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Original article

Relation between Placental Thickness Measurements and Fetal Outcome in Patients with Intra-Uterine Growth Restriction [IUGR]

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ABSTRACT

Background: Placental thickness appears to be a promising parameter for estimation of gestational age of the fetus due to steady increase in placental thickness with gestational age.

Aim of the work: To investigate the relationship between placental thickness and fetal outcome in patients with intrauterine growth restriction [IUGR].

Patients and Methods: This study included patients with fetuses diagnosed clinically and by ultrasound as IUGR [estimated fetal weight <10th percentile for gestational age], singleton pregnancy, gestational age between 28 – 40 weeks of gestation, maternal age between 20-40 years old and body mass index between 18-30 kg/m². The placental thickness was measured at the second and third trimesters and correlated with the fetal outcome.

Results: Results revealed that, estimated fetal weight significantly increased in normal placenta when compared to either thin or thick placentae. In addition, thin placentae had significantly low fetal birth weight [1936.4±409.2] when compared to thick placentae [2236.4±410.1] or normal placentae [2636.4±421.4]. Also, Apgar score was significantly higher and need for NICU admission were significantly lower with normal placentae. In addition, there is significant positive correlation between 3rd trimester placental thickness and fetal birth weight, placental weight and APGAR score.

Conclusion: Placental thickness could predict deviations from norms of birth weight in late pregnancy. It seems to be promising for estimation of gestational age of the fetus and predicting fetal outcome.

Keywords: Third trimester; Placental thickness; Birth weight; Fetal; Intrauterine growth restriction.

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* Main subject and any subcategories have been classified according to research topic.

INTRODUCTION

Intrauterine growth restriction [IUGR] refers to fetus with marked reduction of birth weight below the tenth percentile [the lower border of normal weight] for that gestational age [1].

IUGR is ascribed to different fetal or maternal factors and placenta is one of the important causes of growth restriction. The placental main function is to provide nutrition and oxygen to the fetus, and fetal growth to normal birth weight depends on the competent delivery of nutrients via normally functioning uteroplacental system [2]. The normal development of placenta is mandatory for normal growth of a healthy baby. At the term, the healthy baby growth is achieved by three significant factors: genetic, healthy mother and efficient uteroplacental system. Placenta is the most important factor. However, it is unfortunately often ignored [3]. Historically document normal weight of placenta at term in normal pregnancy is about 1/5 of fetal weight. Both fetus and placenta are exposed to the same stress in utero life. Any maternal disease will exert its impact on the fetus and placenta. Thus, placental measurements like its thickness must reflect the status of the fetus and its outcome [4]. On the other side, any development impairment of the placenta could have a significant impact on fetal growth and outcome. The ratio of the fetal birth weight to placental weight has been used since the 1940s as an indicator for the normal fetal growth [2].

The definitive placenta could be demonstrated by ultrasound at 9–10 gestational weeks, with a uniform granular echogenic outline. Ultrasound [US] permits placental evaluation and the detection of different placental abnormalities using different variables such as its thickness and volume [5].

Abnormal placental thickness arises the suspicion of underlying pathological process. Small placentas were found to be related to chromosomal abnormalities, chronic fetal infections, preeclampsia, diabetes & intrauterine growth restriction [IUGR] [6].

Several studies have reported an association between small placenta and low birth weight [LBW], and IUGR, secondary to abnormal villous development and defective fetoplacental circulation, and blood vessel formation [7].

Some pregnancies suspected of IUGR are constitutionally small but healthy; however, others

fail to attain their growth potential due to factors that affect growth, such as lack of proper nourishment, chromosomal aberrations, drugs or infections. Prenatal identification of IUGR is important for improving the perinatal outcome [8].

The hypothesis that decreased placental size precedes the onset of IUGR makes placental thickness abnormalities with the corresponding gestational age [GA], one of the early warning signs for development of IUGR. Using two-dimensional [2D] ultrasound [US] assessment for placental size provides a safe, simple, easy, cheap, feasible and non-invasive diagnostic tool. This is more suitable in developing and low-income countries, to avoid the obstacles encountered with using three dimensional systems, being more expensive, time-consuming, and need more training [9].

AIM OF THE WORK

The aim of this study is to investigate the association between placental thickness and fetal outcome [estimated fetal birth weight as primary outcome & secondary outcome include birth weight, Apgar score, NICU admission] in patients with IUGR.

PATIENTS AND METHODS

The study had been conducted at Obstetrics and Gynecology Department, Al-Azhar University Hospital [New Damietta]; from May to November 2019. The study included 45 pregnant women diagnosed with intrauterine growth restriction [IUGR]. The study protocol approved by the local Institution Research Board [IRB] of faculty of medicine Al-Azhar University Damietta [ADIM-IRB18032019]. In addition, an informed verbal consent had been obtained from each participant sharing in the study. Confidentiality and personal privacy had been respected in all levels of the study.

The inclusion criteria were: 1] Fetuses diagnosed as IUGR [by U/S estimated fetal weight <10th percentile for gestational age as patient sure from date of LMP]; 2] Singleton pregnancy; 3] Gestational age 20 – 40 weeks of gestation; 4] Maternal age 20-40 years old; 5] Body mass index [BMI] 18-30 kg/m²; 6] Patient at risk [diabetes mellitus, hypertension, Preeclampsia]. On the other side, exclusion criteria were: 1] Chromosomal abnormalities; 2] Polyhydramnios; 3] Suspected placental anomaly; 4] Poor sonographic visualization of the placenta; 5] Presence of uterine or adnexal gross pathology

The sample size calculated according to formula of Daniel^[10], and frequency of intrauterine growth retardation in developing countries [3%] according to Radon et al.^[11]; and accordingly, 45 subjects were reasonable sample size.

Patients were subjected to complete history taking, thorough clinical examination, calculation of BMI, and obstetric examination. Then, ultrasound was carried out to measure placental thickness [two-dimensional ultrasound; Medison ultrasound with transabdominal 3.5 MHz probe]. The placental site had been determined in a longitudinal section using two-dimensional real-time mode. The thickness of the placental had been measured at the level of umbilical cord insertion in longitudinal course from lateral chorionic plate to the insertion of the cord apart from the retro placental area. The ultrasound determination of gestational age was determined by calculating the mean BPD, HC, AC, and FL. The thickness of the placental and gestational age was then correlated. The estimated fetal weight was calculated by the measurement of BPD, AC, and FL, using the formula proposed by Hadlock. Subsequently, the fetal outcome was evaluated and correlated with other outcome parameters of postpartum fetal weight [categorizing into groups of baby weights < 2,500 and > 2,500 g].

The technique of Transabdominal ultrasound: The sonographer uses full bladder as a 'porthole' to your uterus, so patients have to drink plenty of water before the test. patients lie supine on an examination table or bed. Gel is applied to patient's abdomen and the sonographer moves the scanner in various positions. The scan usually takes about 30 minutes. The thickness of the placental in mm had been measured at the level of cord insertion site. The transducer had been focused on to scan perpendicular to the chorionic and basal plates as tangential scan. The identification of the site of cord insertion by doppler was vitally significant for gaining correct measurement values.

Outcome measures of the study were:

- Primary outcome includes estimated fetal birth weight had been correlated with secondary outcome which include birth weight, Apgar score, NICU admission. An abnormal pregnancy outcome was recognized as birth weight < the 10th percentile or fetal weight < 2,500 g. The mean values of the

placental thickness along with the standard deviation were calculated for the diverse gestational ages [from the 20th to 40th gestational weeks].

Data management and Statistical Analysis: Data collected throughout history, examination, lab investigations and outcome measures were coded, documented and statistically analyzed using Microsoft Excel software. Data were then transferred to Statistical Package for the Social Sciences [SPSS version 20.0] software for analysis. Qualitative data represent in number and percent. But quantitative variables represented by arithmetic mean \pm SD [standard deviation]. Student [t] and Chi square tests were used to test differences for significance when appropriate. Correlation was calculated by Pearson's or Spearman's. P value was set at <0.05 for significant results.

RESULTS

In the present study, the patient age ranged between 20 and 30 years; the mean age was 25.0 \pm 3.1 years. Patient BMI ranged between 18.8 and 38.9kg/m²; the risk factors were in the form of gestational diabetes among 5 patients [11.1%], gestational hypertension among 10 patients [22.2%] and preeclampsia among 5 patients [11.1%]. The mode of delivery was normal vaginal delivery [NVD] among 15 patients [33.3%] and cesarean section among 30 patients [66.7%] [Table 1].

The placental thickness at the second trimester ranged from 16.9 to 29.7, while at the third trimester, it ranged from 27.3 to 55.1; the mean values were 20.82 \pm 3.169 and 30.27 \pm 2.1 at the second and third trimesters respectively. In addition, EFW ranged from 200 to 800 [mean value 365.54 \pm 53.48] and from 1200 to 2448 [mean value 1423.62 \pm 372.08] at the second and third trimesters respectively. The birth weight ranged from 2120 to 2590g [mean value 2436.4 \pm 430.01] and APGAR ranged between 3 and 10 at first the fifth minutes, [the mean value was 6.8 \pm 1.2, and 6.9 \pm 1.12 at first and fifth minutes respectively] [Table 2]. Estimated fetal weight and the second and third trimester significantly increased in normal placenta when compared to either thin or thick placentae. In addition, thin placentae had significantly low fetal birth weight [1936.4 \pm 409.2] when compared to thick placentae [2236.4 \pm 410.1] or normal placentae [2636.4 \pm 421.4]. Also, Apgar score was significantly higher and need for NICU

admission were significantly lower with normal placentae [Table 3]. Results of the present work indicated that, placental thickness in both second and third trimesters showed significant, moderate, proportional correlation with each of estimated fetal weight, AGAR score and fetal birth weight [Table 4].

Table [5] shows that changes in fetal weight can be predicted by placental thickness 2nd trimester by 12.5 %, also changes in fetal weight can be predicted by placental thickness 3rd trimester by 10 %.

Table [1]: Characteristics of the study sample size

Variables		Statistics
Age [years]		25.0±3.1; 20-30
Weight [kg]		78.0±12.0; 55-115
Height [m]		1.7±0.07; 1.55-1.78
BMI		27.1±3.7; 18.8- 38.9
Risk Factors	Gestational diabetes	5[11.1%]
	Gestational hypertension	10[22.2%]
	PE	5[11.1%]
Mode of delivery	NVD	15[33.3%]
	CS	30[66.7%]

BMI: Body mass index; PE: preeclampsia; NVD: Normal vaginal delivery; CS: Cesarean section

Table [2]: Placental thickness, EFW, and birth weight

Variables	Second trimester	Third trimester
Placental thickness	20.82±3.169; 16.9-29.7	30.27±2.1; 27.3- 55.1
EFW [g]	365.54±53.48; 200-800	1423.62±372.08; 1200-2448
Outcome		
Birth weight [g]	2436.4±430.01; 2120- 2590	
APGAR score 1 minute	6.8±1.2; 3-10	
APGAR score 5 minute	6.9±1.12; 3-10	

EFW: Estimated fetal weight.

Table [3]: Relation between placental thickness and outcome

Placental thickness	Thin placenta [n=20; 48.9%]	Normal placental thickness [n=22; 44.4%]	Thick placenta [n=3; 6.7%]		
Estimated Fetal weight second trimester	360.54±53.48	375.54±53.48	365.54±53.48	10.6	<0.001*
Estimated Fetal weight third trimester	1745±35.82	2383±23.48	2076±48.52	10.52	<0.001*
Fetal birth weight [g]	1936.4±409.2	2636.4±421.4	2236.4±410.1	10.43	<0.001*
APGAR 1 minute	4.4±1.0	9.1±0.9	4.1±1.2	99.9	<0.001*
APGAR 5 minute	6.8±0.81	9.1±0.91	6.3±0.81	30.9	<0.001*
NICU admission	10[50.0%]	5[22.7%]	2[66.7%]	7.71	0.033*

* = Significant; p < 0.05

Table [4]: Correlation between placental thickness and outcome

Variable	Placental thickness [2 nd trimester]	
	r	P
Estimated Fetal weight second trimester	0.412	0.031*
Fetal weight	0.454	0.04*
APGAR score	0.423	0.042*
Placental thickness [3 rd trimester]		
	r	P
Fetal birth weight	0.319	<0.05*
APGAR score	0.414	<0.05*

* = Significant; p < 0.05

Table [5]: Linear regression of placental thickness second and third trimesters for prediction of fetal birth weight

Variable	fetal birth weight				
	B	SE	Beta	p	R 2
Placental thickness second trimester	51.1	19.5	0.354	<0.05*	0.125
Placental thickness third trimester	36.4	15.6	0.319	<0.05*	0.10

* = Significant; p < 0.05

DISUCSSION

The placenta 'the sprightliness of fetus in utero' functions diversely to reinforce the maturation of the fetus and interacts with the two individuals- mother & developing fetus. The placenta, a highly vascular fetal organ, maintains the feto-maternal circulation via its connection: the umbilical cord [7]. A normally developed placenta with efficient function is crucial for normal fetal development and growth. The size of placenta increases during fetal growth period to allow it to carry out its vital functions. If the fetal growth is compromised it is due to the abnormal functioning of the placenta which can be detected by the abnormal placental measurements [12].

Placental thickness is very much related to fetal development and may be a key in perinatal outcome. According to Sadler et al. [13], at term placenta is approximately 3 cm thick and measures 15-25 cm in diameter.

A 'warning limit' of 1.8cm of placental diameter and 2cm of placental thickness at 36 weeks predict low birth weight neonates. Small placentas are associated with preeclampsia, chromosomal abnormalities, severe maternal diabetes mellitus, chronic fetal infections and intrauterine growth restriction [14]. The placentas over 4 cm thick at term have been observed in conditions like diabetes mellitus, perinatal infections, hydrops fetalis [both immune & non-immune]. The incidence of perinatal morbidity and mortality was considerably higher among gravida with thick placenta, related to higher rates of fetal irregularities and higher incidences of both IUGR and large for gestational age term neonates [15]. Some pregnancies suspected of IUGR are constitutionally small but healthy; however, others fail to attain their normal growth potential due to different factors, such as lack of proper nourishment, chromosomal aberrations, drugs or infections. Prenatal identification of IUGR is important for improving the perinatal outcome [8].

The hypothesis that decreased placental size precedes the onset of IUGR, makes placental thickness abnormalities with the corresponding gestational age [GA], one of the early warning signs for development of IUGR]. Using two-dimensional [2D] ultrasound [US] assessment for placental size provides a safe, simple, easy, cheap, feasible and non-invasive diagnostic tool. This is more suitable in

developing and low-income countries, to avoid the obstacles encountered with using three dimensional systems, being more expensive, time-consuming, and need more training [9].

The main objective of this study was to investigate the association between placental thickness and fetal outcome [estimated fetal birth weight as primary outcome & secondary outcome include birth weight, Apgar score, NICU admission in patients with IUGR.

Our results are in agreement with study of Adeyekun & Ikubor [9] as they reported that study subjects were 29.1 ± 4.9 years. The mean maternal weight was 71.4 ± 13.6 kg and mean height was 1.6 ± 0.5 m. Nagpal et al. [16] found that, mean age of their study population was 23.1 ± 3.02 years. Majority of women were in age group of 19–23 years.

Both fetus and the placenta exposed to the same strain during uterine life, and any maternal disease affects both placenta and fetus. Thus, placental health and measurements could reflect the health and nutritional status of the fetus and could predict pregnancy outcome. Placental thickness is the simplest measure, reflecting placental size [4].

As regard risk factors and mode of delivery, 33.3% of cases had a normal vaginal delivery and 66.7% of cases had cesarean section. Gestational diabetes represented 11.1% of cases, Gestational hypertension represented 22.2% and preeclampsia 11.1%.

Placental wellbeing and maternal health, in addition to genetically determined growth potential, are known factors that influence fetal growth. Indeed, placental disease has been shown to be the most clinically relevant of all potential underlying processes that may result in intrauterine growth restriction. Fetal weight estimation is important because birth weight has been shown to be the single most important parameter that determines neonatal survival [17].

The present study show that mean of Placental thickness 2nd trimester was 20.5 ± 2.5 with range of [16.9-29.7], mean of Placental thickness 3rd trimester was 30.27 ± 2.1 with range of [27.3-55.1], mean of EFW [g] second trimester was 165.54 ± 53.48 with range of [160-370], mean of EFW [g] third trimester was 1423.62 ± 372.08 with range of [1200-2448], mean Birth weight [g] was 2436.4 ± 430.01

with range of [2120-2590] and Mean APGAR score 1 minute 6.8 ± 1.2 with range [3-10]. Mean APGAR6.9 \pm 1.12 score 5 minutes with range [3-10].

Our results are supported by study of Adeyekun & Ikubor^[9] as they reported that the mean values of placental thickness [PT] and EFW throughout gestation were 35.5 ± 7.0 mm and 1555.0 ± 1004 g; respectively. Nagpal et al.^[16] reported that, at 32 and 36 weeks, mean placental thickness were 33.45 ± 1.62 and 35.7 ± 2.08 mm respectively.

In the current study, placental thickness < 10th percentile was recognized as abnormally thin placentae. Also, placentae with thickness > 95th percentile were defined as abnormally thick placentae. Placental thickness between 10th and 95th percentile was considered normal at 32 and 36 weeks. Mahale et al.^[18] observed that the range for thickness of placenta measured between 12–41 weeks was 1.3–3.9 cm and the mean placental thickness was 2.748 cm.

A healthy full-term baby is the results of three significant factors: a healthy mother, normal genes, and good placental implantation [which considered the most important, and ignored factor]^[19]. The current study shows that there is high significant relation between placental thickness second trimester and Fetal weight 2nd trimester, also there is high significant relation between placental thickness third trimester and fetal birth weight. Our results agree with study of Afrakhteh et al.^[20], as they reported that there was a significant positive correlation between placental thickness and fetal weight in the second and third trimesters [$r=0.15$, $p=0.03$; $r=0.14$, $p=0.04$ correspondingly]. Schwartz et al.^[4] investigated placental measurements in 1909 singleton pregnancies between 18 and 24 gestational weeks and reported that mean placental diameter and thickness were significantly smaller in small-for-gestational-age infants. Nagpal et al.^[16] reported that, there was a significant correlation between placental thickness and biometric fetal parameters [$r = 0.67$ and $r = 0.735$ at 32 weeks and 36 weeks respectively]. In addition, there was a significant proportional correlation between placental thickness and fetal weight [$r = 0.55$ and $r = 0.740$ at 32 weeks and at 36 weeks successively]. Furthermore, Abu et al.^[21], noted significant positive correlation between placental thickness and estimated fetal weight [EFW] in the second and third

trimesters. Mahale et al.^[18], reported that, the correlation coefficient between placental thickness and gestational age was found to be 0.838 and 0.916 in the second and third trimesters respectively, and significant correlation were observed between placental thickness and each of BPD and AC in the second and third trimesters respectively. Ohagwu et al.^[12] conducted a study on 666 pregnancies in Nigeria. They demonstrated a significant positive correlation between placental thickness and ach of BPD and AC. They found that subnormal placental thickness for a specific gestational age may be the earliest sign of IUGR. They advocated the placental thickness measurement during usual obstetric ultrasound scan. Karthikeyan et al.^[22] conducted a study on 211 women at 11–40 weeks gestations. They observed significant correlation between placental thickness and estimated fetal weight at first, second and third trimesters [$r =0.609$, $r = 0.812$ and $r = 0.814$ respectively]. They advocated the use of the placental thickness to predict gestational age. Ohagwu et al.^[12] conducted a study on 730 females. They found a fairly linear relation between gestational age and placental thickness, and obtained various regression equations to correlate placental thickness with gestational age in each trimester

In the clinical trial at our hands, 48.9% of cases had normal thickness placenta in the second trimester, 44.4% had abnormally thin and 6.7% had abnormally thick placenta. In the 3rd trimester 48.9% of cases had normal thickness of placenta, 44.4% had abnormally thin and 6.7% had abnormally thick placenta. Our results support the BaGhel et al.^[7] study and Li et al.^[23]. They reported that, mean placental thickness was 24.5 mm at 24 weeks, 31.8 mm at 32 weeks and 35.5 mm at 36 weeks. So, the thickness of placenta in millimeters almost coincides with gestational ages. It suggests a significant positive association between placental thickness and biometric parameters at different gestational ages. Nagpal et al.^[16] study demonstrated that, placental thickness < 3.0cm at 32 weeks and 3.1 cm at 36 weeks gestations are associated with low-birth-weight babies and poor fetal outcome. Comparable results were reported in the study of Habib^[24]. Also, the association between placental thickness and gestational age has been reported by many researchers^[25].

The present study shows that there is high significant relation between placental thickness second and third trimester and Apgar score at 1 minute. Also, there is statistically significant relation between placental thickness second trimester and Apgar score at 5th minute. These results support that of Nagpal et al. [16] who reported that there was proportional correlation between placental thickness and Apgar score at 32 and 36 weeks.

The current study shows that there is significant relation between thickness of placenta second and third trimester and NICU admission. These results are comparable to Nagpal et al. [16] who reported increased incidence of perinatal complications in full-term neonates of low Apgar scores and increased NICU admissions in those with placental thickness >4.0 cm at 36 weeks, and our study showed increased incidence of low-birth-weight babies in women with abnormally thick placenta.

The neonatal outcome was better in females with normal placental thickness than those with abnormally thin or thick placentae. This can be used to recognize the fetuses at risk by identifying women with thin placenta or thick placenta. Ahn et al. [26] reported that, the abnormal placental thickness-to-estimated fetal weight ratio at 18–24 weeks gestation was associated with small-for-gestational-age infants.

In the current work, there is significant positive correlation between 2nd trimester placental thickness and estimated fetal weight 2nd trimester and 3rd trimesters, fetal birth weight, and APGAR score. Changes in fetal weight can be predicted by placental thickness 2nd trimester by 12.5 % and changes in fetal weight can be predicted by placental thickness 3rd trimester by 10%. Balla et al. [27] investigated placental thickness in 53 pregnant females in their second and third trimesters. They concluded that, placental thickness < 25 mm in third trimester could be an indicator of IUGR and thickness > 45 mm might be an indicator of maternal comorbidity as diabetes and hypertension or fetal abnormalities as hydrops fetalis. Furthermore, Abu et al. [21] reported proportional correlations between placental thickness and estimated fetal weight in the second and third trimesters. Damodaram et al. [28], revealed a positive correlation, with increasing placental volume with increasing gestational age, but it was reduced in the growth-restricted fetuses. The

decreased placental thickness for a gestational age may be the earliest sign of fetal growth restriction. Mathai et al. [29], reported a positive significant correlation between placental thickness and gestational age.

In short, placental thickness measured by ultrasound seems to be a promising predictor for estimation of gestational age of the fetus and predicting fetal outcome as placental thickness almost equals gestational age in weeks, placental thickness below 10th percentile was found to be associated with low birth weight and IUGR.

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None

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