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RESEARCH ARTICLE

PREDICTION OF GESTATIONAL AGE BY ULTRASONOGRAM USING LINEAR REGRESSION MODEL

¹Rajathi, G., ^{2,*}Johnson, W.M.S., ³Archana, R. and ³Rahe, R.

¹Assistant Professor, PRIMST,

²Director, Research Centre for Cellular Genomics, Sree Balaji Medical College and Hospital ³Assistant Professor, Dept of Anatomy, Sree Balaji Medical College and Hospital

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ABSTRACT

Introduction: Estimation of an accurate due date is of both social and medical significance. Care providers are dependent on gestational age to schedule maternal and fetal investigations, to gauge parameters of fetal growth and apply interventions timely for the management of prenatal complications. This study was done to develop a linear regression model using ultrasound measurement of fetal parameters to predict the gestational age in pregnancy.

Methodology: This study was carried out as a multicentre cross sectional study in one government and one private tertiary care hospitals in Chennai among 145 antenatal women. Gestational age was determined by measuring fetal parameters like Mean sac diameter, Biparietal diameter, Crown rump length, Abdominal circumference, Head circumference, Femur length and Effective fetal weight.

Results: The mean age of the participants was 27.5 years. About 57 % of subjects were between 25-30 years and nearly 23 % of the subjects were in the age group 20-25 years. Overall, 55(37.9%) of the participants were in 3rd trimester. There was a statistically significant correlation between the fetal parameters and gestational age in the second trimester (p<0.001).

Conclusion: Fetal parameters are key predictors of gestational age. They are useful to detect fetal abnormalities. It is essential to assess the gestational age using multiple parameter. It is likely that the technological development of USG will continue and increases in ultrasound frequency will further improve image resolution of early pregnancies. A 3D and 4D USG will also improve our ability to assess early pregnancy viability and multiple gestations.

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INTRODUCTION

Ian Donald, a Scottish physician in 1958 published the first scientific report on medical use of ultrasound entitled "Investigation of abdominal masses by pulsed ultrasound (Ian Donald, 1958). Initially ultrasound was done in antenatal women only for those with any medical problem or at high risk pregnancy. It was introduced in routine medical practice in 1970's and in antenatal women to confirm the fetal viability, to assess gestational age and to detect whether single or multiple pregnancies. Radiographic techniques were used to measure fetal dimensions prior to ultrasound, which had the drawback of exposing radiation to the fetus. Currently with increasing use of ultrasound, a non invasive diagnostic procedure, there is a decrease in maternal morbidity and mortality. Estimation of an accurate due date is of both social and medical significance. Providers of obstetric care are dependent on gestational age to

schedule maternal and fetal investigations, to gauge parameters of fetal growth and apply interventions timely for the management of prenatal complications. Proper timing of a repeat caesarean section also needs accurate dates. When an anomaly is detected, interventional modality is influenced by gestational age. For this, ultrasonography is one of the methods commonly used. Accuracy depends on the quality of images obtained. Gestational age is approximately 280 days calculated from first day of last menstrual period and so dating of pregnancy starts even before fertilisation. Ultrasonography is commonly used to estimate gestational age by measuring fetal dimensions like gestational sac diameter, crown rump length, biparietal diameter, abdominal circumference, circumference and femur length. When ultrasound is performed with quality and precision, it is far superior and reliable compared to clinical and other methods of dating the pregnancy (Butt, KimberlyLim et al.)

Objectives

To develop a linear regression model using ultrasound measurement of fetal parameters to predict the gestational age in pregnancy. Materials and Methods

Study Settings

This study was carried out as a multicentre cross sectional study between February and April 2015. All the tertiary care hospitals were approached for permission. The study was carried out in one government and one private tertiary care hospitals in Chennai.

Study Population

All pregnant women who attended the study facility during the study period and fulfilled the study criteria were selected for the study. The participants were selected consecutively. A total of 145 antenatal women participated in the study.

Inclusion Criteria

- Singleton pregnancy (5 40 weeks)
- Known last menstrual periodul
- History of regular menstrual cycles

Exclusion Criteria

- Gestational Diabetes
- Hypertension (Systemic and pregnancy induced)
- Anaemia
- Maternal Disease
- Fetal anomalies
- Multiple Pregnancy
- Placental anomalies
- Unknown last menstrual period / irregular menstrual cycles

Ethical approval and informed consent

Approval from Institutional Ethics committee was obtained prior to data collection. The study participants were explained in detail about the study and informed consent was obtained prior to data collection.

Data collection

Subjects were made to lie down in a supine position with full bladder while doing ultrasonogram. Ultrasonography machine used was Siemens Acuson X 300,3-5 MHz transducer. Each fetus was measured only once during the whole study. Gestational age was determined by measuring fetal parameters like Mean sac diameter, Biparietal diameter, Crown rump length, Abdominal circumference, Head circumference, Femur length and Effective fetal weight.

Operational Definitions

 Gestational sac diameter: Gestational sac is an echo free space containing the fluid, embryo and extra embryonic structures. It is measured inside the hyperechoic rim, including only the echo free space (MacGregor, 2008)

- Biparietal diameter: The biparietal diameter is imaged in the transaxial plane of the fetal head at a level depicting thalami in the midline, equidistant from the temporal bone and usually the cavum septum pellucidum anteriorly (MacGregor, 2008)
- Crown-Rump length: Crown rump length is a measurement of embryo along its longest axis. The technique involves measurement of the fetal length from the tip of cephalic pole to the tip of caudal pole. (MacGregor, 2008)
- Head circumference: Head circumference is measured by tracing the outer perimeter of the head.(MacGregor, 2008)
- Abdominal circumference: Abdominal circumference is measured in the transaxial view at the level of fetal liver using the umbilical portion of the left portal vein as the landmark.(MacGregor, 2008)
- Femur length: Femur length is measured along the long axis of the bone, disregarding the curvature. (MacGregor, 2008).

Data analysis

Data was computed in Microsoft Excel 2010 and statistical analysis was performed using SPSS ver. 21 software. Mean and standard deviation was calculated for all the fetal parameters. Correlation co-efficient was calculated and linear regression was used for developing a predictor model.

RESULTS

This study was carried out among 145 pregnant mothers visiting one government and one private health facility. The mean age of the participants was 27.5 years. About 57 % of subjects were between 25-30 years and nearly 23 % of the subjects were in the age group 20-25 years. Nearly 1 1 % of the subjects belonged to the age group of 30 -35 years and nearly 7 % of the subjects belonged to the age group of 35 -40 years. 1 % belonged to 1 5 -20 age group and 0. 7 % to 40-45 years. The age distribution of the study participants is given in Figure 1.

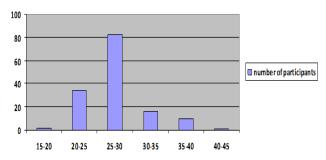


Figure 1. Age distribution of the study participants

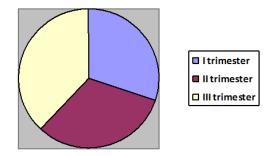


Figure 2. Distribution of the participants based on the gestational week

Table 1. First trimester fetal parameters among the study participants

S. No	Gestational age in weeks	No. of participants N	MSD (Mean ±S.D)	CRL (Mean ±S.D)
1	6	7	1.8 ± 0.045128	0.49 ± 0.078372
2	7	7	2.45±0.21923	1.03±0.195784
3	8	13	3.22±0.110752	1.73±0.08136
4	9	11	3.84±0.168257	2.34±0.149644
5	10	3	4.23±0.143422	2.83±0.108281
6	12	3	5.76±0.286844	5.00±0.416664

Table 2. Second trimester fetal parameters among the study participants

S. No	Gestational Age in	No. of	BPD	FL	НС	AC
	weeks	participants N	$(Mean \pm S.D)$	$(Mean \pm S.D)$	$(Mean \pm S.D)$	$(Mean \pm S.D)$
1	12	4	1.8±0.0692	1.10±0.0092	7.5±0.34	6.5±0.2386
2	13	10	2.2 ± 0.058	1.1±0.0345	8.2 ± 0.191	6.9 ± 0.2248
3	14	6	2.5±0.1457	1.3±0.0839	9.5 ± 0.282	7.9 ± 0.262
4	15	4	2.8 ± 0.0375	1.5±0.414	10.4±1.69	8.8 ± 0.6920
5	16	2	3.4 ± 0.127	1.9 ± 0.4447	12.3 ± 6.035	9.8 ± 6.988
6	17	4	3.6 ± 0.15	2.2±0.284	13.6±1.0373	10.8±1.394
7	19	4	4.4±0.204	2.9 ± 0.1097	16.2±1.5449	13.3 ± 0.21
8	20	3	4.6±0.1434	3.01 ± 0.68	17 ± 0.496	15.3±3.229
9	21	3	4.8 ± 0.4418	3.5±0.1864	18.4 ± 1.804	15.5±1.536
10	23	2	5.4±1.27	4.1±0.381	20.2 ± 0.44	18.3±8.51
11	24	2	6.5±1.27	4.9±1.27	24±5.0824	20.3±1.905
12	26	2	6.5±1.27	4.9±1.27	24±5.0824	20.3±1.905

Table 3. Third trimester fetal parameters among the study participants

S. No	Gestational Age in weeks	No. of participants N	BPD (Mean ±S.D)	FL (Mean ±S.D)	HC (Mean ±S.D)	AC (Mean ±S.D)
1	31	4	7.79 ± 0.10	5.94 ± 0.67	28.89 ± 0.85	27.09 ± 2.53
2	32	6	7.93 ± 0.22	6.17 ± 0.16	28.75 ± 0.74	28.02 ± 0.64
3	33	11	8.39 ± 0.16	6.38 ± 0.16	30.04 ± 0.55	28.95 ± 0.57
4	34	10	8.48 ± 0.24	6.60 ± 0.15	31.47 ± 1.25	30.23 ± 0.38
5	35	4	8.69 ± 0.23	6.73 ± 0.35	31.98 ± 1.14	30.07 ± 1.34
6	36	3	8.85 ± 0.52	6.93 ± 0.55	32.68 ± 0.55	31.4 ± 3.11
7	37	6	9.04 ± 0.22	7.1 ± 0.16	32.77 ± 0.78	32.78 ± 1.40
8	38	3	9.42 ± 0.30	7.51 ± 0.22	33.89 ± 1.33	34.07 ± 3.25
9	39	2	9.36 ± 3.05	7.95 ± 3.18	34.54 ± 2.03	34.13 ± 15.57

The distribution of the participants based on the trimesters is given in figure-2. Overall, 55(37.9%) of the participants were in 3rd trimester. About 44(30.3%) and 46(31.7%) were in 2nd trimester. The mean and standard deviation of the fetal parameters for first trimester are given in Table-1. During the first trimester Mean Sac Diameter (MSD) and Crown Rump Length (CRL) were measured. The mean and standard deviation of the fetal parameters for second trimester are given in Table-2. During the first trimester Mean Sac Diameter (MSD) and Crown Rump Length (CRL) were measured. The mean and standard deviation of the fetal parameters for third trimester are given in Table-3. During the first trimester Mean Sac Diameter (MSD) and Crown Rump Length (CRL) were measured. To prove a correlation between BPD ,FL,HC,AC and gestational age in the second trimester correlation coefficient was calculated and found to be statistically significant 0. 997, 0. 991, 0.994, 0.992 and the values were less than 0.001, there by showing positive correlation between the variables.(Table-4,5). The linear regression was computed for the 1st trimester parameters with the dependent variable being gestational age. Statistically significant results were obtained (Table-6). From Table 7, As per Anova, Regression model was accepted and the equation was given as follows GA (USG) = 3.797 + 1.335(MSD) + 0.59(CRL). Both CRL and MSD were contributing towards gestational age assessment and highly significant. Linear regression and coefficients were computed for 2nd trimester, with Gestational age as dependent variable and BPD, FL and AC as predictor variables.

The results were statistically significant (Table-8, 9). From Table 10 and 11, As per Anova, Regression model was accepted and the equation was given as follows: GA (USG) = 14.657+0.965 (BPD) +0.894 (FL) +0.002 (EFW). EFW was highly significant than BPD and FL. HC and AC were excluded in this model since they are not contributing. From Table 12 and 13, As per Anova, Regression model was accepted and the equation was given as follows GA (USG)=6.624+0.816 (BPD) +0.927 (FL)+0.480 (AC). BPD, FL, AC were highly significant. HC was excluded in this model since it was not contributing.

DISCUSSION

This study was carried out to predict the gestational age based on ultrasound measurements of fetal parameters using linear regression model. Patricia M .Dietz et al ., (2007 in their study provided evidence that substantial amount of misclassification results on using LMP based gestational age estimates and this can lead to preterm delivery rates. Estimation of gestational age by USG is of high importance for diagnosis, investigation and treatment of fetus. The importance and use of ultrasound in estimating the gestational age has been well emphasized in studies done by Nielson (1998) Caroline A Crowther et al., (2005) Daniel Salpou, Torvid Kiserud (2008), Verburg Bo et al., (2008) and George M Graham (2010). According to Laing et al. (2000) during the first 3 to 5 menstrual weeks an intrauterine pregnancy is first signalled by the presence of gestational sac.

Table 4. Correlation between the GA and first trimester measurements

S. No	Pearson Correl	Pearson Correlation Coefficients				Lower Limit	of Correla	tion Coe	fficients		Upper Limit of Correlation Coefficients				
	GA/ USG	BPD	FL	HC	AC	GA/ USG	BPD	FL	HC	AC	GA/ USG	BPD	FL	НС	AC
GA/USG	1	0.99	0.99	0.99	0.99		0.99	0.98	0.98	0.98		0.99	0.99	0.99	0.99
BPD	0.99	1	0.98	0.99	0.98			0.97	0.99466	0.97			0.99	0.99	0.99
FL	0.99	0.98	1	0.98	0.98				.968	0.97				0.99	0.99
HC	0.99	0.99	0.98	1	0.98					0.97					0.99
AC	0.99	0.98	0.98	0.98	1										

Table 5. Correlation between GA and 2nd/3rd trimester measurements

S. No	Pea	Pearson Correlation Coefficients				Lower Limit	of Correla	ation Coef	ficients		Upper Limit of Correlation Coefficients				
	GA/USG	BPD	FL	HC	AC	GA/ USG	BPD	FL	HС	AC	GA/USG	BPD	FL	HC	AC
GA/USG	1.00	1.00	1.00	0.99	1.00		0.99	0.99	0.99	1.00		1.00	1.00	1.00	1.00
BPD	1.00	1.00	0.99	1.00	0.99			0.99	0.99	0.99			1.00	1.00	1.00
FL	1.00	0.99	1.00	0.99	0.99				0.99	0.99				1.00	1.00
HC	0.99	1.00	0.99	1.00	0.99					0.99					0.99
AC	1.00	0.99	0.99	0.99	1.00										

Table 6. Liner Regression for 1st trimester

S.No	Model	Sum of Squares	df	Mean Square	F	Sig.
1	Regression	95.99		48.00	13917.99	0.0001
2	1 Residual	0.15	42	0		
	Total	96.14	44			

Dependant variable: GA – USG

Table 7. Coefficients for 1st trimester

S. NO		Unstandardize	ed	Standardized		
	Model	Coefficients		Coefficients	t	Sig.
		В	Std. Error	Beta		_
1	(Constant)	3.797	.076		49.844	.0001
2	1MSD (in cms)	1.335	.048	0.955	27.602	.0001
3	CRL (in cms)	.059	.045	0.045	1.297	.0001

Dependant variable: GA – USG

Timor-Tritsh IE *et al.* (1988) stated that the gestational sac represents the chorionic cavity, and its echogenic rim represents the implanting chorionic villi and associated decidual tissue. The smallest gestational sac size that can be clearly distinguished by high frequency transvaginal transducers is 2 to 3 mm, which corresponds to a gestational age of about 32 to 33 days as per Rowling *et al.* (1999).

The MSD is a commonly used, standardized, way to estimate gestational age during early pregnancy. It is less reliable when the MSD exceeds 1 4 mm or when the embryo can be identified according to Nyberg DA *et al.* (1987).MacKenzie AP *et al.*, (2008) stated that the growth of the MSD is approximately 1 mm per day. CRL is measured transabdominally from 6th - 7th week.

Table 8: Liner Regression for 2nd trimester

S.NO	Model	Sum of Squares	Df	Mean Square	F	Sig.
1	Regression	874.15	1	874.15	7020.31	0.0001b
	Residual	5.85	47	0.12		
	Total	880.01	48			
2	Regression	876.18	2	438.09	5262.55	0.0001c
	Residual	3.82	46	0.08		
	Total	880.01	48			
3	Regression	876.76	3	292.25	4053.64	0.0001d
	Residual	3.24	45	0.07		
	Total	880.01	48			

- a. Dependent Variable: GA BY USG
- b. Predictors: (Constant) BPD
- c. Predictors: (Constant) BPD, FL
- d. Predictors: (Constant) BPD, FL, AC

Table 9. Coefficients for 2nd trimester

S.NO	Model	Unstanda	rdized Coefficients	Standardized Coefficients	t	Sig.
		В	Std. Error	Beta		
1	(Constant)	6.57	0.13		48.86	0.0001
	BPD	2.92	0.03	0.99	83.78	0.0001
2	(Constant)	7.36	0.19		37.75	0.0001
	BPD	2.06	0.17	0.70	11.71	0.0001
	FL	1.00	0.20	0.29	4.93	0.0001
3	(Constant)	7.16	0.19		36.94	0.0001
	BPD	1.74	0.19	0.59	8.76	0.0001
	FL	0.74	0.21	0.22	3.52	0.001
	AC	0.17	0.06	0.18	2.85	0.007

Dependent Variable: GA BY USG

Table 10. Liner Regression for 3 rd trimester

S. No	Model	Sum of Squares	df	Mean Square	F	Sig.
1	Regression	273.74	1	273.74	716.43	0.001 B
	Residual	18.72	49	0.38		
	Total	292.46	50			
2	Regression	276.71	2	138.35	421.49	0.001c
	Residual	15.75	48	0.33		
	Total	292.46	50			
3	Regression	279.02	3	93.01	325.25	0.001 D
	Residual	13.44	47	0.29		
	Total	292.46	50			

Dependent Variable: GA-USG Predictors: (Constant), EFW Predictors: (Constant), EFW, BPD Predictors: (Constant), EFW, BPD, FL

Table 11 coefficients for 3rd trimester

S. No	Model	Unstandardized Coefficients	Standardized	Coefficients	t	Sig.
		В	Std. Error	Beta		
1	(Constant)	24.97	0.35		69.62	0.000
	EFW	0.00	0.00	0.96	26.76	0.000
2	(Constant)	18.87	2.05		9.18	0.000
	EFW	0.01	0.00	0.75	9.86	0.000
	BPD	.95	0.31	0.23	3.00	0.004
3	(Constant)	14.66	2.42		6.04	0.000
	ÈFW	0.01	0.00	0.56	5.78	0.000
	BPD	0.96	0.29	0.23	3.27	0.002
	FL	0.89	0.31	0.21	2.84	0.007

a. Dependent Variable: GA - USG

In present study, with each fetus being measured only once the data was analyzed with gestational age as a dependent variable and equations were generated. It was evident that both parameters increased as gestational age advanced. Pregnancy could be detected by ultrasonography as early as 5th week of gestational period, when the gestational sac size can be measured. The present study was also comparable to study carried out by Bhusari Prashant *et al* (2012). Thus accuracy and reliability of ultrasonographic measurement was established.

Koch ,Sarah *et al.* (2014) had insisted that use of Crown Rump Length for estimation of gestational age was not associated with an increased post term male to female ratio .It can therefore be used for the estimation of due date without risk of sex bias that occurs when using BPD in 2nd trimester of pregnancy . From this study it became obvious that GA by USG and MSD,CRL were strongly correlated with each other as well as are found to be statistically very highly significant (P < 0.001) and Regression Equation derived was GA(USG) = 3.797 + 1.335(MSD) + 0.59(CRL).

Table 12. Liner Regression for 2nd and 3rd trimester

S. No	Model	Sum of Squares	df	Mean Square	F	Sig.
1	Regression	8581.56	1	8581.56	16021.56	0.0001b
	Residual	52.49	98	0.54		
	Total	8634.05	99			
2	Regression	8598.16	2	4299.08	11621.14	0.0001c
	Residual	35.88	97	0.37		
	Total	8634.05	99			
3	Regression	8603.01	3	2867.67	8868.81	0.0001d
	Residual	31.04	96	0.32		
	Total	8634.05	99			

Dependent Variable: GA BY USG Predictors: (Constant), AC Predictors: (Constant), AC, FL Predictors: (Constant), AC, FL, BPD

Table 13 Coefficients for 3rd trimester

S.NO	Model	Unstandardized Coefficients		Standardized Coefficients Beta	T	Sig.
		В	Std. Error			
1	(Constant)	6.703	.168		39.929	.0001
	AC	.912	.007	.997	126.57	.0001
					6	
2	(Constant)	7.260	.162		44.713	.0001
	AC	.586	.049	.641	11.952	.0001
	FL	1.398	.209	.359	6.700	.0001
3	(Constant)	6.624	.224		29.625	.0001
	AC	.480	.053	.524	8.977	.0001
	FL	.927	.230	.238	4.036	.0001
	BPD	.816	.211	.238	3.870	.0001

Oh, Wright G, Coulam GB (2002) demonstrated that there was no difference in gestational sac diameter at 28 -35 days from LMP in normal and abnormal pregnancies. However smaller than expected sac diameter in pregnancies 36-45 days from LMP is predictive of spontaneous miscarriage. Kalish RB *et al.* (2004) have stated that ultrasound assessment of gestational age is very accurate and is marginally better in the 1 st trimester compared with 2nd trimester. Weinraub *et al.* (1979) showed that the biparietal diameter was the most reliable parameter for estimation of gestational age. Campbell *et al.* (1985) demonstrated that Biparietal diameter obtained between 1 4 and 20 weeks is a better predictor of estimated date of confinement than an optimal menstrual history and ultrasound cephalometry before 18 weeks was the single best dating parameter.

The accuracy of fetal age assessment based on Biparietal Diameter was dependent on gestational age. Between 12 and 26 weeks gestation, the Biparietal Diameter was accurate to +/-10-11 days. After 26 weeks gestation, the accuracy of BPD measurement progressively decreased and was +/- 3 weeks near term. In o ur s tudy als o BPD was highly s ignificant and contributing for gestational age assessment. In the second trimester next to BPD, BPD in combination with FL contributed towards gestational age assessment which was similar to the study conducted by Sachita Shah et al. (2009) Honarvar et al., (2000)(22) and E.Shalev et al., (1985) in their articles stated that measurement of fetal femur length appeared to be a reliable method for assessing gestational age which can compensate for the limitations of Biparietal Diameter. Tahilramaney Golde (1991) demonstrated that femur length could be used along with biparietal diameter and placental grade as an alternative to amniocentesis in term non diabetic pregnancies. The Abdominal circumference was less accurate than all other predictors in all gestational age intervals. The study conducted by Loetworawanit (2006) demonstrated that the intrapartum fetal abdominal circumference measurement was useful in predicting fetal macrosomia.

An AC measurement of > or =3.5 cm was the best value of fetal macrosomia prediction. From this study it became obvious that GA by US G and BPD, FL and AC were correlated with each other as well as BPD was found to be statistically very highly significant (P < 0.001) and Regression Equation derived was GA(USG)= 7.169+1.744 (BPD)+0.741 (FL)+0.171(AC). The parameters used in 3 rd trimester were BPD, FL, HC, AC and EFW. These parameters were correlated towards GA. EFW was highly significant and contributing towards gestational age assessment in our study. And EFW in combination with BPD and FL were also contributing. From this study it became obvious that GA by USG and EFW, BPD and FL were strongly correlated as well as found to be statistically very highly significant (P < 0.001) and Regression Equation derived was GA(USG)=14.657+0.894 (FL)+0.965 (BPD)+0.002 (EFW). The common parameters in 2nd and 3rd trimester i. e, BPD, FL, HC and AC were taken and correlated with gestational age. AC alone contributed towards gestational age assessment in our study. From this study it became obvious that GA by USG and AC,BPD and FL were strongly correlated with each other as well as found to be statistically very highly significant (P < 0.001) and Regression Equation derived was GA(USG)= 6. 624+0. 480 (AC)+0.927 (FL)+0.816(BPD).

Conclusion

From our study it is concluded that

- There is a linear relationship between MSD, CRL and GA (USG) in the first trimester, BPD,HC,AC,FL and GA(USG) in the second trimester, EFW, BPD, HC,AC, FL and GA(USG) in the third trimester.
- There is a positive correlation between MSD ,CRL andGA (USG) in the first trimester, BPD, AC, FL,HC and GA(USG) in the second trimester, EFW, BPD, FL, HC, AC and GA(USG) in the third trimester, BPD,AC, FL,HC and GA(USG) in the combined second and third trimester.

- In case of abnormal measurements of fetal parameters disease conditions should be addressed.
- Multiple parameters should be used to assess gestational age.
- It is likely that the technological development of USG will continue and increases in ultrasound frequency will further improve image resolution of early pregnancies.
 3D and 4D USG will also improve our ability to assess early pregnancy viability and multiple gestations.

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