Section: Anatomy

Original Research Article

DETERMINATION OF GESTATIONAL AGE BY FETAL FEMUR LENGTH ESTIMATION

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Abstract

Background: Sonographic determination of fetal size, for the purpose of gestational age determination or the detection of fetal growth anomalies is an extremely important part of modern prenatal care. Objective: To establish normal ranges of fetal growth for femur length measurement from 11 weeks of gestational age onwards using linear and multiple regression analysis of data. **Materials and Methods:** This study was conducted in Department of Anatomy, in collaboration with Department of Obstetrics and Gynaecology and Department of Radiology at Rohilkhand medical College and Hospital, Bareilly. **Results:** Most of the females in this study group belonged to urban area (Bareilly district). The age of females in this study ranged from 18 years to 42 years, mean age was 24.98yrs with maximum women upto 90% falling between 21 to 30 yrs of age.Femur length which has been measured was earliest available in a pregnancy of 11 weeks 4days in our study. It has been measured up to maximum of 42 weeks 3 days. The measurement of femur length ranged from 7.05 mms to 74.5 mms during above mentioned period of gestation. Femur Length has been measured in a plane where the full femoral diaphysis is seen almost parallel to the transducer and the measurement is made from one end of the diaphysis to another. **Conclusion:** The predicted femur length in the present study is almost equal to the predicted femur length in the study done by Hadlock. The standard deviation in our study is sometimes greater than those of other studies.

INTRODUCTION

The move toward measurement of several parts of the fetal anatomy has been called fetal biometry. Since a significant proportion of pregnant women are unsure of their last menstrual period, gestational age determination frequently is based on sonographic measurements as more accurate information on gestational age can be provided by ultrasound assessment that is why it is currently widely recognized to be the method of choice.

Predicting gestational age from femur length is ± 9.5days between 12-23 weeks but between 23-40 weeks variability is ± 22days.[1] Fetal femur length can be used as a adjunct in estimating menstrual age and as a screening tool for diseases that effect fetal limb growth e.g. dwarfism, osteogenesisimperfecta.[2] Shortening of femur length in the second trimester appears to be useful screening parameter for fetal Down syndrome.

With advancing gestational age, physical examination also tends to be inaccurate. In vitro fertilization, with known date of conception, is likely the most accurate means of predicting gestational age (±1 day). However, in most pregnancies, the date of ovulation or conception cannot be as accurately predicted so establishment of gestational age by other methods is required. In limited number of cases, basal body temperature and luteinizing hormone surge indicator are also used in estimation of gestational age with an accuracy of ±6 days.

The advent of ultrasound has allowed a more direct means of assessing fetal structures and development. Measurement of various fetal body parts is known as fetal biometry. Ultrasound assessment of gestational age is feasible in a majority of pregnancies and may be used to establish gestational age with greater accuracy than physical examination.

Apart from these transcerebellar diameter.[3,4] (occipitofrontal diameter, orbital diameters, binocular distance , thoracic circumference, thigh circumference, fetal heel ossification, foot length measurements).[5] are other biometric parameters for determination of gestational age. Recently Nasal bone length, Naso-Frontal Angle, Naso-Maxillary

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Angle have also been reported to provide some information with respect to growth in the fetus.

The measurement of fetal femur length is however easily done with the use of improved real time Ultrasound scanners under the conditions in which biparietal diameter is difficult to measure.

Many ultrasonographic studies have been done with respect to fetal limb growth since the early 1980s, in second and third trimester of pregnancy.[6,7] Most of them aimed to predict gestational age and fetal weight to detect intra-uterine growth- retardation at an early stage. Few authors have described the growth of all separate limb bones.[5,8] Most studies have reported the normal values of only the femur or humerus and femur both.[9] Tibia/ fibula and radius/ulna were often measured as complex rather than individually.[9] Often, measurements were limited to a certain period of pregnancy like second and third trimester in case of limb bones. Most of the studies were cross-sectional and some were longitudinal.

The aim of the fetal size chart should be to depict how infant should grow under optimal condition rather than how they should often grow and to achieve this it is necessary to consider factors that influence growth. A number of such factors are well established like maternal smoking, maternal disease e.g chronic hypertension, diabetes, pregnancy induced hypertension, pre-eclampsia, abnormal karyotype, congenital anomalies, preterm delivery, stillbirth. The use of locally developed charts means that the factors that may influence fetal biometry, including maternal age and nutritional status, maternal weight and size can be identified, facilitating accurate prediction of small for date and growth retarded foetuses. Therefore here in this study we have tried to establish normal ranges of fetal growth for femur length measurement from 11 weeks of gestational age onwards using linear and multiple regression analysis of data.

MATERIALS AND METHODS

This prospective, cross sectional, observational was conducted in Department of Anatomy, in collaboration with Department of Obstetrics and Gynaecology and Department of Radiology at Rohilkhand medical College and Hospital, Bareilly and associated hospital (R K Nursing Home, Bareilly).

Study group: Our study group consisted of pregnant women from Rohilkhand region, Bareilly (U.P.) who were referred to Department of Radiology for their routine antenatal sonographic assessment as a part of antenatal care. Among 815 pregnant women scanned, 700 women fitted the inclusion criteria. A total of 115 women were excluded.

No foetuses were excluded on the basis of abnormal biometry or birth weight. All the women whether primigravida or multigravida were included in this study those between 12 to 42 weeks of gestation. We included in the study, measurement of femur length in foetuses of 700 women. Ultrasound has noknown harm to the pregnant females and to their unborn foetuses. Informed consent was taken from the pregnant females and they participated voluntarily, protocol acknowledged by the medical ethical committee has been followed.

The subjects name, demographic data like age, habitat –urban (subjects belonging to proper Bareilly city) or rural (subjects belonging to villages or town in the periphery of Bareilly), last menstrual period (first date of last menstrual period) was asked and recorded. The menstrual age was established by reference to last menstrual period in patient with history of regular menses i.e known date of the beginning of the last menstrual period. Besides these femur length (in millimetres) and presentation of the foetus were recorded. The nutritional status of the pregnant female was also taken into account, because in the context of North Indian females excluding women with poor nutritional status or antenatal infections in the study population would create a healthy pregnant cohort, and will produce appropriate mean and centile values for that population.

Data Acquisition

For fetal biometric measurements, real-time transabdominal ultrasonogram was taken using "Model - Logiq V5 (Making - GE)" ultrasound machine equipped with a 3.5-MHz convex transabdominal probe. The measurements were taken to the nearest millimetre.

Fetal Biometrics

The technique originally described by O`Brien et al. was used to align the transducer along longest axis of the femur. The long axis of the fetus is found by obtaining a longitudinal section through fetal spine and aorta. The transducer is then turned 90 degrees to produce a cross sectional image of the fetal trunk at the level of umbilical vein. The transducer is then moved down the fetus, maintaining this angle, to the fetal pelvis. Since the fetal femur is usually flexed, the transducer must be rotated 30 to 45 degrees towards the fetal abdomen in order to visualize the longest possible image of femur.

Lateral and medial aspects of femur have different appearance. The lateral aspect is straight, whereas the medial aspect is curved. If a medial femur length is obtained, the femur may then be thought to be bowed. To ensure that one has the longest femoral length, measurements are taken along an axis that shows both the round echogenic cartilaginous femoral head and the femoral condyles. The straight lateral surface is measured rather than medial surface which is bowed. Femur Length has been measured in a plane where the full femoral diaphysis is seen almost parallel to the transducer and the measurement is made from one end of the diaphysis to another. In the third trimester, particular care was taken not to include the epiphysis in the measurement.13 The distal femoral epiphyses are visible after 32 weeks. The proximal tibial epiphysis

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becomes visible at around 35 weeks. A Statistical analysis was performed on the data thus obtained.

Statistical Analysis

The data was entered and analyzed in a computer, using MS Excel 07 and Statistical Package for Social Sciences (SPSS) version 10.0. The descriptive statistics (mean and standard deviation) were performed for the measurements of femur lengths at weekly intervals. Each interval was centred on a week, so that from 11 weeks and 4 days up to 12 weeks and 3 days has been considered as 12th week.

RESULTS

Among 815 pregnant women scanned, a total of 115 women were excluded for the following reasons: no information of the date of their last menstrual period (n=71), femur too small to be visible (n=39), multiple foetuses (n=3) and fetal malformation (n=2). The measured Femur length was recorded in 700 women who fitted the inclusion criteria.

Most of the females in this study group belonged to urban area (Bareilly district). The percentage of females belonging to rural area (villages and towns in the periphery of Bareilly) were less.

The age of females in this study ranged from 18 years to 42 years, mean age was 24.98yrs. Femur length which has been measured was earliest available in a pregnancy of 11 weeks 4 days in our study. It has been measured up to maximum of 42 weeks 3 days. The measurement of mean femur length ranged from 7 mms to 74.5mms during 12 to 42 weeks period of gestation. The group has been so divided that from 11 weeks and 4 days up to 12 weeks and 3 days gestation has been considered as 12th week.

Subjects in early and late period of gestation were few constituting about 10% of the group studied. Standard deviation and mean were calculated for each period of gestation.

The presentations of foetuses as seen through ultrasound were mostly cephalic. Other presentations were breech, transverse, variable.

Regression Analysis

To facilitate comparison of the observed variability associated with determining the femur length from menstrual age, regression analysis (linear and multiple) was performed. Linear (FL = a + b × GA), square (FL= a + b × GA + c × GA2) and cubic (FL = a + b × GA + c × GA2 + d × GA3) equations were generated. The best fit model was chosen based on the value of r2 (r square). r squared statistic compares the strength of association for the regression model.

Table 1: The regression equations and their r^2 value

Linear regression equation:	**FL=2.289GA-13.93**	**(r^2=0.888)**
Square regression equation:	**FL=-0.026GA^2+3.736GA-32.61**	**(r^2=0.932)**
Cubic regression equation	**FL=-0.0013GA^3+0.077GA^2 +1.082GA-11.22**	**(r^2=0.933)**

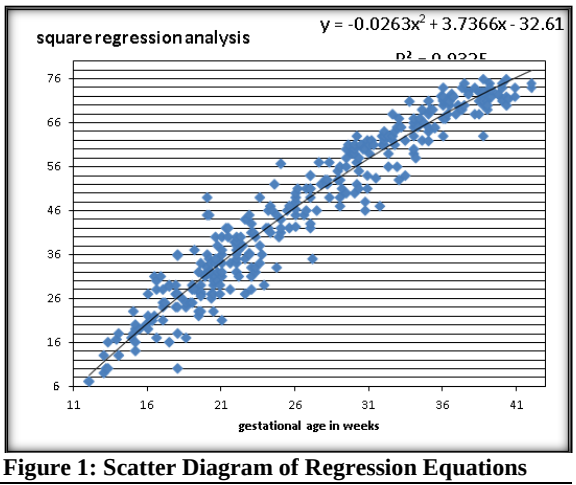

Figure 1: Scatter Diagram of Regression Equations

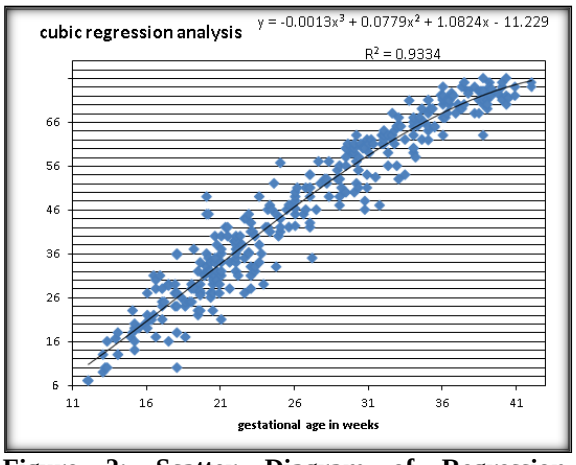

Figure 2: Scatter Diagram of Regression Equations

Here FL is femur length in millimetres with 2 decimal places and GA is menstrual gestational age (gestational age calculated by last menstrual period) in exact weeks i.e. 11 weeks 1day is 11.14 weeks, 11 week 2 day is 11.29 weeks, 11
weeks 3 day is 11.43 weeks, 11 weeks 4 day is 11.57 weeks, 11 weeks 5 day is 11.71 weeks and 11 weeks 6 day is 11.86 weeks and so on. These

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regression analyses showed that femur length correlated significantly with gestational age at 99% confidence limit (P-value is less than 0.01). Raw data was fitted in Linear, square and cubic equations and tables for femur length were generated. The best fit model for estimating femur length from gestational age, in our study was cubic regression equation.

To facilitate comparison of the observed variability associated with determining the femur length from menstrual age, femur length was predicted from the regression analysis equation in various studies.

Table 2: Mean Femur Length and Standard Deviation

Gestation(weeks)	Femur length(mm)	S.D (mm)
12	7.05	0.07
13	11.6	2.71
14	14.73	2.28
15	18.25	2.62
16	22.74	3.99
17	25.5	4.76
18	25.98	6.55
19	26.28	4.7
20	32.23	5.72
21	34.79	5.1
22	35.71	3.38
23	36.48	5.77
24	41.42	6
25	43.97	6.14
26	46.99	3.18
27	48	5.39
28	53.25	2.57
29	53.62	3.63
30	57.71	3.71
31	58.08	4.82
32	60.58	4.75
33	61.67	4.79
34	63.71	3.98
35	66.89	2.94
36	69.59	2.8
37	71.27	2.17
38	71.31	2.28
39	71.69	2.84
40	72.58	1.99
41	73	1.41
42	74.5	0.71

Table 3: Comparison of Mean and Standard Deviation of Femur Length

Gestationalage(Weeks)	Presentstudy	SD1	ES Madoretal. Nigeria	SD2
14	14.7	2.28	16.3	4.8
15	18.2	2.62	19	3.1
16	22.7	3.99	22.9	6.3
17	25.5	4.76	25	2.9
18	25.9	6.55	29	5.2
19	26.2	4.7	31.6	4.3
20	32.2	5.72	33.5	3.8
21	34.7	5.1	36.7	3.9
22	35.7	3.38	38.7	3.5
23	36.4	5.77	41.1	2.9
24	41.4	6	43.8	3.0
25	43.9	6.14	46.2	3.8
26	46.9	3.18	49.1	3.6
27	48	5.39	50.9	2.3
28	53.2	2.57	53.6	3.4
29	53.6	3.63	55.4	3.8
30	57.7	3.71	58.3	3.5
31	58.0	4.82	60.3	3.4
32	60.5	4.75	62.1	3.3
33	61.6	4.79	64.1	2.4
34	63.7	3.98	66.2	3.4
35	66.8	2.94	68.5	2.4
36	69.5	2.8	70.6	3.3
37	71.2	2.17	71.7	5.5
38	71.3	2.28	73.9	4.7
39	71.6	2.84	76.7	3.0
40	72.5	1.99	78.8	3.7

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41	73	1.41	79.9	5.4

SD-standard deviation

Table 4: Comparison of Mean and Standard Deviation of Femur Length

Gestational age (weeks)	Piyamas et al. Thailand		Snijders et al. London		Shahida et al. Pakistan		This study	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
11	NA	NA	8	2	NA	NA	NA	NA
12	NA	NA	10	2.5	NA	NA	7.05	0.07
13	NA	NA	11	2.5	NA	NA	11.6	2.71
14	13.28	1.02	15	3	15.2	1.7	14.73	2.28
15	18.29	2.01	17	3.5	17	2	18.25	2.62
16	18.87	2.94	22	4	21.5	2.6	22.74	3.99
17	24.16	3.43	25	4	23.7	3.1	25.5	4.76
18	26.51	2	28	5	27.2	2.2	25.98	6.55
19	28.35	2.82	30	5	30.2	3.9	26.28	4.7
20	32.61	3.4	32	6	33	2.1	32.23	5.72
21	34.85	2.49	34	6	35.3	2.4	34.79	5.1
22	36.61	3.05	37	5	39.2	2.6	35.71	3.38
23	40.21	2.8	43	5	40.1	3.1	36.48	5.77
24	42.22	1.71	45	4	44.3	2.6	41.42	6
25	47	5.88	48	5	46	3.4	43.97	6.14
26	46	2.65	49	5	50	2.1	46.99	3.18
27	49.01	2.01	50	5	51.2	1.9	48	5.39
28	50.11	5.92	54	4	53.3	2.2	53.25	2.57
29	53.6	2.02	55	5.5	55.7	2.2	53.62	3.63
30	56.25	2.45	58	6	58.4	2.9	57.71	3.71
31	59.44	2.62	59	5.5	59.4	1.6	58.08	4.82
32	58.85	2.26	62	6	62.1	1.8	60.58	4.75
33	60.71	2.43	65	4	63.6	2.4	61.67	4.79
34	62.16	2.91	66	4	65.9	2.3	63.71	3.98
35	65.22	2.07	67	6	68.1	1.9	66.89	2.94
36	67.57	1.89	69	6	69.6	6.25	69.59	2.8
37	68.36	1.89	72	5	68.8	2.7	71.27	2.17
38	69.86	3.43	73	5.5	71.9	1.6	71.31	2.28
39	71.09	3.46	75	6	NA	NA	71.69	2.84
40	73.5	4.34	76	4	NA	NA	72.58	1.99
41	73.67	3.04	77	5	NA	NA	73	1.41
42	NA	NA	NA	NA	NA	NA	7.05	0.07

NA= not availabl

Gestational age was calculated from femur length by fitting into linear, square and cubic equation. Femur length varied from minimum of 7mm to maximum of 75mm in our study with increase in gestational age from 10.7weeks to 37.8 weeks as depicted from regression equation.

Values of femur length and gestational age when calculated from each other by fitting into standard equation have correlated well and were comparable, hence we have come out with the result that gestational age when calculated from femur length best fitted into cubic regression equation.

Linear regression equation:	**GA=0.398FL +7.912**	**(r^2=0.927)**
Square regression equation:	**$GA=0.00237FL^2+0.1837FL+12.04$**	**(r^2=0.935)**
Cubic regression equation:	**$GA= 0.0000002145FL^3-0.00042FL^2+0.292FL+10.83$**	**(r^2=0.936)**

Significance of above calculation is to cross check our findings and to derive regression equation charts based on North Indian standards and to compare that with charts of Western standard.

This showed that femur length is a reliable indicator for assessment of gestational age.

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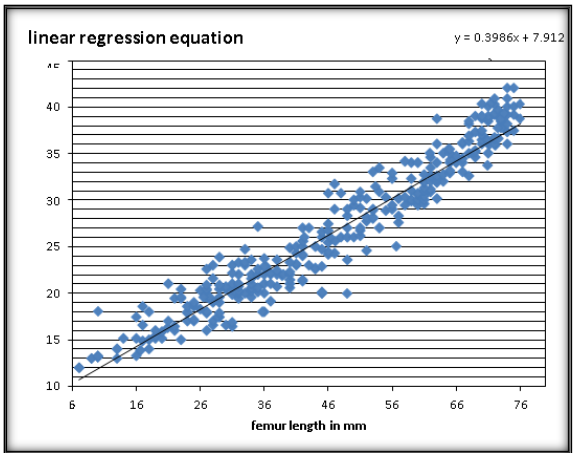

Figure 3: Scatter Diagram of Regression Equations

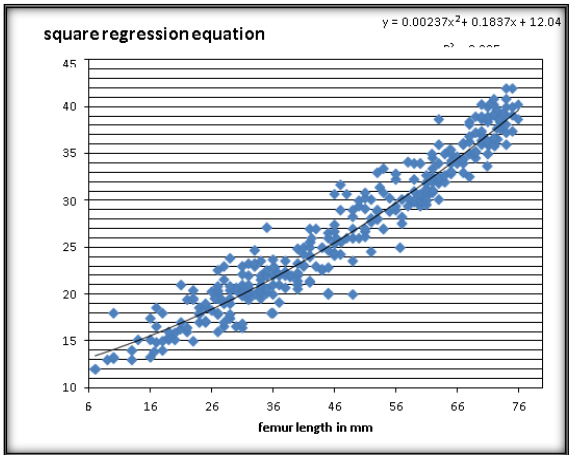

Figure 4: Scatter Diagram of Regression Equations

DISCUSSION

Ultrasound is probably the most important innovation in obstetric care in the past 50 yrs. It looks into the anatomy of unborn foetus and determines the gestational age, any fetal and placental anomaly and assesses the amniotic fluid volume.

In this cross sectional study we have tried to establish normal ranges for femur length for the North Indian population. Each women contributed to one set of measurement, taken during a routine ultrasound examination.

We have studied femur length in 700 singleton pregnancies in Bareilly district of north India. 58% of females belonged to urban area and the rest 42% were from rural area. Their age of women studied ranged from 18 years to 42 years. We have reported femur length from when it is visible and measurable, earliest in our study is 11 weeks 4 days. The maximum gestational age at which femur length measured was 42 weeks 3 days.

Presentation of the foetus studied were cephalic (60.43%), breech (15%), Transverse lie (2.57%) and variable lie (22%).

Menstrual age was centred to a week so that 11 week interval is from 10 weeks 4 days to 11weeks 3 days (10.57 weeks to 11.43 weeks). The mean (average) and standard deviation of femur length in millimetres was calculated for each week. The mean of femur length increased as the menstrual gestational age increased. The mean of femur length increased suddenly from 12 to 17weeks (7.05mms in 12th week to 25.5mms in 17th week). A gradual growth of about 1.5mm to 3 mm was seen every week, as the weeks progressed in late 2nd trimester. But the growth was less (1- 1.5mm) from 36 weeks onwards.

The predicted femur length in the present study is almost equal to the predicted femur length in the study done by Hadlock et al.[10]

Much difference is seen in the predicted value of femur in the study carried by Jeanty et al.[9] The difference in femur length gradually increases from 12 to 40 weeks. The predicted femur length is greater in their study than ours by 3mms from 18 to 19 weeks, by 5mms from 20 to 21 weeks, by 6mms from 22 to 23 weeks, by 7mms from 24 to 25, by 9 mms from 26 to 27 weeks, by 10mms from 27 to 30 weeks, by 11 mms from 31 to 40 weeks.

Comparison of the mean of femur length obtained in this study with those of study carried in North-eastern Thailand by PiyamasSaksiriwutthoet al.11 suggested the femur length greater in their study when compared with this study (the difference of mean femur length being 1-3mms respectively). These differences were found significant at some instances. The differences could be attributed to racial factors and dietary habits.

The mean femur length of Pakistan foetuses, in the study carried by Shahida et al.[12] was slightly greater than ours by 3-4mm in most of the weeks.

1. In early 2nd trimester mean femur length of foetuses was slightly lesser than present study but differences were not significant.
2. The differences were found significant in late 2nd and 3rd trimester.

It may be contributed to their non-vegetarian (high protein) diet.

Comparison of our results with the two studies carried out in United Kingdom, showed varied results. There were few statistically significant differences on comparing the mean femur length with the study of Snijderset al.[13] The femur length of their foetuses was higher than ours by 3-4mms with p value being significant in 10 out of 30 weeks.

Predicted femur length by TamyShohatet al.14 in Israel is about 2-5mms more than predicted femur length of our study.

Predicted femur length by Shahida Zaidi et al.[12] in Pakistan is about 3- 14mms more than predicted femur length of our study.

Predicted femur length by Leung TN et al.[15] In China is about 1- 5mms less than the predicted femur length of our study.

Predicted femur length by Pam Loughna et al.[16] in United Kingdom is about 1- 2mms more than the predicted femur length of our study.

The standard deviation in our study is sometimes greater than those of other studies in the 2nd

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trimester. This may be because of wide variability of data collected from females of varied socioeconomic strata having different nutritional status, racial variation and physical structure.

Regression analysis was done to find out best fit model to derive gestational age from femur length. We found cubic regression equation as best fit model for Rohilkhand population. The equation derived was:

GA = 0.0000002145 FL3 + 0.00042FL2 + 0.292FL + 10.83

This study provides us a chart derived from cubic regression equation to determine gestational age from femur length measurement of foetuses in Rohilkhand region of North India. So far gestational age estimation was dependent on western charts based on previous studies.

Charts generated based on our study clearly demarcates from studies done on other population. This can be because of difference in racial, nutritional and many other factors between different populations studied.

CONCLUSION

The predicted femur length in the present study is almost equal to the predicted femur length in the study done by Hadlock. Predicted femur length by T N Leung in China was lesser than the predicted femur length of our study. The standard deviation in our study is sometimes greater than those of other studies.

On comparing the mean femur length with those of study done by Snijdersetal in 1994 carried out in London showed mean femur length greater than this study. The t test showed significant p value in late 2nd and late 3rd trimester at most instances. This could be attributed to racial and dietary factors.. We found cubic regression equation as best fit model for Rohilkhand population.

This study provides us a chart derived from cubic regression equation to determine gestational age from femur length measurement of fetuses in Rohilkhand region of North India. So far gestational age estimation was dependent on western charts based on previous studies.

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