent variable.

V. Discussion

In Hadlock etal study in USA on 338 normal foetal FL, the linear function was an accurate model for describing the relation between femur length and menstrual age with r^2=96.6% but the linear quadratic function was the optimal model for predicting menstrual age from femur length with r^2=97.3%. The regression equation for their data was "menstrual age =10.38+0.2256 (FL) + 0.001948$(FL)^2$"(4) where MA in weeks and FL in millimetres. [6]

In Chaithra Rao BR et al in Karnataka, India, study on 152 pregnant women established the linear relation between the diaphyseal length of femur and gestational age. They develop simple linear regression equation of "gestational age = 5.994+4.370 Femur length" (5) where GA in weeks and FL in cm. The correlation coefficient between GA and diaphyseal length of femur was 0.9893 and was highly significant with p< 0.001. [7]

In L. J. Salomon et al constructed new reference charts and equations for foetal Femur Length, Bi-parietal Diameter, head circumference and abdominal circumference using a large sample of 19647 of foetuses

examined at 15 to 40 weeks gestation. Raw data were fitted satisfactorily with a cubic polynomial model for each biometric parameter as follows: "FL = -27.085 + 2.9223 × GA + 0.0148 × GA^2 - 0.0006 × GA^3" (6) with R^2 = 96.33, where FL is in mm and GA is in weeks. [8]

T. N. Leung constructed new reference charts and equations for foetal biometry in Hong Kong ethnic Chinese population involving 709 women with singleton pregnancies between 12 to 40 completed weeks of gestation. The foetal biometric measurements recorded included Bi-parietal Diameter, Abdominal Circumference, Head Circumference and FL. For each measurement, regression model were fitted to estimate the mean and SD at each GA. The raw data were fitted to the Gestational Age in weeks satisfactorily with a cubic polynomial model. The formula for the regression model of FL and its correlation co-efficient R^2 are as follows: "FL = -4.445082 + 0.492073 × GA -0.0067 × GA^2 + 0.000042 × GA^3" (7) with R^2 =0.986 where FL is in cm and GA is in weeks. [9]

In Mador ES et al study in Nigeria on FL measurement in 13,740 pregnant women between 12 to 42 weeks gestation, the best fitted regression model to describe the relationship between FL and GA was second order polynomial regression equation "$Y = -0.017x^2 + 3.2794x-25.282$" (8) with a correlation of r^2=0.999 & $p<0.001$ where Y is FL in mm and x is GA in weeks. [10]

In the present study, the simple linear regression equation derived for the calculation of menstrual age using the length of foetal femur is "MA = 7.86 + 4.03 × FL" (9) and that for the calculation of femur length is "FL= -1.77 + 0.24 × MA" (10) where MA is the menstrual age in weeks and FL is the length of femur in cm. Femur lengths plotted against menstrual age showed a linear growth curve. Similar observations were made in the previous studies [6, 7, 8, 9, 10.].

VI. Conclusion

Ultrasonography is the most effective way to date pregnancy nowadays. The relationship between the foetal femur length and the menstrual age is Linear as shown by the regression equations "MA = 7.86 + 4.03 × FL" (11) & "FL= -1.77 + 0.24 × MA"(12). The length of foetal femur is a good predictor of Menstrual Age in second and third trimesters. We can predict the femur length or the menstrual age of any Meitei foetus by using the regression equations derived from the present study. Thus, foetal femur length is an important additional parameter for estimating menstrual age along with other parameters like Bi-parietal diameter, Head circumference. Foetal femur length shows a high correlation with menstrual age and a low inter-observer variation, thus suggesting their usefulness in the assessment of the menstrual age as an alternative basis, when it is impossible to obtain reliable measurements of the bi-parietal diameter like in deep pelvic engagement of the vertex, dolichocephaly etc. A mildly foreshortened femur is used as a minor marker for Down syndrome but a dramatically foreshortened one prompts an evaluation for a lethal skeletal dysplasia. Limitation of the present study is the small sample size and better results can be expected from larger study population.

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