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ULTRASONOGRAPHIC MEASUREMENTS OF FETAL FEMUR LENGTH IN NORMAL PREGNANT WOMEN : A CASE SERIES STUDY

Anatomy

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ABSTRACT

Background: The femur is generally preferred over the other long bones as a means of predicting gestational age (GA) because of its size, visibility and ease of measurement.

Objectives: 1. To establish a reference table for femur length (FL) in normal pregnant women of 20 to 38 weeks of gestation from Belagavi District, Karnataka. 2. To find out the predictive accuracy of gestational age determined by FL with gestational age determined by LMP method.

Materials and Methods: The data was collected by using predesigned pretested questionnaire from September 2016 to January 2018. Total 768 singleton pregnant women with minimum 30 cases for each gestational week from 20 to 38 weeks of gestation, fulfilling inclusion and exclusion criteria were studied.

Statistical Analysis: The data was analyzed using Statistical Package for Social Sciences (SPSS) version 20. For each gestational week percentages, mean, standard deviation, range, standard error, percentiles and regression equation etc. were performed for femur length.

Results: The regression equation derived for FL measurements was ***GA = 5.358 + (4.40 X FL in cm)*** where correlation coefficient 'r' = 0.977 (highly correlated) and proportion of variation in dependent variable (GA) - R^2 = 0.955. By this regression equation, the accuracy in prediction of gestational age by FL measurement alone was ranging from 96.12 % at 38 weeks to 99.96 % at 23 weeks of gestation.

Conclusion: The present study findings confirmed that the fetal FL measurements significantly vary among different population groups due to genetic, racial, and ethnic factors. So generation of population specific reference tables and regression equations for various fetal biometric parameters by a large scale study at national level is required for more precise reporting of GA and expected date of delivery (EDD) by ultrasonography.

KEYWORDS

Fetal femur length, Gestational age, Ultrasonographic measurements

Introduction

Successful obstetric care needs an accurate knowledge of age of an unborn baby i.e. GA. Uncertain gestational age has been associated with adverse pregnancy outcomes including low birth weight, spontaneous preterm delivery and perinatal mortality, independent of maternal characteristics[1]. Ultrasonographic fetal biometry is the most widespread method used to establish gestational age, estimate fetal size and monitor its growth. Many curves and reference tables for fetal biometry have been published in the literature, using mean values for the biparietal diameter, head circumference, abdominal circumfer ence, and femur length, which allow estimation of the fetal weight[2,3].

On the basis of the data derived from pregnancies with known conception dates, ultrasound determines the fetal age to within 5 days in first trimester and less than 7 days in second trimester in 95% of cases[4].

Fetal biometry is influenced by different variables like physiological and pathological changes such as maternal height and weight, drug or tobacco exposure, fetal sex, ethnicity, genetic syndromes, congenital anomalies and placental failure[5,6]. Several standard charts of various fetal parameters have been fed into ultrasound machines for ready reference.[7,8]. A study by Lim et al[9] in 2000 found that Indian fetuses have significantly longer FL as compared to Non-Indian (Malay and Chinese) fetuses. Prashant Acharya et al[10] concluded that if western parameters are applied to all, intrauterine growth restriction (IUGR) will be over diagnosed and correct dating will be wrong for other patients. Various other studies have determined that our fetal measurements are smaller than Caucasian fetal measurements [4,11-15]. Use of charts derived from a different population may lead to errors in diagnosis of gestational age and over-diagnosis of intrauterine growth restriction, over or under estimation of gestational age and expected date of delivery[16]. Femur is generally preferred over the other long bones as a means of predicting GA because of its size, visibility and ease of measurement. Most studies suggest that FL is an accurate predictor of menstrual age in early second trimester (2 SD = $\pm$ 1 week), but again variability increases as pregnancy advances[17].

The difference in mean values with other ethnic groups indicate that single formula cannot be used for calculation of GA by FL and each population needs different growth charts for accurate calculations.[4]

Therefore, the present study was designed to determine the relationship between fetal FL and GA with $\pm$ 2 SD, to form a reference table for FL and to find out the predictive accuracy of gestational age determined by FL with GA determined by last menstrual period (LMP) method in normal pregnant women from 20 weeks to 38 weeks of gestation from Belagavi District, Karnataka, India.

Aims and Objectives:

1. To establish a reference table for FL in normal pregnant women of 20 to 38 weeks of gestation from Belagavi District, Karnataka.
2. To find out the predictive accuracy of gestational age determined by FL with gestational age determined by LMP method.

Materials and Methods:

A random case series study was done from September 2016 to January 2018. 768 pregnant women with minimum 30 cases for each gestational week from 20 to 38 weeks of pregnancy referred to the Department of Radiology, Belagavi Institute of Medical Sciences (BIMS), Belagavi by antenatal clinic of Department of Obstetrics and Gynaecology (OBG) for routine antenatal scanning were studied after clearance from Institutional Ethics Committee. Antenatal cases with knowledge about exact date of last menstrual period (LMP) with regular menstrual cycles of 26-33 days[18] for at least 3 cycles before conception, with delivery of a live baby with birth weight more than or equal to 2500 grams, fundal height corresponding to duration of pregnancy as per obstetricians finding, who delivered within one week of the expected date of delivery (EDD) and who delivered a newborn baby without any congenital abnormality were included in the study for analysis. Exclusion criteria were - pregnant women with age below 18 and above 35 years, with height below 140 cm, history of drug abuse, tobacco / gutkha use before and during pregnancy, oral contraceptive pills for 3 months prior to conception, and previous baby with low birth weight. women with Diabetes mellitus, hypertension detected during examination or developing later during pregnancy, women with multiple gestations, oligohydromnios, polyhydromnios, intrauterine growth retardation, or intrauterine death, women with uterine abnormalities like fibroids, bi-cornuate uterus, etc.

Method of collection of data:

A predesigned, pretested, structured proforma was used for each subject separately. Ultrasonographic examination of each pregnant

woman fulfilling inclusion criteria was done after submission of completely filled 'Form F' in compliance to Pre-Conceptional and Pre-Natal Diagnostic Techniques (PCPNDT) Act, duly signed by the women undergoing ultrasonography and the radiologist conducting ultrasonography. Using standard methodology, the reading of only first examination of each patient was included for the study purposes, although some patients underwent multiple ultrasonographic examinations during their pregnancy period.

The patients or close relatives were contacted for information about delivery like date of delivery, onset of labor (spontaneous or induced), mode of delivery (vaginal or caesarean section or assisted one), place of delivery, birth weight of the baby, any congenital anomaly detected in newborn baby, etc. The ultrasound examination was done by a single radiologist on one ultrasound machine - iU22 Philips make real-time machine with 3.5 MHz electronic curvilinear transducer.

Sample size calculation:

A sample size of 15 – 18 cases for each gestational week from 20 to 38 weeks was calculated by using the following formula. $\mathbf{n = (Z^2 X S^2) \div d^2}$ Where, n = required sample size, Z= value for α error (99%) = Z value, S = Standard Deviation from reference studies [4,19], d = Clinically expected variation (5% of mean value).

Adjusted sample size of 26 for each gestational week was calculated by considering around 30% exclusion of cases for various reasons mentioned in inclusion and exclusion criteria. Of the total 1037 cases initially included for the study, 269 cases were excluded after their follow up till delivery for various reasons as mentioned above in inclusion and exclusion criteria. Thus, finally present study included 768 cases for data analysis.

Statistical Analysis:

The data was analyzed using MS Excel and SPSS version 20. The basic categorical variables were reported as frequencies and percentages. A box plot of the mean, first quartile, third quartile and extreme measurements of FL for each gestational week from 20 to 38 weeks of gestation by LMP in study subjects was also plotted. The descriptive statistics (mean, standard deviation and range, standard error, percentiles and regression equation) were performed for FL measurements for each gestational week.

Results:

The present study included total 768 cases between 20 to 38 weeks of gestation for analysis ranging from 34 to 51 cases per gestational week as shown in Table 1. The average age of the study subjects was 23.59 ± 3.28 years ranging from 18 to 35 years. The mean height observed was 151.13 ± 3.43 cm. Majority of the subjects (53.65%) were educated up to secondary school, followed by higher secondary school (20.05%) with average education status of 9.14 ± 3.14 standard. 42 subjects (5.47%) were illiterates. Almost all (99.61%) were housewives/home makers and around 2/3rd cases were from rural area. 42.97% cases were primigravidae and 427 (55.60%) were from below poverty line family. Majority (79.30%) of the cases delivered in a government health institutes and 89.19% cases delivered normally. 47.79% newborns were females and 62.89% newborns were weighing between 2500 to 2700 gms with average birth weight of 2712.22 ± 181.66 gms.

The average GA observed in the present study with reference to FL measurements is as shown in Table 2. The gestational week wise descriptive statistics of FL measurements is as shown in Table 3. The difference in minimum and maximum FL values went on increasing with advancing GA (0.4 cm at 20 weeks to 1.4 cm at 37 weeks of gestation).

Figure 1 shows the graph of 5th, 50th and 95th percentile values of fetal FL values according to gestational week which shows increasing FL with advancing gestational age. The regression equation derived for FL measurements was **GA = *5.358 + (4.40 X FL in cm)*** where correlation coefficient 'r' = 0.977 (highly correlated) and proportion of variation in dependent variable (GA) - $R^2 = 0.955$. By this regression equation, the accuracy in prediction of gestational age by FL measurement alone was ranging from 96.12 % at 38 weeks to 99.96 % at 23 weeks of gestation. Table 4 shows different regression equations for FL measurements by different studies.

Figure 2 shows box plot of the mean, first quartile, third quartile and extreme measurements of FL for each gestational week from 20 to 38 weeks of gestation by LMP in study subjects.

Table 1: Socio-demographic profile of study cases:

Sr No	Particulars	Total Cases N = 768 (%)	Mean ± SD
1	**Age (18-35 years)**	143 (18.62)	**23.59 ± 3.28 years**
	- < 20	451 (58.72)	
	- 21 to 25	151 (19.66)	
	- 26 to 30	23 (02.99)	
	- 31 to 35		
2	**Height (cm)**	36 (04.69)	**151.13 ± 3.43 cm**
	- 141 - 145	337 (43.88)	
	- 146 – 150	332 (43.23)	
	- 151 – 155	58 (07.55)	
	- 156 – 160	05 (00.65)	
	- > 160		
3	**Education Status**	42 (05.47)	**9.14 ± 3.14**
	- Illiterate	131 (17.06)	
	- Primary School	412 (53.65)	
		154 (20.05)	
	- Secondary School	29 (03.78)	
	- Higher Secondary School		
	- Graduate & Above		
4	**Parity**	330 (42.97)	**0.74 ± 0.77**
	- 0	325 (42.32)	
	- 1	96 (12.50)	
	- 2	17 (2.21)	
	- >2		
5	**Birth weight of Newborn (grams)**	483 (62.89)	**2712.22 ± 181.66 gm**
	- 2500 – 2700	247 (32.16)	
		29 (03.78)	
	- 2800 – 3000	09 (01.17)	
	- 3100 – 3300		
	- > 3300		

Table 2: Average Gestational Age for FL Measurements (3.1 to 7.6 cm)

Femur Length in cm	No of Cases	Average Gestational Age ± SD	Femur Length in cm	No of Cases	Average Gestational Age ± SD
3.1	10	20.30 ± 0.35	**5.4**	35	29.09 ± 0.96
3.2	15	20.61 ± 0.46	**5.5**	19	29.96 ± 1.21
3.3	18	20.64 ± 0.43	**5.6**	19	30.15 ± 1.26
3.4	9	20.93 ± 0.71	**5.7**	26	30.29 ± 1.41
3.5	14	21.40 ± 0.46	**5.8**	21	31.04± 0.69
3.6	14	21.94 ± 0.63	**5.9**	17	31.72 ± 0.79
3.7	15	22.08 ± 0.51	**6.0**	23	32.60 ± 1.48
3.8	15	22.39 ± 0.75	**6.1**	21	32.83 ± 1.59
3.9	15	23.09 ± 0.58	**6.2**	19	33.17 ± 1.58
4.0	10	23.45 ± 0.49	**6.3**	19	33.23 ± 1.57
4.1	12	23.71 ± 0.81	**6.4**	16	34.25 ± 1.46
4.2	18	24.16 ± 1.09	**6.5**	14	34.72 ± 1.57
4.3	14	24.53 ± 0.72	**6.6**	24	35.10 ± 1.35
4.4	14	25.14 ± 1.07	**6.7**	18	35.58 ± 1.52
4.5	18	25.34 ± 0.84	**6.8**	25	35.91 ± 1.49
4.6	24	25.50 ± 0.94	**6.9**	27	36.56 ± 1.34
4.7	24	26.09 ± 0.94	**7.0**	14	36.93 ± 1.25
4.8	11	26.77 ± 0.85	**7.1**	19	37.47± 1.00
4.9	23	26.90 ± 0.95	**7.2**	08	37.64 ± 0.80
5.0	13	27.61 ± 0.92	**7.3**	09	37.87 ± 1.33
5.1	16	27.88 ± 0.83	**7.4**	04	38.08 ± 0.53
5.2	20	28.28 ± 1.01	**7.5**	05	38.29 ± 0.66
5.3	21	28.46 ± 0.83	**7.6**	03	38.48 ± 0.36
			Total Cases	**768**	

Table 3: Descriptive Statistics of FL in study subjects

Gestational Age	Mean ± SD	Min	Max	Std Error	95% Confidence Interval	
					Lower	Upper
20	3.25 ±0.11	3.1	3.5	0.02	3.21	3.28
21	3.51±0.18	3.1	3.8	0.03	3.45	3.56
22	3.79±0.18	3.4	4.2	0.03	3.73	3.86
23	4.10±0.25	3.6	4.6	0.04	3.6	4.6
24	4.26±0.21	3.8	4.7	0.04	4.18	4.33
25	4.59±0.21	4.2	5.2	0.03	4.53	4.66
26	4.67±0.21	4.2	5.1	0.03	4.61	4.73
27	5.05±0.24	4.5	5.7	0.04	4.98	5.12
28	5.26±0.21	4.7	5.7	0.03	5.2	5.32
29	5.44±0.19	5.0	5.7	0.03	5.38	5.49
30	5.69±0.23	5.3	6.3	0.03	5.63	5.76
31	5.97±0.24	5.4	6.5	0.04	5.89	6.05
32	6.02±0.34	5.5	6.8	0.06	5.91	6.14
33	6.25±0.24	5.7	6.7	0.04	6.17	6.32
34	6.48±0.3	6.0	7.0	0.05	6.37	6.58
35	6.66±0.24	6.2	7.3	0.04	6.58	6.74
36	6.86±0.23	6.3	7.3	0.04	6.78	6.94
37	6.92±0.28	6.1	7.5	0.05	6.82	7.01
38	7.18±0.26	6.6	7.6	0.04	7.09	7.27

Figure 1: Graph showing the percentile values of fetal FL measurements

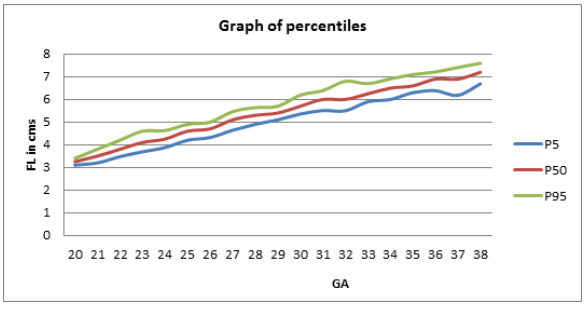
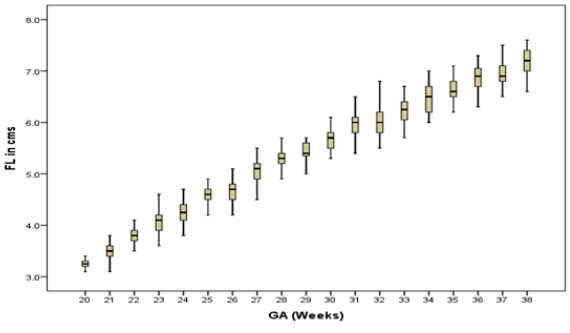


Figure 2: Box plot of fetal FL measurements with gestational age



Discussion:

Determination of GA by ultrasound examination has now become an integral part of antenatal care. Different studies have shown that fetal FL measurement is one of the reliable and valid parameter for fetal age estimation[4,16,17,20,22,24,25]. As seen in Table 5, there was difference in mean values of FL in present study and that of the other study findings[20,21,23]. In comparison with values of present study and Hadlock's and other study values, the observed difference in was more with advancing gestational age. The observed difference was found to be statistically significant (P value less than 0.05). The local Radiologists and Obstetricians follow the reference values published by Hadlock et al for assessment of gestational age and fetal well-being, but however, there are more chances of over-diagnosis of intra-uterine growth retardation and wrong prediction of expected date of delivery especially at advancing gestational age For 3.2 cm FL value, the mean gestational age found was 19.44 weeks in this study while that in other studies it was found to be 19.6 weeks[20], 20.1 weeks [21], 18.7 weeks[23] and for 7.6 cm FL value, the gestational age was found to be 38.8 weeks in the present study, while for the same FL value in other similar studies, it was 38.8 weeks[20], 38.2 weeks[21] and 40 weeks[23].

Jeanty et al[21] reported a uniform variability for the FL age estimate of ± 2.1 weeks throughout the second and third trimesters of pregnancy, suggesting that the FL is just as accurate in predicting age at 40 weeks as it is at 14 weeks. The variability in estimation of gestational age in this study by FL measurements was ± 3 to 4 days while it was ± 8 days in a similar study by Gupta et al[4], ± 5 days[26], ± 5 days[27] and ± 3-3.5 weeks [28]. Hence, we need to have reference tables prepared on local population for more accurate and reliable estimation of gestational age and also for diagnosis of overall fetal growth and well-being.

Table 4: Comparison of equations for predicting GA (weeks) from FL measurements

1	Present study	*GA = 5.358 + (4.400 X FL in cm)*
2	Hadlock et al[20]	GA = 10.38 + 0.2256 x F + 0.001948 x F^2
3	Jeanty et al[21]	GA = 9.541 + 0.298 x F + 0.002 x F^2
4	O' Brien et al[22]	GA = 3.786 + 0.32 x F
5	Hohler CW et al[23]	GA = 9.18 + 0.267 x F + 0.002 x F^2

F=FL in mm

Table 5: Comparison of Mean GA derived from FL measurements by regression equations by different studies

FL (cm)	Present studyGA(Weeks)	Hadlock et al[20]	Jeanty P et al[21]	Hohler et al[23]
3.2	19.44	19.6	20.1	18.7
3.4	20.32	20.3	20.9	19.4
3.6	21.20	21.0	21.6	20.1
3.8	22.08	21.8	22.4	20.8
4.0	22.96	22.5	23.1	21.5
4.2	23.84	23.3	23.9	22.3
4.4	24.72	24.1	24.7	23.1
4.6	25.60	24.9	25.4	24.0
4.8	26.48	25.7	26.2	24.9
5.0	27.36	26.5	27.0	25.8
5.2	28.24	27.4	27.8	26.7
5.4	29.12	28.2	28.6	27.6
5.6	30.00	29.1	29.5	28.6
5.8	30.88	30.0	30.3	29.7
6.0	31.76	30.9	31.1	30.7
6.2	32.64	31.9	32.0	31.8
6.4	33.52	32.8	32.9	32.9
6.6	34.40	33.8	33.7	34.0
6.8	35.28	34.7	34.6	35.2
7.0	36.16	35.7	35.5	36.4
7.2	37.04	36.7	36.4	37.6
7.4	37.92	37.7	37.3	38.8
7.6	38.80	38.8	38.2	40.0

Conclusion:

Fetal FL is one of the most accurate and important parameter for estimation of gestational age. The present study findings confirmed that the fetal FL measurements significantly vary among different population groups due to genetic, racial, and ethnic factors. Thus there is strong possibility of overestimation or underestimation of GA and EDD when the fetal biometry parametric measurements of one population is used for other racial or ethnic groups. So generation of population specific reference tables and regression equations for various fetal biometric parameters by a large scale study at national level is required for more precise reporting of gestational age and EDD by ultrasonography.

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