

Ultrasonographically Observed Grade III Placenta at 36 Weeks' Gestation: Maternal and Fetal Outcomes

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ABSTRACT:

BACKGROUND:

Current ultrasound assessment of placental calcification relies on Grannum grading. The ultrasonographic appearance of grade III placental maturation, if it occurs before 37 weeks, may signify placental dysfunction and is found to be associated with development of pre-eclampsia and low birth weight.

OBJECTIVE:

To look at the prevalence of a grade III placenta at 36 weeks' gestation in a low-risk obstetric population, and to explore the association between premature aging observed ultrasonographically and pregnancy outcome.

METHODS:

Scans were performed at 36 weeks' gestation in 591 low-risk pregnant women to determine placental maturity. The prevalence of grade III placenta at 36 weeks' gestation was determined. Follow-up was performed for the group of women demonstrating a grade III placenta in comparison to those not demonstrating a grade III placenta for determining pregnancy outcome.

RESULTS:

The prevalence of grade III placenta at 36 weeks' gestation was 3.9%. A grade III placenta at 36 weeks' gestation was significantly associated with young maternal age $P = 0.01$. The Grannum grade III of the placenta at 36 weeks' gestation was statistically associated with increased risk for development of proteinuric pregnancy-induced hypertension (PIH) later in pregnancy (RR 4.94; 95% CI 1.15-21.26), $P = 0.021$. Women demonstrating a grade III placenta at 36 weeks' gestation had a significant high risk of induction of labour for suspected fetal compromise (RR 4.7; 95% CI 1.76-12.59), $P = 0.001$. The risk for delivering a baby with a weight <10th centile at birth was significantly higher in women with grade III placentas in comparison to those with grades 0-II (RR 3.19; 95% CI 1.23-8.27), $P = 0.017$.

CONCLUSION:

In a low-risk obstetric population, ultrasound detection of Grannum grade III placenta at 36 weeks' gestation helps to identify at risk pregnancy. It appears to predict subsequent development of proteinuric PIH and may help in identifying the growth-restricted baby.

KEYWORDS: ultrasound, grade III, placenta, outcomes

INTRODUCTION:

The placenta is essential to fetal well-being, growth and development; it can be demonstrated reliably and accurately by ultrasound ⁽¹⁾. The association of ultrasonically detectable placental changes with increasing gestational age was first reported by Winsberg ⁽²⁾, but it was Grannum *et al.* ⁽³⁾ who introduced a grading system based on the ultrasonographic appearance of placentas. They graded placentas from 0 (Immature) to III (mature) on the basis of changes in the appearance of the chorionic plate, placental structure and basal layer. By 38 gestational weeks, 5-10% of placentas present

as grade III ^(3, 4). It used to be thought that a Grannum grade III placenta was associated with mature fetal lung and placental dysfunction ⁽⁵⁾. Brown *et al.* have shown that a grade III placenta before term is associated with maternal smoking ⁽⁶⁾. Furthermore, in the unselected obstetric population a grade III placenta at or below 35 weeks' gestation has been shown to be associated with subsequent development of pre-eclampsia ⁽⁷⁾ and pregnancies so identified are at increased risk of neonatal morbidity and mortality ^(8, 9). McKenna *et al.* in 2005 suggested a link with accelerated placental maturation and maternal disease ⁽¹⁰⁾. It has been substantiated by smaller studies ⁽¹¹⁾. A recent study by Cooley *et al.* in 2010 further substantiates this association ⁽¹²⁾. This study was

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designed to look at the prevalence of grade III placentas at 36 weeks' gestation in a low-risk obstetric Iraqi population, to evaluate the relationship between a grade III placenta at 36 weeks' gestation and maternal characteristics that may be considered relevant in pregnancy and to determine the impact of placental architecture on pregnancy outcome in this low-risk obstetric population.

MATERIALS AND METHODS:

The study was conducted in the Department of Obstetrics and Gynaecology at Al-Yarmouk Teaching Hospital, Baghdad, Iraq during the period from the 1st of August 2009 to the end of July 2010. The local ethics committee approved the study. The inclusion criteria to the study were singleton pregnancies and known gestational age confirmed by ultrasound at <20 weeks' gestation. The exclusion criteria were multiple pregnancy; known maternal medical problem; obstetric complication in a previous pregnancy; obstetric complication in this pregnancy prior to 36 weeks' gestation; and known fetal abnormality. All recruited pregnant women gave informed consent to participate in this study. The study was carried out on two steps. Step one: cross-sectional study for determining the prevalence of grade III placenta at 36 weeks' gestation in a low-risk obstetric population. Step two: follow-up cohort study of those with grade III placenta at 36 weeks' gestation in comparison to those patients not demonstrating a grade III placenta for determining pregnancy outcome.

The ultrasound examination was performed at 36 weeks' gestation to determine placental maturity using a 2.0-5.0 MHz curvilinear transabdominal probe, of SIEMENS G-50 equipment. Particular attention was directed to the placenta. Placental maturity was determined using the Grannum classification by grading the placenta on a scale of 0 through III. Grading was done according to the sonographic appearance of the chorionic plate, the

placental substance, and the basal plate. The grading was based on the appearance of the bulk of the placenta rather than the edges. For the purpose of the study, the original Grannum grades 0 and I was combined into a single category named grade I. A grade 0 placenta has an easily delineated, relatively straight chorionic plate and a homogeneous texture throughout. A grade I placenta is characterized by an undulatory chorionic plate and scattered echogenic areas within. A grade II placenta is recognized by the presence of small echogenic areas along the basal layer of the placenta and the division of the placenta by comma-like echogenic densities that originate at the chorionic plate. A grade III placenta is characterized by echogenic indentations extending from the chorionic plate to the basal layer dividing the placenta into discrete components, resembling cotyledons. In addition irregular densities that cast acoustic shadows are occasionally present near the chorionic plate.

The studied pregnant women were allocated into two groups: grade III placenta group comprised those patients demonstrating a grade III placenta at 36 weeks' gestation; and the grade 0-II placenta group comprised patients not demonstrating a grade III placenta. Both groups were compared for maternal age, parity, maternal smoking, proteinuric pregnancy-induced hypertension, fetal distress in labour, mode of delivery, Apgars, need for neonatal resuscitation at delivery, birth weight and admission to neonatal intensive care unit (NICU).

Statistical analysis:

Data were analyzed using the computer facility with the available statistical software packages of Epi-Info version 6 (WHO recommended). Data were presented as frequency and percentage. Odds ratio (OR) and its 95% confidence interval (CI) was calculated for the part one data, while relative risk (RR) and its 95% confidence interval (CI) was calculated for the part two data. *P* value was calculated using the χ^2 -test and a *P* ≤ 0.05 was considered a significant difference.

Table 1: Maternal and Fetal characteristics

Characteristics	Grade III placenta (n=23) No (%)	Grade 0-II placenta (n=568) No (%)	Odds ratio (95% CI)	P value
Nulliparous	13 (56.5%)	233 (41%)	1.87 (0.75-4.68)	0.139
Maternal age <25 years	12 (52.2%)	156 (27.5%)	2.88 (1.16-7.17)	0.01*
Smoking	2 (8.7%)	48 (8.5%)	1.03 (0.25-4.27)	0.967
Male fetus	13 (56.5%)	291 (51.2%)	1.24 (0.5-3.1)	0.619

CI, Confidence interval

* Significant difference

RESULTS:

In this low-risk obstetric population scanned at 36 weeks' gestation, placentas from 591 patients were examined, of which 23 (3.9%) demonstrated a grade III placenta (Grannum classification). A grade II

placenta was demonstrated in 108 (18.3%) of patients and 460 (77.8%) demonstrated a grade 0 or grade I placenta.

Figure 1 illustrates the ultrasound appearances associated with a Grannum grade III placenta.



Fig.1:Grannum grade III anterior placenta at 36 weeks' gestation

Maternal and fetal characteristics are presented in table 1.

A grade III placenta was more likely to be found in a nulliparous patient, 56.5% (13/23) vs.41% (233/568), but the differences were insufficient to reach statistical significance (Table1). A grade III placenta at 36 weeks was found to be significantly associated with young maternal age (age <25 years; 12 (52.2%) grade III vs. 156 (27.5%) grades 0-II), *P* = 0.01. A non-significant association with maternal smoking was observed: 2 (8.7%) women with grade III

placentas were smokers compared with 48 (8.5%) women with grades 0-II. Also a non-significant association was found with fetal sex: 13 (56.5%) women with grade III placentas were pregnant with male fetus compared with 291 (51.2%) women with grades 0-II.

The pregnancy outcomes are compared between the study groups and are summarized in table 2.

Table 2: Pregnancy Outcomes

	Grade III placenta (n=23) No (%)	Grade 0-II placenta (n=568) No (%)	Relative risk (95% CI)	P value
Proteinuric PIH	2 (8.7%)	10 (1.8 %)	4.94 (1.15-21.26)	0.021*
Induction for suspected fetal compromise	4 (17.4 %)	21 (3.7 %)	4.7 (1.76-12.59)	0.001*
Spontaneous labour	12 (52.2 %)	339 (59.7 %)	0.87 (0.59-1.3)	0.472
Abnormal CTG	4 (17.4 %)	71 (12.5 %)	1.39 (0.56-3.48)	0.490
Meconium-stained liquor	3 (13 %)	70 (12.3 %)	1.06 (0.36-3.11)	0.918
Normal vaginal delivery	14 (60.9 %)	361 (63.6 %)	0.96 (0.69-0.34)	0.793
Apgar <7 at 5 minutes	1 (4.3 %)	23 (4 %)	1.07 (0.15-7.61)	0.943
Neonatal resuscitation	17 (73.9 %)	410 (72.2 %)	1.02 (0.8-1.31)	0.856
Birth weight <10 th centile	4 (17.4 %)	31 (5.5 %)	3.19 (1.23-8.27)	0.017*
Birth weight >90 th centile	2 (8.7 %)	55 (9.7 %)	0.9 (0.23-3.46)	0.875
Admission to NICU	1 (4.3 %)	24 (4.2 %)	1.03 (0.15-7.28)	0.977

CI, Confidence interval; PIH, pregnancy- induced hypertension; CTG, cardiotocography; NICU, neonatal intensive care unit.

*Significant difference

Two patients (8.7%) demonstrating a grade III placenta at 36 weeks' gestation subsequently went on to develop proteinuric pregnancy-induced hypertension. This compares with 10 (1.8%) patients with grades 0-II, $P = 0.021$. The relative risk of developing pre-eclampsia later in the pregnancy was 4.94 (1.15-21.26) among those demonstrating a grade III placenta. Interestingly, none of these patients had proteinuria or hypertension at the time of their 36-week scan (Table 2). In this low-risk group of 591 patients, a total of 26 patients had their labour induced for suspected fetal compromise at a later stage in their pregnancy. A grade III placenta at 36 weeks' gestation helped to identify these compromised pregnancies, 17.4% (4/23) vs. 3.7% (21/568), relative risk 4.7 (1.76-12.59), $P = 0.001$. In those demonstrating a grade III placenta, 17.4% (4) delivered babies less than the 10th centile for weight at birth. This compares with 5.5% (31) in the grade 0-II group, $P = 0.017$. The relative risk of delivering a baby less than the 10th centile for weight at birth was 3.19 (1.23-8.27) among those demonstrating a grade III placenta.

A grade III placenta was not associated with a poor perinatal outcome. Fetal distress in labour (abnormal cardiotocograph and meconium-stained liquor) was not associated with a grade III placenta, nor was it associated with a low Apgar score, an increased need for neonatal resuscitation, or admission to neonatal intensive care unit (Table 2).

DISCUSSION:

The placenta mediates the intrauterine interaction between a mother and her baby, it is directly responsible for mediating and/or modulating the maternal environment necessary for normal fetal development⁽¹³⁾. As the placenta ages, it begins to thin and in the third trimester may calcify. These changes are variable, but in approximately 15% of cases the calcifications extend completely through the substance of the placenta, completely outlining the cotyledons. These are termed grade III changes and should not occur before 34 weeks⁽¹⁴⁾.

Eighty percent of pregnancies are considered antenatally to be "low-risk", increased surveillance, as the result of an ultrasound scan, has helped to identify the high-risk fetus in a low-risk antenatal population⁽¹⁵⁾.

In this low-risk population scanned at 36 weeks, 3.9% of placentas demonstrated a grade III placenta. This finding was comparable to the work done by McKenna *et al.*⁽¹⁰⁾, who demonstrated a grade III placenta in 3.8% of a low-risk population at 36 weeks' gestation. A grade III placenta was associated with pregnancies that we know are more likely to be complicated: the young, nulliparous patient, who

smokes^(6, 10). This study has confirmed a statistical significant association between the presence of a grade III placenta and young maternal age. The study also confirmed that a mother demonstrating a grade III placenta at 36 weeks' gestation on scan was

nearly about two times more likely to be nulliparous although the latter did not reach statistical significance. In addition, a non-significant association between a grade III placenta at 36 weeks' gestation and maternal smoking was observed, this disagree with the findings reported by McKenna *et al.*⁽¹⁰⁾. This may be explained by the fact that Asian women almost invariably did not smoke. In fact, smaller numbers were smokers in our study population in comparison to the numbers reported by McKenna *et al.* The study findings also confirmed a non-significant association of a grade III placenta with male fetus. This was also the case in the work done by McKenna *et al.*⁽¹⁰⁾.

Placental grading has been used to predict an increased antepartum risk and can be used in evaluating fetuses at risk for intrauterine growth retardation (IUGR)⁽¹⁶⁾. Premature placental maturation to a grade III configuration has been found in patients with chronic hypertension, pre-eclampsia, and IUGR^(17, 18). Grannum and Hobbins⁽⁴⁾ stated that finding a grade III placenta before 35 weeks may precede the diagnosis of pre-eclampsia, or IUGR and should prompt close follow-up of the patient for the duration of the pregnancy. Interest in these placental ultrasound findings remote from term has found a link to fetal death, IUGR, fetal distress, and meconium staining in labour⁽¹⁹⁾. A British pilot randomized controlled trial found that reporting Grannum grade III placentas at 36 weeks, followed by a plan of fetal monitoring reduced the risk of perinatal death⁽⁹⁾. Placental grading on ultrasound examination – the Grannum classification – has been incorporated in the biophysical profile to give an overall score of 12 rather than 10⁽²⁰⁾. McKenna *et al.* in 2005 suggested that ultrasound detection of a grade III placenta at 36 weeks' gestation in a low-risk population may identify a subgroup of women at increased risk of developing proteinuric PIH in the later stages of pregnancy and to have their labour induced for suspected fetal compromise. Furthermore, mothers demonstrating a grade III placenta at 36 weeks' gestation were more likely to deliver a baby less than the 10th centile for weight at birth⁽¹⁰⁾. A recent study by Cooley *et al.* in 2010 also suggested that higher Grannum grades were associated with an increase in the incidence of pre-eclampsia, obstetric intervention, and small for gestational age (SGA) infants⁽¹²⁾.

In the present study, a mother demonstrating a grade III placenta at 36 weeks' gestation was nearly five times more likely to develop pre-eclampsia later in the pregnancy, and was three times more likely to deliver a baby less than the 10th centile for weight at birth. Furthermore, in this low-risk population, mothers demonstrating a grade III placenta at 36 weeks' gestation need nearly five times more likely to have their labour induced for suspected fetal compromise at a later stage in their pregnancy. A grade III placenta at 36 weeks' gestation helped to identify these compromised pregnancies.

In a low-risk obstetric population at 36 weeks' gestation, these results do provide a basis for using placental grading as a screening tool to identify the high-risk fetus. An ultrasound scan can be performed in a matter of minutes by accoucheurs with modest training and skills. Once identified as high risk, pregnancy outcome can be optimized by using tools (Doppler ultrasound, etc.) reserved for previously identified high risk pregnancies, such as previous stillbirth and a previous pregnancy complicated by IUGR.

CONCLUSION:

Ultrasound detection of a grade III placenta at 36 weeks' gestation in a low-risk population helps to identify the "at risk" pregnancy. It appears to predict subsequent development of pre-eclampsia and may help in identifying the growth-restricted baby. It may be used as an appropriate screening tool in the low-risk obstetric population, to verify the low-risk and identify the high-risk fetus.

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