

Sonographically abnormal placenta: an association with an increased risk poor pregnancy outcomes

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Abstract

Background. The placenta is a most interesting but unfortunately often ignored and misunderstood organ. Placental abnormalities, therefore, can be an “early warning system” for fetal problems. A complete prenatal sonographic examination of the placenta is an essential component as its abnormalities can have a direct effect on fetal or maternal outcomes, obstetrical management and future fertility.

Objective To determine whether any association exists between the finding of an increased thickness of placenta, abnormal placenta shape, placental calcification, placental lake and abnormal cord insertion site at 20-22 and 30-32 weeks gestation with an increased risk of uteroplacental complications or a poor pregnancy outcome.

Methodology. A real-time ultrasound was used at the time of detail scan (at 20-22 weeks gestation) and at 30-32 weeks gestation to look for placenta appearance, fetal growth and anomaly. The main outcome measures were risk of hypertension disease in pregnancy, fetal growth restriction and poor fetal outcomes such as low Apgar score and low cord pH.

Results. The majority of the participants were Malay (77.9%). Abnormal placenta found at both gestations were placental lakes and thickness, and only one case had marginal cord insertion. Approximately 6% of the cases were confirmed placenta previa. No abnormal shape or abnormal calcification found at both gestations. About 10% patient developed hypertensive disease in pregnancy, 15% of the fetus was found to have growth restriction and another 16% have low umbilical cord pH. Majority of them delivered at term (90%) and via vaginal delivery (81%). There was no significance between presence of abnormal placental lake and thickness at both gestations with the maternal and fetal outcome.

Conclusion. Presence of abnormal placental thickness and lakes at 30-32 weeks scan associated with maternal hypertensive disease, fetal growth restriction and low umbilical cord pH, however these were not statistically significant. *Clin Ter 2017; 168(5):e283-289. doi: 10.7417/CT.2017.2021*

Key words: placenta abnormality, maternal hypertensive disease, fetal complications

Introduction

The placenta is an interesting but unfortunately often ignored and misunderstood organ. Placental abnormalities can be an “early warning system” for fetal problems. Perinatal death and extreme preterm delivery before 32 weeks of gestation due to intrauterine growth restriction (IUGR) and or pre eclampsia are strongly associated with underlying placental pathology following delivery (1,2).

Recognition of placental variants is important and its degree of abnormality as well as the clinical implications of these findings must be understood to help guide management of the pregnancy (3).

Placental size has been shown to be an important factor in abnormal fetal growth. An increased thickness is non-specific and can be found with maternal diabetes, maternal anemia, abnormalities of fetal growth, fetal hydrops, whether immune or non-immune which can be caused by several infection such as syphilis, cytomegalovirus as toxoplasmosis or fetal cardiac smaller in fetuses with karyotypic anomalies (4).

Circumvallate placenta has been linked to adverse prenatal outcome such as placental abruption, fetal hemorrhage and mortality. However, circummarginal placenta has a questionable clinical significance. Another morphological abnormal placenta is the succenturiate placenta, including one or more small accessory lobes that develop at a distance from the main placenta. The antenatal recognition of this condition is important since intramembranous vessels connecting the main placenta with the succenturiate placenta may rupture during labor with rupture of the membranes and fetal death may ensue. In addition, retention of this accessory lobe may lead to postpartum hemorrhage (4). Bilobate or succenturiate placenta had an odds ratio of 22.1 as an independent risk factor for vasa previa (5). A further rare variant not yet described by ultrasound is the girdle placenta. The placenta is annular or horse-shoe shaped. It has been associated with antepartum bleeding and/or IUGR.

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Significant placental calcifications are rarely seen before 37 weeks gestation. The classification is commonly used consisted of four grades (0 – 3)(6). The presence of grade 3, early in pregnancy, may suggest significant placental dysmaturity that associated with IUGR, chronic hypertension, SLE, diabetes and other vascular diseases 6. While it seems to be clinically valid that premature aging (grade 3 before 37 weeks gestation) is associated with more perinatal complications (7), many authors have shown a lack of direct correlation with IUGR, nor was it found useful to predict post maturity and fetal distress. Nevertheless, McKenna et al. concluded that ultrasound detection of a grade 3 placenta at 36 weeks gestation might help to identify the “at-risk” pregnancy, in terms of subsequent development of gestation hypertension and delivery of a growth-restricted neonate (8).

Placental lakes are described as homogenous, sonolucent villous vascular spaces. There is little clinical information available regarding these lesions and their possible clinical significant (9). Previously reported associated clinical findings include early pregnancy bleeding and an increase risk of IUGR (10,11).

Since complete prenatal sonographic examination of placenta was not routinely done, this study’s aim was to look at significant pathology that afflicts the placenta, often before affecting fetus.

Objective

To determine prospectively whether any association exists between the finding of an abnormal placenta at 20-22 and 30-32 weeks of gestation with an increased risk of uteroplacental complications and a poor pregnancy outcome.

DEFINITION OF TERMS:

1)Increased thickness of placenta: Placenta thickness of 3 cm and more at 20-22 weeks scan, and of 4 cm and more at 30-32 weeks scan. It is measured at the level of cord insertion when the cord is centrally located or at the centre of the placenta if the cord is not a centrally located.

2)Abnormal placenta shape: If the placenta is either circumvallate, circummargina or succenturiate lobe.

3)Abnormal placental calcification: presence of grade 3 placental calcification before 37 weeks gestation.

4)Abnormal placental lake: presence of small placental lakes more than 3, or less than 3 but large (more than 2 cm in diameter)

5)Abnormal cord insertion: The umbilical cord insertion that may be not located central or lateral onto the placental plate.

6)Uteroplacental complications and poor pregnancy outcome in this study includes:

1. Intra uterine Growth Restriction (IUGR)
2. Low birth weight fetus (<5th centile) or 3) low Apgar score < 4 at 1 minute or low pH (< 7.20)
3. Hypertension disease in pregnancy

Methodology

Study Design

This was a prospective study involving patients who undergoing detail scan in the antenatal clinic PPUKM. It was conducted over a period of 12 months.

Study Population

Patients who came for detail scan at 20-22 weeks gestation were invited to participate in this study. The inclusion criteria included accurately dated, singleton pregnancy, consented to participate in this study and patients who understand English or Bahasa Melayu. The exclusion criteria includes patients with multiple gestations, patients with fetal anomalies, patients with preexisting hypertension and diabetes mellitus and refused to participate in this study.

Study Procedures

All participants were given the information sheet and explained regarding the nature and purpose of the study, including clear definitions of terms and informed consent. Clinic staffs and attended sonographer were briefed about the placental morphology before commencement of the study.

A detail scan including scan for placenta morphology was performed by designated sonographer and the findings were recorded in the patient’s data collection sheet. All patients with normal or abnormal placental findings will have a repeat scan for placental abnormality and fetal growth at 30-32 weeks gestation, and will further follow up until delivery. Obstetric complications in which maternal hypertension disease, fetus with restricted growth or with poor Apgar score and umbilical cord pH will be recorded if present. Socio-demographic data recorded included maternal age, parity, ethnicity, smoking habits, and presence of any medical illness.

Instruments

The 3D ultrasound machines used for detail scan were Voluson 730 Expert (GE Healthcare) and Aplio MX (Toshiba). Designated sonographers chosen performing the detail scan and placenta morphology were Puan Nazatulfahya Bt Mujamil, Puan Nooriyan bt Yahya and Encik Sharul Rizam Bin Samsury. The designated Fetomaternal O&G Specialists involved were Associate Prof Dr Shuhaila Ahmad and Associate Prof Dr Norzilawati Mohd Naim.

Ethical consideration

Approval by PPUKM ethical committee was obtained before commencing this study. The patients were informed about this study both verbally as well as in written form as in the patient information sheet. Written consent then will be issued for participant. Once written consent to participate was obtained, patient was recruited into this study. They were assured of their anonymity and the confidentiality of the data obtained. The study ethical code was FF-342-2009.

Statistical analysis

To ensure confidentiality, respondents were identified numerically. In this study, the level of significance is 5%. The collection data was analyzed using SPSS version 19. The data was normally distributed, hence parametric test was used. The chi-square test was used to test the association between abnormal placentas with obstetrics outcome. A *p* value of less than 0.05 was considered to be statistically significant.

Results

A total of 113 patient who are fulfilled the criteria were recruited in this study. Out of 113 participants, 68 patients had scan done both at 20-22 weeks and at 30-32 weeks. Another 45 patients did not turn up for a repeat scan at 30-32 weeks gestation for many reasons. Hence, only 68 patients with complete scans would be analyzed in this study.

The mean age of participants completed this study was 34 ± 5.046 years old Majority of them were Malay (77.9%) and of para 2 to 4 (48.5%). Only 1 of them was a smoker (1.5%) and 29 (42.6%) of them had medical illness which included thyroid disease, systemic lupus erythematosus, chronic rheumatic heart disease, asthma, thalassemia and nephrotic syndrome (Table 1).

At 20-22 weeks scan, all patients were found to have normal shape of the placenta (discoid shape) and 5 patients were found to have low lying placenta (7.3%). Only one patient (1.5%) had an abnormal cord insertion (marginal). There was no placental calcification noted the mean thickness was 2.82 ± 0.757 cm. Twenty five patients (36.8%) had an increased placental thickness of 3 cm and more . Furthermore eight patients (11.8%) were found to have abnormal placental lakes either there were more than 3 or the diameters were more than 2 cm.

At 30-32 weeks scan, 4 patients (6.0%) with low lying placenta noted at 20-22 weeks scan were confirmed to have placenta previa (either anterior or posterior) and none

were found to have increased calcification (grade three and more). The mean placenta thickness at 30-32 weeks scan was 4.16 ± 0.926 cm. Abnormal placental thickness of 4 cm and more were found in 25 patients (52.9%), whereas 29 patients (42.6%) were found to have abnormal placental lakes of either more than 3 lakes or diameter of more than 2 cm in diameter (Table 2).

From total of 68 patients involved in this study, most of the patients delivered vaginally (80.9%), followed by via emergency lower segment caesarean section (LSCS) 13.2% and via elective LSCS 5.9%. Almost 90% of them delivered at term and those delivered prematurely were due to severe pre eclampsia (1.5%), premature labour (7.3%) and bleeding placenta previa (1.5%). Seven patients (10.3%) developed hypertensive disease in pregnancy. Ten fetuses (14.7%) were found to have growth restriction. Although none of them with low apgar score of less than 4 at one minute, 11 babies (16.2%) were found to have low umbilical cord pH of less than 7.20 at delivery.

The marked abnormal placental changes were placental thickness and placental lakes. The obstetrics complications that were chosen to be analysed further were the hypertensive disease in pregnancy, fetal growth restriction and low cord pH (Table 3).

The placental abnormalities at 20-22 weeks and at 30-32 weeks of gestation were not significantly associated with hypertensive disease in pregnancy (HDP). At 30-32 weeks, mothers with ultrasound findings of abnormal lakes and abnormal thickness had 3.4 and 2.2 times respectively higher risk of developing hypertensive disease during pregnancy. However this findings were not statically significant and may have occurred by chance in this study (Table 4).

Table 1. Sociodemographic characteristics

	Characteristics	N = 68	(%)
Parity	Para 1	17	(25.0)
	Para 2-4	33	(48.5)
	Para > 5	18	(26.5)
Ethnic	Malay	53	(77.9)
	Chinese	12	(17.6)
	Indian	2	(2.9)
	Others	1	(1.5)
Smoking	Yes	1	(1.5)
	No	67	(98.5)
Medical illness	Yes	29	(42.6)
	No	39	(57.4)

Table 2. Placental findings

Placenta findings	At 20-22 weeks gestation N = 68 (%)	At 30-32 weeks gestation N = 68 (%)
Site:		
Low lying	5 (7.3)	
Not low	63 (92.7)	
Placenta Previa		4 (6.0)
Upper segment		64 (94.0)
Calcification:		
Normal	68 (100.0)	68 (100.0)
Abnormal	0 (0.0)	0 (0.0)
Lakes:		
Normal	60 (88.2)	39 (57.4)
Abnormal	8 (11.8)	29 (42.6)
Thickness:		
Normal	43 (63.2)	32 (47.1)
Abnormal	25 (36.8)	36 (52.9)
Cord insertion:		
Normal	67 (98.5)	67 (98.5)
Abnormal	1 (1.5)	1 (1.5)
Shape		
Normal	68 (100.0)	68 (100.0)
Abnormal	0 (0.0)	0 (0.0)

Table 3. Obstetric outcomes

Obstetric outcome	N = 68 (%)	
Mode of delivery		
Spontaneous Vertex Delivery (SVD)	55	(80.9)
Emergency Lower Segment Caesarean Section (LSCS)	4	(5.9)
Elective LSCS	9	(13.2)
Time of delivery		
Premature	7	(10.3)
Term	61	(89.7)
Hypertensive Disease in pregnancy		
Yes	7	(10.3)
No	61	(89.7)
Fetal Growth Restriction		
Yes	10	(14.7)
No	58	(85.3)
Low cord pH fetus		
Yes	11	(6.2)
No	57	(83.8)
Low Apgar score fetus		
Yes	0	(0.0)
No	68	(100.0)

Although abnormal placental lakes at 20-22 and 30-32 weeks of gestation were not significantly associated with intrauterine growth restriction, its presence may likely to predispose to IUGR with relative risks of 3.21 at 20-22 weeks and 2.01 at 30-32 weeks of gestation respectively. Abnormal placental thickness at both gestations carried no significance at all (Table 5).

Low umbilical cord pH was not significantly associated with abnormal placental lakes or thickness at any gestation this study was done. Neither presence of any of these abnormalities at any gestation increased the risk of developing this complication (Table 6).

Discussion

Ultrasonic imaging is widely used in antenatal care, both as a screening tool and as an aid to diagnosis. An abnormal placental morphology findings on ultrasound presents a dilemma because the lack of information regarding its pathophysiology and clinical significance. It is well known that placental morphology changes as pregnancy progresses. This study was conducted to determine whether any association exists between the finding of an abnormal placenta with an increased risk of uteroplacental complications and a poor pregnancy outcome. A total of 113 patients who came for detail scan and fulfilled the criteria participated in this study. But 68 of them completed the study. This small sample size limited the clinical importance that can be proved to the findings.

Harris et al proposed that the clinical significance of placental lakes depends on the time of appearance and size of the spaces, important lesions appearing before 20-25 weeks or being numerous (>3), or large (>2 cm)¹². There is no doubt that in some pregnancies the presence of placental lakes is associated with a poor or complicated outcome¹³. In a case report by Jauniaux and Nicholaides, the presence of lakes prior to 20 weeks was associated with IUGR¹¹. In this study, presence of abnormal lakes at 20-22 weeks and 30-32 weeks scan was associated with 37.5% and 20.7% fetus with growth restriction respectively. Besides IUGR fetus, presence of abnormal lakes also associated with hypertensive disease in pregnancy (17.2%) and fetus with low umbilical cord pH (10.3%) even though these were not statistically significant. A similar findings found in the study by Reis et al, which showed no statistically significant difference was observed in birth weight, gestational age at delivery and adverse obstetric outcome in cases presenting with placental lakes (14).

Table 4. Association between abnormal placenta findings with hypertensive disease in pregnancy

Abnormal placenta findings	Hypertensive disease in pregnancy			
	Yes N = 7 (%)	No N = 61(%)	P value	RR (95% CI)
At 20-22 weeks:				
Abnormal Lakes				
Yes	0 (0.0)	8 (100.0)	0.689	0.0
No	7 (11.7)	53 (88.3)		
Abnormal thickness			1.000	1.29 (0.31,5.30)
Yes	3 (12.0)	22 (88.0)		
No	4 (9.3)	39 (90.7)		
At 30-32 weeks:				
Abnormal Lakes				
Yes	5 (17.2)	24 (82.8)	0.222	3.36 (0.71,16.12)
No	2 (5.1)	37 (94.9)		
Abnormal thickness			0.525	2.22 (0.46,10.67)
Yes	5 (13.9)	31 (86.1)		
No	2 (6.3)	30 (93.8)		

Table 5. Association between abnormal placenta findings with growth restricted fetus

Abnormal placenta findings	Intrauterine Growth Restriction			
	Yes N = 10 (%)	No N = 58 (%)	P value	Relative Risk
At 20-22 weeks: Abnormal Lakes				
Yes	3 (37.5)	5 (62.5)	0.160	3.21 (1.04,9.99)
No	7 (11.7)	53 (88.3)		
Abnormal thickness				
Yes	3 (12.0)	22 (88.0)	0.016	0.74(0.21,2.60)
No	7 (16.3)	36 (83.7)		
At 30-32 weeks: Abnormal Lakes				
Yes	6 (20.7)	23 (79.3)	0.392	2.02 (0.63,6.50)
No	4 (10.3)	35 (89.7)		
Abnormal thickness				
Yes	5 (13.9)	31 (86.1)	1.000	0.89 (0.28,2.79)
No	5 (15.6)	27 (84.4)		

Table 6. Association between abnormal placenta findings with low umbilical cord pH fetus

Abnormal placenta findings	Low cord pH			
	Yes N = 11 (%)	No N = 57 (%)	P value	Relative Risk
At 20-22 weeks: Abnormal Lakes				
Yes	0 (0.0)	8 (100.0)	0.417	0.0
No	11 (18.3)	49 (81.7)		
Abnormal thickness				
Yes	4 (16.0)	21 (84.0)	1.000	0.98(0.32,3.03)
No	7 (16.3)	36 (83.7)		
At 30-32 weeks: Abnormal Lakes				
Yes	3 (10.3)	26 (89.7)	0.428	0.50 (0.15,1.74)
No	8 (20.5)	31 (79.5)		
Abnormal thickness				
Yes	3 (8.3)	33 (91.7)	0.062	0.33 (0.10,1.15)
No	8 (25.0)	24 (75.0)		

Sonographically thick placenta has been associated with an increased perinatal morbidity and mortality (15). Raio et al also reported that the sonographic presence of thick heterogeneous placenta is strongly associated with an adverse pregnancy outcome and often with perinatal death (16). Varying cut offs have described for placental thickness, for example 4 cm maximum at any gestation and 3.5 cm between 18-24 weeks respectively (17,18). Study done by Mital et al also showed from the 22nd week to the 35th week of gestation the placental thickness coincide almost exactly with the gestational age in weeks (19). A cut off of 3.0 cm corresponding to the 95th centile at 18-20 weeks was chosen for this study (20). Abnormal thickness of the placenta at (20-22) weeks and at 30-32 weeks in this study were found to have lack of association with hypertension disease in pregnancy, fetal growth restriction and low cord pH.

Besides abnormal placental lakes and thickness found in this study, there was no abnormal placenta shape and significant abnormal cord insertion and calcification found in this study.

Significant placental calcifications are rarely seen before 37 weeks gestation. The presence of grade 3, early in pregnancy, was described as signifying placental dysmaturity and associated with IUGR8. McKenna et al concluded that ultrasound detection of a grade 3 placenta at 36 weeks gestation might help to identify the “at-risk” pregnancy, in terms of subsequent development of gestation hypertension and delivery of a growth-restricted neonate (8). Kazzi et al found the fetus with a small biparietal diameter and a grade 3 placenta to be more likely to be small for gestational age at delivery in a high risk group of 224 patients21. Proud & Grant found that patients with a grade 3 placenta were at

increased risk of problems during labour and that their babies had an increased risk of being of low birthweight, in poor condition at birth or of perinatal death (22).

Biswas and Ghosh noted in a study that a number of macroscopic changes including the shape of the placenta and the site of umbilical cord insertion have been noted between normal placentas and those from intra-uterine growth restriction and pre-eclampsia (23). A study done by Toal M. et al showed women with abnormal placental shape at 19-23 weeks of gestation ($n = 28$) had higher odds of intrauterine fetal death (odds ratio, 4.5; 95% CI, 1.3-15.6), delivery at <32 weeks of gestation (odds ratio, 4.7; 95% CI, 1.6-14.1), and intrauterine growth restriction (odds ratio, 4.7; 95% CI, 1.4-15.1) than di women with a normal placental shape (24). Cai et al found a 3.69-fold increased risk of IUGR in the presence of abnormal UCI (odds ratio 3.69, 95% CI 1.62–8.42) (25).

This study showed an association between abnormal placenta lakes with hypertensive disease in pregnancy and intrauterine growth, even though these were not statistically significant. An increased placental thickness was not significantly associated with any of the obstetrics complications as above. On the other hand, present of placental calcification observed in this study showed no significant calcification of grade 3 and more at 30-32 weeks scan. There were also no significant abnormality detected on placenta shape, and abnormal cord insertion (besides marginal) noted in this study most probably because of the small sample size.

The conflicting data from different studies implies that there is a need to define placental morphology more rigorously at different gestations if we are to make use of these findings in practice. Although we found an association between abnormal placental thickness and lakes with poor obstetric outcome, the study size was not adequate to conclusively demonstrate statistical significance.

Limitation of the study

The numbers of respondent were limited due to several reasons such as only patients scheduled for detail scan were involved in the study and other patients with normal fetus and fulfilled the criteria for the study but was not scheduled for detail scan were not included. The ultrasound for the study was only performed by designated sonographers and fetomaternal specialist using the same model of ultrasound machine in order to reduce bias. Some of the patients defaulted a repeat scan at 30-32 week of gestations or delivered at other hospitals were also not included.

Conclusion

Presence of abnormal placental lakes at 30-32 weeks scan associated with maternal hypertensive disease, fetal growth restriction; however these were not statistically significant. A further study with a bigger sample size involving all patients who attended the antenatal clinic need to be carried out in order to achieve statistical significant.

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References

1. Vireo S, Chaddha V, Alkazaleh F, et al. Prognostic value of placental ultrasound in pregnancies complicated by absent end-diastolic flow velocity in the umbilical arteries. *Placenta* 2004; 25(8-9):735-41
2. Moldenhauer JS, Stanek J, Warshak C, et al. The frequency and severity of placental findings in women with preeclampsia are gestational age dependent. *Am J Obstet Gynecol* 2003; 189(4):1173-7
3. Kanne JP, Lalani TA, Fligner CL. The placenta revisited: Radiologic-Pathologic Correlation. *Curr Probi Diagn Radiol* 2005; 34(6):238-55
4. Abramowicz J, Sheiner E. Ultrasound of the placenta: A Systemic Approach. *Placenta* 2008; 29(3):225-40
5. Baulies S, Maiz N, Munoz A, et al. Prenatal ultrasound diagnosis of vasa praevia and analysis of risk factors. *Prenat Diagn* 2007; 27(7):595-9
6. Grannum PA, Berkowitz RL, Hobbins JC. The ultrasonic changes in the maturing placenta and their relation to fetal pulmonary maturity. *Am J Obstet Gynecol* 1979; 133(8):915-22
7. Baeza Valenzuela A, Garcia Mendez A. Premature aging of the placenta. *Ultrasonic diagnosis. Ginecol Obstet Mex* 1995; 63:287-92
8. McKenna D, Tharmaratham S, Mahsud S, et al. Ultrasonic evidence of placental calcification at 36 weeks gestation: maternal and fetal outcomes. *Acta Obstet Gynecol Scand* 2005; 84(1):7-10
9. Thompson M, Vines S, Aquilina J, et al. Are placental Lakes of any Clinical Significance? *Placenta* 2002; 23(8-9):685-90
10. Jauniaux E, Campbell S. Ultrasonographic assessment of placental abnormalities. *Am J Obstet Gynecol* 1990; 163(5):1650-8
11. Jauniaux E, Nicolaides KH. Placenta lakes, absent umbilical artery diastolic flow and poor fetal growth in early pregnancy. *Ultrasound Obstet Gynecol* 1996; 7(2):141-4
12. Harris R, Cho C, Wells W. Sonography of the placenta with emphasis on pathological correlation. *Semin Ultrasound CT MR* 1996; 17(1):66-89
13. Cooperberg P, Wright V, Carpenter C. Ultrasonographic demonstration of a placental maternal lake. *J Clin Ultrasound* 1979; 7(1):62-4
14. Reis NS, Brizot ML, Schultz R, et al. Placental lakes on sonographic examination: Correlation with obstetric outcome and pathologic findings. *J Clin Ultrasound* 2005; 33(2):67-71
15. Dombrowski M, Wolfe H, Saleh A, et al. The sonographically thick placenta : a predictor of increased perinatal morbidity and mortality. *Ultrasound Obstet Gynecol* 1992; 2(4):252-5
16. Raio L, Ghezzi F, Cromi A. The thick heterogeneous (jellylike) placenta: a strong predictor of adverse pregnancy outcome. *Prenat Diagn* 2004; 24(3):182-8
17. Hoddick W, Mahony B, Callen P, et al. Placental thickness. *J Ultrasound Med* 1985; 4(9):479-82

18. Kelly R, Nyberg D, Mack L, et al. Sonography of placental abnormalities and oligohydromnios in women with elevated alpha-fetoprotein levels: comparison with control subjects. *AJR Am J Roentgeno* 1989; 153(4):815-9
19. Mital P, Hooja N, Mehndiratta K. Placental thickness: a sonographic parameter for estimating gestational age of the fetus. *Indian Journal of Radiology and Imaging* 2002; 12(4):553-4
20. Jauniaux E, Ramsay B, Campbell S. Ultrasonographic investigation of placental morphologic characteristics and size during the second trimester of pregnancy. *Am J Obstet Gynecol* 1994; 170(1):130-7
21. Kazzi G, Gross T, Sokol R, et al. Detection of intrauterine growth retardation: a new use for sonographic placental grading. *Am J Obstet Gynecol* 1983; 145(6):733-7
22. Proud J, Grant A M. Third trimester placental grading by ultrasonography as a test of fetal wellbeing. *Br Med J (Clin Res Ed)* 1987; 294(6588):1641-4
23. Biswas S, Ghosh S. Gross morphological changes of placentas associated with intrauterine growth restriction of fetuses: A case control study. *Early Hum Dev* 2008; 84(6):357-62
24. Toal M, Sarah K, Geoff M, et al. Determinants of adverse perinatal outcome in high-risk women with abnormal uterine artery Doppler images. *Am J Obstet Gynecol* 2008; 198(3):330-37
25. Cai L, Izumi S, Koido S, et al. Abnormal placental cord insertion may induce intrauterine growth restriction in IVF-twin pregnancies. *Hum Reprod* 2006; 21(5):1285-90