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Ultrasonographic estimation of gestation age and growth pattern of foetuses in second trimester of pregnancy by multiple growth parameters

Dr. Rajeev. R. Desai
Professor, Department of Anatomy, Rural Medical College. Pravara Institute of Medical Sciences. DU. Loni- 413736. Maharashtra

Dr. Manoj. P. Ambali*
Professor, Department of Anatomy Krishna Institute Of Medical Sciences University, Karad-415110, Maharashtra
*Corresponding author

Dr. Ashwini R Desai
Assistant Professor, Department of Anatomy, Rural Medical College. Pravara Institute of Medical Sciences. DU. Loni- 413736. Maharashtra.

***Abstract*---**Background and Aim- Fetal biometry rely on racial segment attributes, sustenance, hereditary qualities, and a lot more on ecological elements of a specific populace. Therefore, this study aimed to assess various fetal parameter and to establish a regression equation to predict the gestational age (GA) of pregnant women among the population of Western Maharashtra. Methodology- A descriptive, prospective study was conducted on 420 pregnant women in their second trimester (i.e. 14 to 27 weeks of gestation). Thirty women from each week of gestation were studied by ultrasonography for estimation of GA of the fetus. Various parameters such as biparietal diameter (BPD), femur length (FL), head circumference (HC), and abdominal circumference (AC) were studied and compared to the normal standards for GA, based on the initial sonogram from first trimester. Result-. Maximum (3.75 mm) and minimum (1.41 mm) increase in BPD was seen in 21-22 and 26 - 27 weeks, respectively. Maximum (4.50 mm) and minimum (0.42 mm) increase in FL was seen in 19 - 20 and 26 - 27 weeks, respectively. Maximum (15.76 mm) and minimum (6.66 mm) increase in AC was seen in 24 - 25 and 18 - 19 weeks, respectively. Maximum (25.31 mm) and minimum (1.96 mm) increase in HC was seen in 25 - 26 and 24 - 25 weeks, respectively. A strong positive correlation between GA and BPD, FL, HC and AC, was

observed (p-values < 0.001). In addition, growth parameters (BPD, FL, HC, and AC) have statistically significant positive correlation with each other also (p-values < 0.001). Conclusion- Fetal parameters (BPD, FL, AC and HC) can be used to estimate gestational age among the population of Western Maharashtra. Derived regression equation is proposed to be a good fit for the estimation of gestational age in the studied population.

***Keywords*---**gestational age, fetus, ultrasonography, maternal age, pregnancy.

Introduction

Gestational age (GA) is a crucial piece of information used to diagnose various fetal abnormalities and to establish the timing of various screenings and evaluation of fetal and maternal health throughout pregnancy by healthcare providers.[1] Therefore, definitive evaluation of GA is crucial as it permits appropriate planning of a woman's antenatal consideration, educates obstetric administration choices, and encourages the right translation of fetal development assessment.[2] Various methods of evaluating GA exists, each requiring diverse gear or abilities and with varying degrees of accuracy. Improved accuracy of estimating gestational age through better diagnostic methodologies would improve clinical management of pregnancy.[1]

Ultrasound evaluation of fetal growth is widely performed.[3] Amongst other assessments, an ultrasound growth scan incorporates the performance of three fetal biometry measurements – head circumference (HC), abdominal circumference (AC) and femur length (FL).[3] Moreover, numerous standard fetal biometric outlines are accessible for assessment of GA. Among the various fetal parameters, the parameters that are predominantly incorporated to estimate the GA includes- measurement of gestational sac, crown rump length (CRL), fetal biparietal diameter (BPD), femur length (FL), abdominal circumference (AC) and head circumference (HC).[4] However, the most often considered parameters in the second and third trimester of pregnancy are BPD, FL, AC and HC. These parameters are considered as the gold standard.[4]

Reference values for these four parameters by ultrasound were first detailed by Hadlock on the populaces of developed nations.[5-8] Fascinatingly, numerous researchers have worked on numerous population groups and have put forth the reference value concerning their own populations due to the difference from the obtained results. Since fetal measurements have been known to rely on racial qualities, hereditary qualities, sustenance and ecological components of a specific populace, biometric curves obtained from one population may not accurately estimate the fetal gestational age when used for another population. [4]

Despite there being numerous studies that have assessed the gestational age concerning different population, region and countries, there is paucity of such research among the population of Western Maharashtra, India. Therefore, this study aimed to assess various fetal parameters (BPD, FL, AC and HC) and to

establish a regression equation to predict the gestational age of pregnant women in Western Maharashtra.

Methodology

A prospective, quantitative, and descriptive study was conducted in the department of anatomy at a tertiary care hospital for a period of one year after obtaining approval from the Institutional Ethics & Research Committee. A total of 420 pregnant women in their second trimester (i.e. 14 to 27 weeks of gestation) aged below 30 years were included by convenient sampling method. Pregnant women less than 14 weeks and above 27 weeks of gestation, aged 30 years or above, with moderate to severe anemia, uncertain dates of last menstrual period, ultrasonography and menstrual age difference of more than 10 days, multiple pregnancy and fetal abnormalities, maternal illness either preexisting or related to pregnancy (hyperemesis, hemorrhage or hypertensive disorders in pregnancy), medical and surgical illness, complicating pregnancy, maternal disease or medication that could affect the growth of the fetus were excluded.

Transabdominal real time ultrasonography (Sanoline sonography machine G50) was used to estimate the gestational age of the fetus using multiple fetal growth parameters. Biparietal diameter (BPD) was measured from the outer edge of the proximal parietal bone to the inner edge of the distal skull.[9] Femur length was obtained by measuring its ossified shaft (Diaphysis). Long axis of the femur, which extends from the head of the femur to condyle, was measured.[10] For HC, the outer perimeter of the cranium, made on the same transaxial image of the fetal head was measured using an electronic ellipse available on ultrasound scanner (Figure 1 (a). (Hadlock et al.1984).[11] The fetal abdominal circumference (AC) was taken as the length of the outer perimeter of the fetal abdomen, measured on transverse scan at the level of the stomach, intrahepatic portion of umbilical vein and appearance of lower fetal ribs symmetrically (Figure 1 (b) .[12]

(a) (b)

Figure 1- USG images

Figure 1(a) -Showing BPD and HC of fetal head at the age of 20 week of gestation

Figure 1 (b) - Showing view of AC of fetus at the age of 20 week of gestation

On subsequent examination, standard fetal measurements (BPD, HC, AC, and FL) were obtained and compared to the normal standards for the gestational age, based on the initial sonogram, to determine whether the fetus growth was appropriate.

Statistical analysis

Data was analyzed using statistical software R version 4.0.2 and Microsoft Excel. Quantitative data was expressed as mean and standard deviation. Pearson's Correlation test was used to check the correlation between gestational age and growth parameters. Linear regression analysis was used to establish equation to get gestational age based on growth parameters. P-value less than or equal to 0.05 indicates statistical significance. Prediction formulae were derived using regression analysis.

Results

The mean GA observed was 20.5 ± 4.04 weeks. The mean BPD was 47.88 ± 13.11 mm, mean FL was 32.39 ± 11.64 mm, mean AC was 151.51 ± 47.14 mm, and mean HC was 174.62 ± 49.81 mm. Table 1 presents the summary of fetal biometry concerning GA. An incremental BPD, FL, AC and HC with advancing GA was observed.

Table-1 -Fetal biometry with respect to Gestational age

Gestational age (Weeks)	Bi-parietal diameter (mm) Mean ± SD [95% CI]	Femur length (mm) Mean ± SD [95% CI]	Abdominal circumference (mm) Mean ± SD [95% CI]	Head circumference (mm) Mean ± SD [95% CI]
14	26.77±1.82 [26.09-27.45]	14.12±1.77 [13.46-14.78]	77.65 ± 8.23 [74.58 - 80.73]	100.56 ± 13.77 [95.42 -105.71]
15	30.13 ± 2.12 [29.34 -30.93]	16.75 ± 1.6 [16.15 -17.35]	91.07 ± 5.39 [89.06 - 93.09]	109.61 ± 7.84 [106.69- 112.54]
16	33.59 ± 1.83 [32.91 -34.28]	19.86±1.61 [19.26 - 20.46]	102.24 ± 6.51 [99.81 - 104.67]	123.26 ± 6.91 [120.68 -125.84]
17	36.86 ± 3.45 [35.57 -38.14]	22.75 ±2.43 [21.84 - 23.66]	112.99 ± 9.97 [109.27 - 116.72]	133.04 ± 13.32 [128.07 -138.01]
18	40.3 ± 3.37 [39.05 -41.56]	25.89 ± 3.16 [24.71 - 27.07]	125.29 ± 13.17 [120.37 - 130.21]	144.67 ± 12.95 [139.84 -149.51]
19	43.57 ± 4.57 [41.86 -45.27]	26.68 ± 4.68 [24.93 - 28.43]	131.95 ± 13.68 [126.84 - 137.06]	150.84 ± 17.96 [144.13 -157.55]
20	46.45 ± 3.85 [45.01 -47.88]	31.18 ± 3.47 [29.88 - 32.47]	145.47 ± 13.52 [140.42 - 150.52]	169.92 ± 14.51 [164.5 - 175.34]
21	49.55 ± 3.31 [48.32 -50.79]	33.82 ± 2.85 [32.76 - 34.89]	156.81 ± 10.36 [152.94 - 160.68]	182.97 ± 13.4 [177.97 -187.98]
22	53.3 ± 1.7 [52.67 -53.94]	37.64 ± 1.68 [37.01 - 38.27]	171.59 ± 7.07 [168.95 - 174.23]	196.24 ± 9.67 [192.63 -199.85]

23	56.04 ± 3.28 [54.81 -57.26]	40.21 ± 2.95 [39.11 - 41.31]	179.26 ± 12.36 [174.64 - 183.87]	209.91 ± 15.63 [204.08 -215.75]
24	59.13 ± 3.71 [57.74 -60.51]	41.56 ± 2.94 [40.47 - 42.66]	189.56 ± 14 [184.33 - 194.79]	215.58 ± 11.86 [211.15 -220.01]
25	62.07 ± 3.78 [60.66 -63.48]	44.98 ± 3.19 [43.79 - 46.17]	205.32 ± 17.1 [198.94 - 211.71]	217.54 ± 42.53 [201.66 -233.42]
26	65.57 ± 1.21 [65.12 -66.03]	48.78 ± 1.16 [48.35 - 49.21]	216.49 ± 6.07 [214.22 - 218.76]	242.85 ± 5.03 [240.97 -244.72]
27	66.99 ± 3.59 [65.65 -68.33]	49.2 ± 3 [48.08 - 50.32]	215.44 ± 39.33 [200.75 - 230.13]	247.69 ± 16.13 [241.67 -253.71]

Figure 2 represents the relationship between various fetal parameter concerning gestational age. From the 14th to 27th weeks, the BPD increased by more than 40 mm without any decrescendo, with a mean BPD of 47.88 ± 13.11 mm. Maximum increase in BPD was seen in 21-22 weeks by 3.75 mm. However only 1.41 mm rise was seen in 26 - 27 weeks (Fig 2a). From the 14th to 27th weeks, the FL increased by more than 35 mm without any decrescendo, with a mean FL of 32.39 ± 11.64 mm. Maximum increase in FL was seen in 19 - 20 weeks by 4.50 mm. However only 0.42 mm rise was seen in 26 - 27 weeks (Fig 2b).

From the 14th to 26th weeks, the AC increased by more than 137 mm without any decrescendo. However, at 26th to 27th weeks AC decreased by 1.05 mm. The mean AC was 151.51 ± 47.14 mm. Maximum increase in AC was seen in 24 - 25 weeks by 15.76 mm and minimum by 6.66 mm in 18 - 19 weeks (Fig 2c). From the 14th to 27th weeks, the HC increased by more than 147 mm without any decrescendo, with a mean HC of 174.62 ± 49.81 mm. Maximum increase in HC was seen in 25 - 26 weeks by 25.31 mm. Minimum increase in HC, 1.96 mm rise was seen in 24 - 25 weeks (Fig 2d).

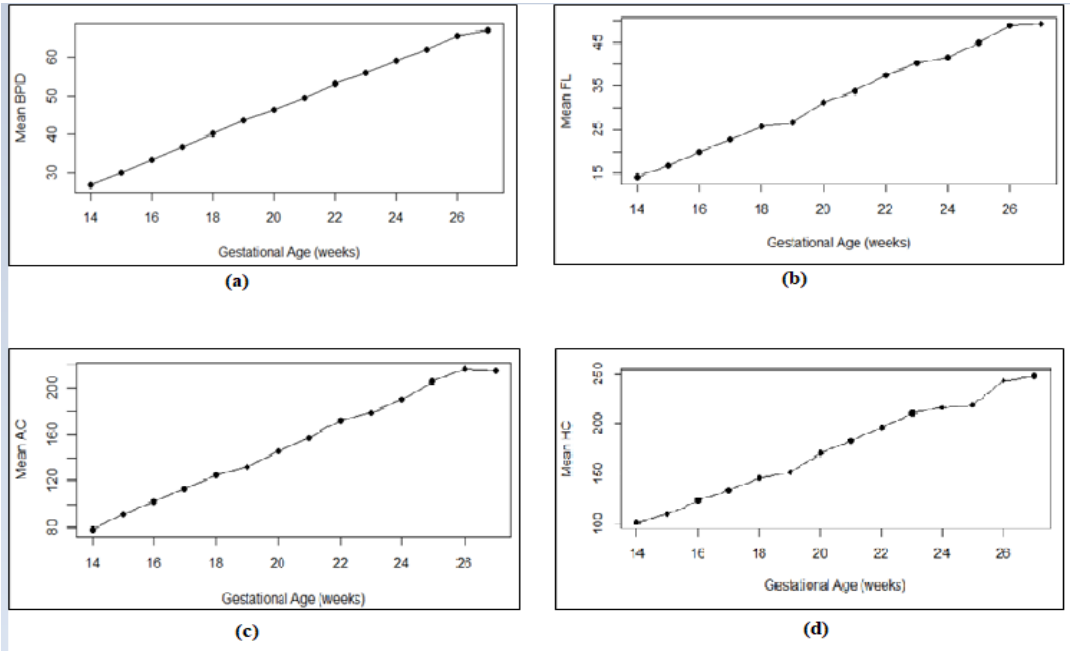

Figure 2- Relationship between various fetal parameter concerning gestational age
(a)- Relationship of Bi-parietal diameter and Gestational age
(b) Relationship of Femur length and Gestational age
(c) Relationship of Abdominal circumference and Gestational age
(d) Relationship of Head circumference and Gestational age

Table 2 presents the correlation of different parameters with each other and with GA. Pearson's correlation test revealed that all the growth parameters (BPD, FL, HC, and AC) had significantly strong positive correlation with gestational age ($p < 0.001$). Moreover, all the growth parameters BPD, FL, HC, and AC had significant positive correlation with each other ($p < 0.001$).

Table 2: Correlation of different parameters with each other and with Gestational Age

Variables		Weeks	BPD	FL	AC	HC
Weeks	r	1	0.971	0.97	0.947	0.94
	p-value		< 0.001*	< 0.001*	< 0.001*	< 0.001*
BPD	r		1	0.985	0.965	0.962
	p-value			< 0.001*	< 0.001*	< 0.001*
FL	r			1	0.964	0.96
	p-value				< 0.001*	< 0.001*
AC	r				1	0.935
	p-value					< 0.001*
HC						1

r – Pearson's correlation coefficient, BPD - Bi-parietal diameter, FL - Femur length, HC - Head circumference, AC - Abdominal circumference, * indicates statistical significance.

Table 3 presents the result of simple linear regression analysis for estimating GA using BPD, FL, AC and HC. With increase of BPD by 1 mm, the GA increased by 0.299 weeks. With increase of FL by 1 mm, the GA increased by 0.3364 weeks. With increase of HC by 1 mm, the GA increased by 0.0762 weeks. With increase of AC by 1 mm, the GA increased by 0.0811 weeks.

Table 3: Estimating GA using Bi-parietal diameter (BPD), Femur length (FL), abdominal circumference (AC), Head circumference (HC)

Variables	Estimate	p-value
Intercept	6.1856	< 0.001*
BPD	0.2990	< 0.001*
Intercept	9.6060	< 0.001*
FL	0.3364	< 0.001*
Intercept	8.2120	< 0.001*
AC	0.0811	< 0.001*
Intercept	7.1981	< 0.001*
HC	0.0762	< 0.001*

Abbreviation: BPD - Bi-parietal diameter, HC - Head circumference AC - Abdominal circumference * indicates statistical significance.

Regression analysis yielded the following linear equations for the relationship of GA with-

BPD

$$GA = 6.1856 + 0.2990 * BPD$$

BPD explains 94.34% variation in GA.

FL

$$GA = 9.6060 + 0.3364 * FL$$

FL explains 94.13% variation in GA.

AC

$$GA = 8.2120 + 0.0811 * AC$$

AC explains 89.74% variation in GA.

HC

$$GA = 7.1981 + 0.0762 * HC$$

HC explains 88.4% variation in GA.

Table 4 presents the result of stepwise multiple linear regression analysis for estimating GA using growth parameters

Variables	Estimate	p-value
Intercept	7.6522	< 0.001*
BPD	0.1512	< 0.001*
FL	0.1460	< 0.001*
AC	0.0054	0.153
HC	0.0003	0.919

BPD - Bi-parietal diameter, FL - Femur length, HC - Head circumference, AC - Abdominal circumference, * indicates statistical significance

Regression analysis revealed that BPD and FL are significant predictors of Gestational age. Holding other parameters constant, GA increases significantly by 0.1512 weeks with 1 mm increase in BPD and by 0.1460 weeks with 1 mm increase in FL. Multivariable regression analysis yielded the following linear equation for the relationship between GA in weeks and growth parameters.

$$GA = 7.6522 + 0.1512\ (BPD) + 0.1460\ (FL) + 0.0054\ (AC) + 0.0003\ (HC)$$

The model explains 94.91% variation in GA.

Discussion

The gestational period in humans is 39 weeks and is divided into trimesters.[13] Despite, the importance of gestational age in the diagnosis of various fetal abnormalities, establishing the timing of various screenings and evaluation of fetal and maternal health being well known, there is paucity of research in evaluating the gestational age in developing countries. Gestational age is traditionally evaluated using fetal measurements. Moreover, since the fetal measurements have been known to rely on racial qualities, hereditary qualities, sustenance, and ecological components of a specific population.[4] Therefore, this study was conducted to establish the regression equation to predict the gestational age of Western Maharashtra population.

Previous studies have revealed that fetal biometric parameters vary widely concerning racial and geographical variation.[4] In a study conducted on 1539 infants of various races including Asian Indian, White, Hispanic, Chinese and others at Northern California, it was found that Hispanic and Asian babies had shorter mean lengths with smaller mean HC compared to white babies.[14] Kinare *et al.*, conducted a study on rural Indian population described the sonographic fetal size and compared it with those in urban Indian populations and European.[15] They reported that all measurements for Indian fetuses were smaller compared to European references.[15] This correlated well with the mean fetal biometry values of the present study are smaller than the means of white fetuses.[5-8]

A strong positive correlation between GA and BPD (r=0.971), FL (r=0.97), HC (r=0.94) and AC (r=0.947) was observed (p-values < 0.001). Kumar et al (2017) conducted a study to evaluate the relationship between (GA) and foot length, mid upper arm circumference (MUAC) and nipple to umbilicus distance.[16] However, they also reported the good correlation of parameters including foot length (r=0.7843), MUAC (0.7832) and nipple to umbilicus distance (r=0.6630) with GA. Thawani et al., also conducted the study to estimate GA using various fetal parameters and reported the strong correlation of GA with head-circumference (r=0.60), birthweight (r=0.72) and MUAC (r=0.67).[17]

In the second trimester (14-26 weeks), the size of the fetus and volume of amniotic fluid are proportionate with each other due to which identification of various anatomical structures of the fetus becomes easier. Additionally, fetus in the second trimester grows faster than near term fetus hence normal growth in second trimester indicates less chances of growth retardation in the third

trimester.[12] During this time frame, various developmental milestones occur as the fetus develops. Additionally, as the fetus grows, it becomes visible via ultrasonography, and laboratory testing can be performed to track progression.In this study, prediction of GA was based on BPD FL AC and HC. The range of error was approximately 3 days after 12 weeks. The fetuses were examined for gross fetal anomaly and GA was estimated by CRL from 11 to 12 weeks of pregnancy, whereas GA from 13 to 40 weeks of pregnancy was determined by measurements of other fetal parameters such as BPD, HC, FL, and AC.

Long bones like femur and humerus are seen from 10 weeks, but measurement of length was technically possible from about 14 to 16 weeks of gestation onwards. Biparietal Diameter (BPD) measurements are taken at the level of the thalamus. A consistent landmark identification is essential to reduce the error inherent in the technique. This method can be utilized from 12 weeks gestation and is most accurate if performed before 28 weeks as growth rate of the fetal head slows down after 32 weeks. The fetal abdominal circumference (AC) is best measured after 14 weeks, as from 20 weeks onwards the growth rate become slow and individual variability becomes progressively more apparent as age advances. (MacGregor et al 2008).[18] This reflects more of fetal size and weight rather than age. Head circumference is most commonly used for evaluation of fetal growth or investigating evidence of fetal anomalies. In this study, the fetal biometric parameters (BPD, FL, AC and HC) were measured in 420 normal pregnancy cases. Head circumference, abdominal circumference, Bi-parietal diameter and femur length had positive significant correlation with gestational age. This finding was in agreement with a study conducted in India by Hussein et al.[19]

Aggarwal et al (2020), who conducted the study on local population of Southern Punjab, India, reported that maximum increase in BPD around 22nd to 23rd weeks by 5 mm and minimum growth of 1.1 mm was observed between 25th and 26th week.[4] In this study, maximum increase in BPD by 3.75 mm was seen between 21st and 22nd weeks whereas, minimum growth by 1.41 mm was seen around 26th – 27th weeks. In this study, uniform growth rate was not observed. However, there was an incremental FL with advancing GA. Maximum increase in FL was seen at 19th - 20th weeks by 4.50 mm. However only 0.42 mm rise was evident at 26th - 27th weeks. Comparatively, in the study conducted by Aggarwal et al, maximum growth was seen between 20th and 21st weeks by 4.8 mm and minimum growth of 0.8 mm between 21st and 22nd weeks.[4] Moreover, they reported maximum growth in the AC between 22nd-23rd weeks by 21.3 mm and minimum growth between 23rd -24th week by 3.4 mm.[4] Whereas in this study, maximum increase in AC was seen between 24 - 25 weeks by 15.76 mm and minimum increase at 26th to 27th weeks by 1.05 mm. Hadlock postulated that AC can be compared with FL and FL / AC ratio and can be studied. He observed that if FL / AC ratio was below 20 then the fetus was macroscopic and if it was above 24, fetus probably had Intrauterine growth Restriction (IUGR).[11] In this study, a maximum increase in HC was seen between 25 - 26 weeks by 25.31 mm and minimum increase was 1.96 mm at 24 - 25 weeks. Similar findings were reported by Thawani et al that maximum growth was seen during 24 to 26 weeks by 25 mm.[17]

The regression equation was formulated in weeks and it was found that there was strong correlation in combination of (BPD,FL,AC) and formulated as $GA =$

$7.6577 + 0.1519\ (BPD) + 0.1466\ (FL) + 0.0054\ (AC)$. This finding was consistent with a study carried out by Yadav et al, and revealed that using a combination of neonatal parameters would offer better prediction of gestational age as compared to individual parameters. [20] Tiruneh et al, inferred the same. [21]

Conclusion

Fetal parameters including BPD and FL have a strong positive correlation with gestational age in the population of western Maharashtra. Hence, gestational age can be successfully estimated from the same. The regression equation derived may be used efficiently for the estimation of gestational age whenever the fetal parameters are known.

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