Study of the Accuracy of Ultrasonography in Predication of Fetal Growth Restriction at Thirty-two versus Thirty-six weeks of Gestation

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ABSTRACT

Background: In some countries, third-trimester ultrasound monitoring of foetal growth is a standard practice, increasing detection rates to 40-80%.

Objective: Evaluation of the effectiveness of standard third-trimester ultrasound examinations at 36 weeks' gestation with those at 32 weeks' gestation for detecting fetal growth restriction (FGR).

Patients and Methods: 132 women who meet the inclusion criteria. Biparietal diameter, head and abdominal circumferences, and length of the femur were used to calculate the estimated fetal weight (EFW). It was determined that an immediate Doppler assessment of the umbilical artery pulsatility index from a free-floating umbilical cord section was necessary when EFW was less than 10th centile by local standard. Automated pulse Doppler measurements were made. After delivery, neonates were assessed by pediatrician to assess fetal growth.

Results: There was a statistical significance increase in EFW at 36 weeks of gestation compared to values at week 32. All US parameters had significant validity in predication of fetal growth restriction (FGR) but with higher accuracy in differentiation than that assessed at 32 weeks of gestation, the most precise was abdominal circumference (AC with) 59.1% accuracy, 65.9% sensitivity and 48.3% specificity for negative cases, then 55.7% and 51.5% for FL and BPD respectively.

Conclusion: Detection of FGR and related perinatal and neonatal outcomes was more accurate when ultrasound was performed at 36 weeks' gestation than when it was performed at 32 weeks' gestation.

Keywords: Ultrasonography, Fetal growth restriction.

INTRODUCTION

Increased risks of bad pregnancy outcomes, such as fetal death, morbidity and mortality in the perinatal and neonatal period, and poor neurodevelopment in the newborn are linked to growth restriction, as are harmful effects in adolescence and adulthood that are delayed [(1)]. If this condition is not detected during pregnancy, it can lead to an increased risk of mortality and difficulties for both the mother and the baby. Prenatal non identification has been recognized as a major cause of preventable prenatal death. Two distinct clinical phenotypes of growth restriction exist, each with its own unique course of development and course of action [(2)].

Deterioration in Doppler parameters and biophysical parameters in children with early-onset growth restriction (generally defined as that identified after 32 weeks) follows a regular progression [(3, 4)]. Normal or slightly raised umbilical Doppler indexes are prevalent in late-onset growth restriction, with moderately aberrant cerebral Doppler but no apparent cardiovascular or biophysical abnormalities [(5)].

While preeclampsia has a strong correlation with early-onset growth restriction, this is not the case with late-onset growth restriction. Using uterine Doppler velocimetry, biochemical markers (angiogenic factors), and maternal features, up to 90% of cases of early-onset growth restriction can be detected in the first or second trimester [(6, 7)]. Detection of early-onset fetal growth restriction (FGR) can be improved by integrating uterine artery Doppler data obtained in the first or second trimester with baseline maternal variables [(8)].

Preeclampsia may be a warning sign in as many as 60% of these pregnancies. Conversely, while accounting for the majority of unfavorable neonatal outcomes and stillbirths, growth restriction in late pregnancy is still widely ignored [(9, 7)].

When it comes to predicting late onset growth restriction, estimates on ultrasound (US) performance have been based on systematic reviews of routine US performance that show detection rates in the vicinity of 50%, which challenges the value of foetal size by US as an established part of the antenatal care [(1)]. Late-onset clinical forms have yet to be differentiated from earlier clinical forms, and no efforts have been made to adjust for potentially significant factors such as baseline risk of the population, the gestational age at scan, or the growth assessment parameter utilised (AC alone vs EFW) [(3)].

Late-onset small-for-gestational-age (SGA) vs late-onset growth restriction performance is another area where current understanding is lacking. SGA is the lowest end of the size range, which accounts for many cases of constitutional smallness. Growth restriction, on the other hand, is a pathological disease [(1)]. Symphysis–fundus height measurements are currently used to track growth in the third trimester. SGA children in low-risk populations, on the other hand, are rarely discovered in this way. Some countries' routine third-trimester ultrasonography surveillance of fetal growth increases detection rates to 40%–80%. It is not yet known, however, if this will have an effect on the perinatal outcome [(10)].

It was the goal of this study to evaluate the effectiveness of standard third-trimester ultrasound

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examinations at 36 weeks' gestation with those at 32 weeks' gestation for detecting fetal growth restriction (FGR) in Zagazig University Hospitals.

PATIENTS AND METHODS

At Obstetrics and Gynecology Department, Zagazig University Hospital, 132 pregnant women were studied in prospective cohort research for accurate prediction of fetal growth restriction.

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee (ZU-IRB#8065). Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Women who match the following inclusion criteria after a standard second-trimester scan are eligible to participate in the study: (1) Singleton non-anomalous fetus that is able to survive and thrive. (2) Ultrasounds taken before 13 weeks + 6 days of pregnancy are used to date pregnancies. (3) Mother' age at recruitment is more than 21 years old.

Exclusion criteria: Medical complications e.g., diabetes with pregnancy, cardiac disease, chronic renal disease. Three months prior to this study, women who had participated in another clinical trial. Women who were unable to follow the study's instructions. Multiple pregnancy, and fetal malformation

All participants were subjected to the following:

1. A thorough review of the patient's medical history and obstetric history.
2. General examination as well as local examination (fundal level) were assessed in all participants.
3. All patients had lab investigation including complete blood picture, random blood sugar, viral screen, coagulation studies (PT/PTT) as well as kidney and liver function tests.

Doppler and ultrasound measurements: Zagazig University's Outpatient Clinic was used for all ultrasonography examinations. Biparietal diameter, head and belly circumferences, and length of the femur were used to calculate the estimated fetal weight (EFW).

Biparietal diameter (BPD): In order to estimate the head's longitudinal axis, the midline echo from the falx cerebri was first located, taking into account the position of the head.

Fig. (1): Biparietal diameter at 32 weeks

Head circumference (HC):
A procedure known as the elliptical method was used to determine HC's value. The Occiput, the outer table of the skull, is the location of the first screen cursor. On the outer table of the skull, a second cursor is then positioned at the sinc axis.

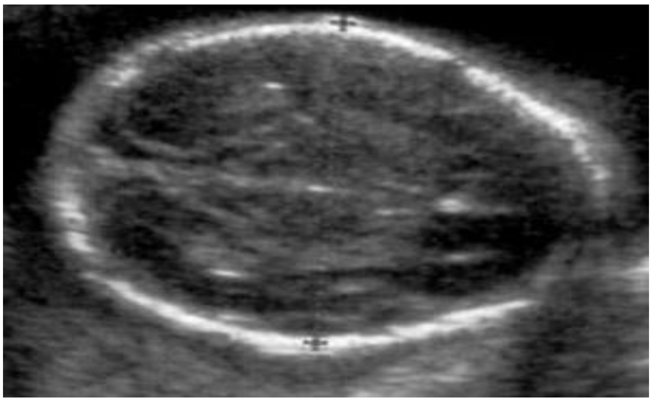

Fig. (2): Head circumference at 32 weeks

Abdominal circumference (AC):
AC was measured using the elliptical method, just like head circumference. Finding the aorta's longitudinal axis provided information about the foetal body's long axis and inclination.

Femur Length (FL):
Greater trochanter to distal metaphysis of the femur is a distance that is measured in inches. (To measure the length of the metaphysis, measure from its center to each end of the bone).

Fig. (3): Femur length at 36 weeks

The umbilical artery pulsatility index (UA-PI), obtained from a free-floating section of umbilical cord, was found to be below the 10th percentile of the EFW, as defined by local regulations. On the basis of at least three consecutive waveforms, automated pulsed Doppler measurements would be carried out.

UA-PI calculation:

In order to compute the Umbilical Artery (UA) Impedance Indices, A free-floating section of the umbilical cord is used to assess blood flow waveforms from the uterine arteries.

Outcome measures:

In the event that pre-eclampsia (PE) occurs, it is defined by the International Society for the Study of Hypertension in Pregnancy as new-onset hypertension at least twice within a four-hour period after the 20th week of gestation, with blood pressure readings of 140 mmHg or higher on either systolic or diastolic measurements, and a proteinuria reading of 300 mg/24 hours or higher.

SBP/DBP 160/110 mmHg on two or more measurements, proteinuria 2g/24h, or the presence of maternal complications were all considered signs of severe PE. Pathological fetal heart rate was used to determine the fetal condition during childbirth. A pediatrician examined the newborn to determine the fetus' development after birth. Following the implementation of adequate warming methods, a core temperature of 36.5°C was shown to be indicative of neonatal hypothermia.

Follow up:

Once assigned, individuals were monitored using a routine technique, which included serial symphysis–fundus height measures after 26 weeks of pregnancy.

Statistical analysis

In order to analyze the data acquired, Statistical Package of Social Services version 20 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed. The quantitative data was presented in the form of mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) was used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X^2) were used to assess qualitatively independent data. $P \leq 0.05$ was considered significant.

RESULTS

Mean age of the studied group was 27.5 years, 31.8% of them were primigravida and 24.2% had pre-eclampsia **(Table 1).**

Table (1): General characteristics of the studied group

Variable		**Studied group N=132**
Age: (years)	Mean ± SD Range	27.5 ± 4.39 20 - 36
		N (%)
Parity:	PG P1 P2 P3 P4 P5 P6	42 (31.8%) 31 (23.5%) 29 (22.0%) 23 (17.4%) 2 (1.5%) 2 (1.5%) 3 (2.3%)
Pre-eclampsia	Yes No	32 (24.2%) 100 (75.8%)

There was a statistical significance increase in all U\S parameters at 36 weeks of gestation compared to values at week 32 **(Table 2).**

Table (2): U\S parameters at 32 and 36 weeks of gestation among the studied group

Parameters		**At 32 weeks**	**At 36 weeks**	**Test**	**P**
BPD:	Mean ± SD Range	7.71 ± 0.17 7.38 - 7.97	8.29 ± 0.12 8.01 - 8.5	45.2	<0.001 HS
FL:	Mean ± SD Range	6.11 ± 0.37 5.1 - 6.5	6.85 ± 0.31 6.1 - 7.1	35.1	**<0.001** **HS**
AC:	Mean ± SD Range	28.1 ± 0.13 27.6 - 28.2	31.4 ± 0.69 30.1 - 32.4	62.9	**0.001** **HS**

There was a statistically significant increase in EFW at 36 weeks of gestation compared to values at week 32 **(Table 3).**

Table (3): Estimated fetal weight at 32 and 36 weeks of gestation among the studied group

Parameters		At 32 weeks	At 36 weeks	Test	P
EFW:	**Mean ± SD** **Range**	**7.71 ± 0.17** **1300 - 1970**	**8.29 ± 0.12** **2200 - 2950**	**45.2**	**<0.001** **HS**

There was a high statistically significant decrease in BPD, FL, AC and EFW with fetal growth restriction group compared to another group **(Table 4).**

Table (4): Relation between U\S parameters at 32 and 36 weeks of gestation and fetal growth retardation among the studied group

Parameters		With FGR N=66	Without FGR N=66	Test	P
BPD (w 32):	Mean ± SD	7.62 ± 0.16	7.81 ± 0.14	7.65	<0.001 HS
BPD (w 36):	Mean ± SD	8.23 ± 0.15	8.34 ± 0.07	**5.46**	**<0.001** **HS**
FL (w 32):	Mean ± SD	6 ± 0.39	6.15 ± 0.33	**2.38**	**0.02** **S**
FL (w 36):	Mean± SD	6.73 ± 0.39	6.97 ± 0.11	**4.87**	**<0.001** **HS**
AC (w 32):	Mean ± SD	27.98 ± 0.14	28.1 ± 0.07	**5.75**	**<0.001** **HS**
AC (w 36)	Mean± SD	31 ± 0.74	31.9 ± 0.21	**9.33**	**<0.001** **HS**
EFW	Mean± SD	1638.2 ± 138.8	1742.8 ± 108.9	**4.95**	**<0.001** **HS**
EFW (w36):	Mean± SD	2472.6 ± 166.8	2680.8 ± 148.2	**7.58**	**<0.001** **HS**

At 32 weeks of gestation there was a statistical significant increase in BPD, FL and AC with Pre-eclampsia group compared to non-pre-eclampsia group. At 36 weeks of gestation there was a statistically significant decrease in BPD, FL, AC and EFW with Pre-eclampsia group compared to non-pre-eclampsia group **(Table 5).**

Table (5): Relation between U\S parameters and occurrence of pre-eclampsia at 32 weeks of gestation among the studied group

At 32 weeks					
Parameters		**Pre-eclampsia** **N=32**	**Non pre-eclampsia** **N=100**	**Test**	**P**
BPD:	Mean ± SD	7.52 ± 0.13	7.76 ± 0.14	8.65	<0.001 HS
FL:	Mean ± SD	5.71 ± 0.37	6.18 ± 0.28	**7.88**	**<0.001** **HS**
AC:	Mean ± SD	27.9 ± 0.14	28.1 ± 0.09	**11.75**	**<0.001** **HS**
EFW	Mean± SD	1621.2 ± 162.4	1712.8 ± 112.3	**2.95**	**0.005** **S**
At 36 weeks					
Parameters		**Pre-eclampsia** **N=32**	**Non pre-eclampsia** **N=100**	**t-test**	**P**
BPD:	Mean ± SD	8.2 ± 0.09	8.36 ± 0.07	13.1	<0.001 HS
FL:	Mean ± SD	6.43 ± 0.37	6.98 ± 0.11	**15.4**	**<0.001** **HS**
AC:	Mean ± SD	30.46 ± 0.58	31.8 ± 0.35	**13.5**	**<0.001** **HS**
EFW	Mean± SD	2335.3 ± 57.9	2653.9 ± 145.7	**12.1**	**<0.001** **HS**

There was a statistically significant positive correlation between EFW at week 36 with all US parameters assessed, while EFW at week 32 was significantly correlated with BPD and AC **(Table 6).**

Table (6): Correlation between EFW and different U\S parameters among the studied groups

Variable	EFW N=132			
	At week 32		At week 36	
	R	P	r	P
Age (years)	-0.23	0.27 NS	0.04	0.86 NS
BPD (week 32)	**0.219**	**0.01 S**	**0.553**	**<0.001 HS**
BPD (week 36)	**0.311**	**<0.001 HS**	**0.612**	**<0.001 HS**
FL (week 32)	-0.19	0.69 NS	**0.344**	**<0.001 HS**
FL (week 36)	-0.002	0.932 NS	**0.515**	**<0.001 HS**
AC (week 32)	**0.353**	**<0.001 HS**	**0.556**	**<0.001 HS**
AC (week 36)	**0.281**	**0.01 S**	**0.611**	**<0.001 HS**
UA PI (week 32)	0.259	0.90 NS	**0.308**	**0.005 S**
UA PI (week 36)	0.295	0.181 NS	**0.573**	**0.001 S**

At 32 weeks all US parameters had significant validity in predication of FGR but with low accuracy in differentiation, the most precise was BPD with 50% accuracy, 75.5% sensitivity but low specificity for negative cases, then 44.7% and 33.3% for FL and AC respectively **(Table 7).**

Table (7): Validity of US parameters at 32 weeks of gestation in prediction of fetal growth restriction among studied group

	cutoff	AUC (95%Ci)	Sensitivity	Specificity	PPV	NPV	Accuracy	P
BPD	<7.5	0.205 (0.125-0.282)	75.5%	23.6%	50.0%	50.0%	50.0%	**0.001**
FL	<6.0	0.387 (0.289-0.484)	69.7%	20.3%	46.5%	39.4%	44.7%	**0.01**
AC	<28.0	0.288 (0.194-0.369)	51.5%	14.3%	37.8%	23.8%	33.3%	**0.001**

At 36 weeks all US parameters had significant validity in predication of FGR but with higher accuracy in differentiation than that assessed at 32 weeks of gestation, the most precise was AC with 59.1% accuracy (65.9% sensitivity and 48.3% specificity for negative cases) then 55.7% and 51.5% for FL and BPD respectively **(Table 8).**

Table (8): Validity of US parameters at 36 weeks of gestation in prediction of fetal growth restriction among studied group

	cutoff	AUC (95%Ci)	Sensitivity	Specificity	PPV	NPV	Accuracy	P
BPD	<8.3	0.313 (0.225-0.402)	55.5%	46.7%	51.4%	48.3%	51.5%	0.001*
FL	<6.95	0.351 (0.289-0.464)	67.8%	42.3%	54.2%	57.4%	55.7%	0.001*
AC	<30.2	0.147 (0.094-0.269)	65.9%	48.3%	56.4%	39.8%	59.1%	0.001*

DISCUSSION

In-utero mortality is 5–10 times greater in growth-restricted foetuses, as are perinatal morbidity and mortality. 7-10% of all pregnancies are plagued by foetal growth restriction, which is described as the failure to grow to the baby's full potential [11]. Using true growth restriction as an outcome criteria rather than merely smallness as a proxy improves third-trimester screening's diagnostic efficacy. Furthermore, there is growing evidence that some babies with BW >10th centile may have had inadequate foetal growth, which could explain the poor diagnostic performance of most index tests. When it comes to defining FGR, the next step would be to incorporate more functional characteristics [1].

In our study, the mean age of the studied group was 27.5 years, 31.8% of them were primigravida and 24.2% had pre-eclampsia. These results agree with **Roma *et al.*** [8] who conducted at 32- or 36-weeks' gestation, 2586 women were randomly assigned to have ultrasound examinations for the identification of foetal growth limitation.

The present study revealed a statistically significant increase in all U\S parameters at 36 weeks of gestation compared to values at week 32. This finding agrees with **Caradeux *et al.*** [1] who discovered that ultrasound examinations performed later in pregnancy had a higher detection rate.

Our study showed a statistically significant increase in EFW at 36 weeks of gestation compared to values at week 32.

In light of our findings, we recommend scanning at 36–weeks' gestation. The perinatal outcome appears unaffected by such a technique. Another option is to delay scanning altogether, but this has been questioned due to large-scale research showing that after this point in pregnancy, the stillbirth rate for highly growth-restrictive pregnancies significantly rises [12, 13]. However, **Roma *et al.*** [8] reported that the scans at 32 and 36 weeks' gestation showed no significant differences in the perinatal outcomes of the two groups.

Prior to delivery, detection of foetal growth retardation (FGR) could provide numerous benefits. For example, UA Doppler has been proven to minimize stillbirths through timely preterm delivery without increasing neonatal mortality, which motivates further exploration [14].

In our study, there was a high statistically significant decrease in BPD, FL, AC and EFW with fetal growth restriction group compared to the other group. This is supported by findings of **Boers *et al.*** [15] study, SGA foetuses who were treated with expectant care had a 2.5-fold increase in the risk of severe FGR compared to those delivered systematically after 36 weeks gestation. As a result, the longer time that passes until a regular scan is performed, the greater the chance of finding a severe case of FGR. While several countries recommend routine third-trimester scanning before 34 weeks' gestation, in majority of these countries it is done before that time [16].

When compared to EFW, which takes into account the intrinsic measurement errors of each individual biometric measurement (including AC and biparietal diameter, circumference of the head, and femur length), this method may have a worse overall predictive performance [1].

The current study showed a statistically significant increase in BPD, FL and AC with Pre-eclampsia group compared to no pre-eclampsia group

This finding goes with several studies suggested that SGA fetuses born before 32 weeks' gestation have a higher risk of pre-eclampsia, which can be minimized with pre-eclampsia screening in the first trimester and aspirin treatment for those in the high-risk group [17, 18].

Concerning relation between U\S parameters and occurrence of pre-eclampsia at 36 weeks of gestation among our studied groups, a statistically significant decrease in BPD, FL, AC and EFW with pre-eclampsia group compared to non-pre-eclampsia group. Predictors of neonatal weight that incorporate measurements of foetal heart rate, amniotic fluid, and foetal hydration (HC, AC, and FL) are superior to those based only on amniotic fluid measurements (AC or AC and FL), according to **Hammami *et al.*** [19].

Our study showed a statistically significant positive correlation between EFW at week 36 with all US parameters assessed, while EFW at week 32 was significantly correlated with BPD and AC. According to **Papageorghiou *et al.*** [20], the gestational age at delivery has an adverse effect on the sensitivity for pre-eclampsia and fetal growth restriction. When delivery occurs before 32 weeks, the sensitivity rises to 93%, 80%, and 56% for all cases of pre-eclampsia with fetal growth restriction, pre-eclampsia without fetal growth restriction, and fetal growth restriction without pre-eclampsia respectively.

In our study, all US parameters had significant validity in predication of FGR but with low accuracy in differentiation, the most precise was BPD with 50% accuracy, 75.5% sensitivity but low specificity for negative cases, then 44.7% and 33.3% for FL and AC respectively. A study of **Sovio *et al.*** [21] reported that 36-week scan performed better than the 28-week scan in detecting SGA (AUC of 88% versus 77%), and for cases with severe SGA below the centile, the AUCs were 93% instead of 82%.

The current study showed that all US parameters had significant validity in predication of FGR but with higher accuracy in differentiation than that assessed at 32 weeks of gestation, the most precise was AC with 59.1% accuracy (65.9% sensitivity and 48.3% specificity for negative cases), then 55.7% and 51.5% for FL and BPD respectively. This finding is in agreement with **Roma *et al.*** [8] where FGR was shown to be more prevalent (38.8% vs. 22.5%) when detected at 36 weeks' gestation (P = 0.001), with positive and negative probability ratios of 6.1% to 2.7%.

Several studies reported that there was a particular focus on the FGR of the last quarter of the year. Pooled sensitivity of EFW 10th centile for FGR prediction was 70%, with a false-positive rate of 5%, based on the observed data [1, 11].

CONCLUSION

It was found that ultrasound at 36 weeks' gestation was more effective than ultrasound at 32 weeks' gestation in diagnosing FGR and accompanying poor perinatal and neonatal outcomes. The detection rate of FGR can be improved by routinely scanning at 36 weeks' gestation rather than 32 weeks' gestation.

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Author contribution: Authors contributed equally in the study.

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