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Influence of placental size and gross abnormalities on intrauterine growth retardation in high-risk pregnancies

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Objective. The aim of the study was to determine a relationship between insufficient fetal growth placental thickness, weight, cord insertion place to placenta and placental gross abnormalities (histological lesions).

Materials and methods. During 1998–2001, 121 patients with suspected intrauterine fetal growth retardation were enrolled into the study. After delivery, all study population was divided into two groups according to newborns' birthweight: the control group (birthweight between the 10th and the 90th percentile) and the research group (birthweight below the 10th percentile). Placental thickness was measured by ultrasound antenatally. After delivery, placental thickness, weight, cord insertion place were estimated and routine histological examinations were performed. Also, the newborns were weighed and the placental ratio (placental weight / birthweight) was calculated.

Results. 121 patients were enrolled into the study, and results from 120 patients were obtained for analysis. Mean placental thickness, measured either before delivery by ultrasound or after delivery, was larger in the control group ($p < 0.05$). Mean placental weight was statistically significally less in the research group than in the control group (425 ± 111.2 g and 608.2 ± 78.3 g, respectively). The placental ratio and cord insertion place didn't show statistically significant differences. Multiple placental infarctions (49.2%) dominated in the study group, but in 21 cases (33.3%) no histological abnormalities were found.

Conclusion. Placental weight and thickness are associated with intrauterine growth retardation, but are less affected than the fetus. Cord insertion place has no influence on fetal growth. Multiple placental infarctions are only lesions found during routine histological examination.

Key words: intrauterine growth retardation, placental thickness, placental weight, gross abnormalities, cord insertion

INTRODUCTION

Small for gestational age babies mostly have small placentas, and this common observation was confirmed by morphometric studies (1). It was believed that the baby is small because the placenta is small. Simple morphological studies of placental lesions have denied this correlation, because extensive perivillous fibrin deposits reducing the functional activity by 30–40% had no discernible influence on fetal growth (2). However, intrauterine growth retardation (IUGR) is associated with impoverished villous development and fetoplacental angiogenesis (3). Decrease of fetal weight is significally larger than placental weight loss, and the placental index (placental weight and fetal weight ratio) of small for gestational age (SGA) infants (birth weight below the 10th percentile) is larger than that of appropriate for gestational age (AGA) infants (4–6). But generally IUGR is related to decreased placental weight and a reduced number of functional placental units (7, 8). In case of IUGR, placental thickness by ultrasound measures may vary widely. The placenta in association with IUGR is more likely to be thick but less in weight (9). Sonographically thick placenta is associated with an increased ratio of both SGA and large for gestational age infants at term (10). Most of gross placental abnormalities do not influence fetal growth (2, 11,

12,). Placentas from IUGR cases had a significantly increased number of villous infarcts, cytotrophoblast proliferation and thickening of the villous trophoblastic basal membrane as compared to AGA cases (13). Placental infarctions usually are small, and only the multiplicity of these lesions has an influence on fetal growth (14). The severity of placental abnormalities expressed as the cumulative number of placental lesions is a significant risk factor for IUGR and perinatal brain injury (15). The aim of the present study was to define the placental thickness, weight, cord insertion place to placenta and placental gross abnormalities (histological lesions) in relationship with insufficient fetal growth.

MATERIALS AND METHODS

The study was performed in 1998–2001. IUGR was suspected to all patients involved in the study. The examinations were performed between the 28th and 40th weeks of gestation. The period between the ultrasound evaluation and delivery was less than 2 days. If US examination was repeated, the last data were taken for analysis. Inclusion criteria were:

– one fetus;
– suspected IUGR (16):
• insufficient fundal height growth;
• inadequate ultrasonographic fetometry.

Exclusion criteria:

– multiple pregnancy;
– impossibility to evaluate pregnancy outcome;
– disagreement of the patient to take part in the study.

Gestational age was calculated according to LMP or, when it was impossible to determine the LMP, by early (up to 12 weeks) ultrasound examination. All pregnancies were terminated because of suspicion of IUGR either by induced vaginal delivery or by cesarean section.

After delivery all patients were divided into two groups: the research and the control. A criterion for division was newborns' weight corresponding to the gestational age: birth weight less than 10th percentile (the research group) and between the 10th and the 90th percentile (the control group) according to the birth standard of Lithuania (17). All results were compared between these two groups.

The GE Logiq 500 ultrasound system version 2.00 was used for the study. In order to avoid placental thickness variations, its thickness was measured by ultrasound at three places: once in the middle part of the placenta and two measurements in the opposite site of the placenta 2 cm from the margin. The mean of three measurements was calculated and used for analysis. Ultrasound examination was performed less than 48 hours before delivery.

Cord insertion place to placenta was determined immediately after placental expulsion. It was evaluated as central (bull's-eye sign), eccentric, marginal (at the edge) or velamentous. The placenta was weighed after the removal of the umbilical cord and membranes. Placental thickness after delivery was estimated by performing three cross-sections: one in the middle part and two cuts 2 cm from the margin of the placenta in the opposite sites. The mean value of these 3 measurements was taken to analysis.

Later the placenta was sent to routine histological examination. The pathologist at the moment of placenta examination didn't know the newborn's weight and its correspondence to the birth standard of Lithuania. The only specification was that pregnancy was terminated under the suspicion of IUGR. Placenta examination was performed according to the requirements to the quality of pathological investigation, set by Ministry of Health of the Republic of Lithuania.

The newborn was weighed in the delivery room immediately after delivery. The placental ratio (placental weight/newborn weight) was calculated.

Statistical analyses were carried out using the SPSS statistical programme for Windows (version 10.0). The values of parameters with standard deviations and 95% confidence interval were calculated. The values in the text are means ± SD. Statistical differences of the values were estimated using Student's t test for parametric variables and the Mann–Whitney U test for nonparametric variables. The bivariate correlation was used for evaluation of interdependence between the variables, and the Pearson correlation coefficient was calculated. For all analysis, the p values <0.05 were considered statistically significant.

RESULTS

121 patients were involved into the study. IUGR was suspected to all of them and they met the inclusion criteria. Results from 120 patients (99.2%) were obtained for analysis. One patient after delivery disagreed to take part in the study. The control group consisted of 55 and the research group of 65 patients according to their babies' birthweight. Pregnancy time varied from 28 to 40 weeks. The average pregnancy time between the groups was similar (Table 1).

The mean placental thickness estimated by ultrasound was 27.4 ± 5.9 mm in the research group and 32.8 ± 5.2 mm in the control group. After delivery, the mean placental thickness in the research and the control groups was 15.8 ± 5.3 and 27.7 ± 6.2 mm, respectively. Mean placental thickness measured before delivery by ultrasound or after delivery was bigger in the control group ($p < 0.05$). Ultrasound examination showed larger measures of placenta thickness than they were estimated after delivery in both groups ($p < 0.05$). Mean placental weight was statistically significally less in the research than in the

control group reaching, 425 ± 111.2 and 608.2 ± 78.3 g respectively (Table 2).

Placental thickness measured by ultrasound correlated with placental thickness after delivery (the Pearson correlation coefficient 0.425, $p < 0.05$). Results after analyzing the correlation separately in the groups showed a good correlation only in the research group, meanwhile in the control group it wasn't statistically significant (Pearson's correlation coefficient 0.297 and 0.065, $p < 0.05$ and $p = 0.64$, respectively) (Fig. 1).

The placental ratio was found to be higher in the research group, but the difference wasn't statistically significant ($p = 0.48$) (Table 3).

The placental ratio had a significant negative correlation with birthweight in all study contingents and in the control and research groups too (Pearson's correlation coefficient –0.605, –0.765 and –0.691, respectively, $p < 0.01$) (Fig. 2).

Central cord insertion to placenta prevailed in the control group (25 cases, 45.5%), meanwhile eccentrical and marginal cord insertion predominated in the research group (46 cases, 70.8%). Velamentous cord insertion was found only in two cases in both groups. There were no statistical differences in cord insertion between the groups ($p > 0.05$) (Figs. 3a and 3b).

Routine placental histological examination was performed and evaluated in 48 cases of 55 in the control group (87.3%) and 63 cases of 65 in the research group (96.9%). In the research group, the main histological finding was multiple infarctions (31 cases, 49.2%), but there were no abnormalities in 21 cases (33.3%). In the control group multiple infarctions were found only in 2 cases (4.2%) and in 37 cases (77.1%) there were no abnormalities. Other placental abnormalities were rare and there were no statistical differences in the groups (Table 4).

DISCUSSION

The placenta and its adaptation to abnormal conditions are very important to fetal growth. Although the placenta adapts itself to a disturbed supply and demand, these compensatory changes are insufficient and result in fetal growth retardation (18). Small fetuses have small placentas with substantial changes in placental morphology (1). Ertan et al. (2003) concluded that in pregnancies at risk the placental weights were significantly lower (216 g *vs.* 385 g) and signi-

Table 1. **Average pregnancy time in the study groups**

	Control group (n = 55)	Research group (n = 65)	Mean difference	95% CI	p
Pregnancy time, weeks	37.1 ± 2.9	36.5 ± 3.4	0.6	0.46–1.76	0.2

Table 2. **Placental thickness and weight in the study groups**

	Research group	Control group	Mean difference	p
Placental thickness by US / range, mm	27.4 ± 5.9 15–46	32.8 ± 5.2 22–48	5.6	< 0.05
Placental thickness after delivery / range, mm	15.8 ± 5.3 8–30	27.7 ± 6.2 10–38	11.9	< 0.05
Placental weight / range, g	425 ± 111.2 200–800	608.2 ± 78.3 450–800	183.2	< 0.05

Table 3. **Placental ratio in the study groups**

	Research group	Control group	Mean difference	95% CI	p
Placental ratio	0.234 ± 0.014	0.219 ± 0.015	0.015 ± 0.021	–0.055–0.026	0.48

Table 4. **Differences in placental lesions in the groups**

	No abnormalities, n (%)	Multiple infarctions, n (%)	Inflammatory changes, n (%)	Other, n (%)
Research group, n = 63	21 (33.3)	31 (49.2)	9 (14.3)	2 (3.2)
Control group, n = 48	37 (77.1)	2 (4.2)	8 (16.6)	1 (2.1)
p	<0.05	<0.05	0.85	0.55

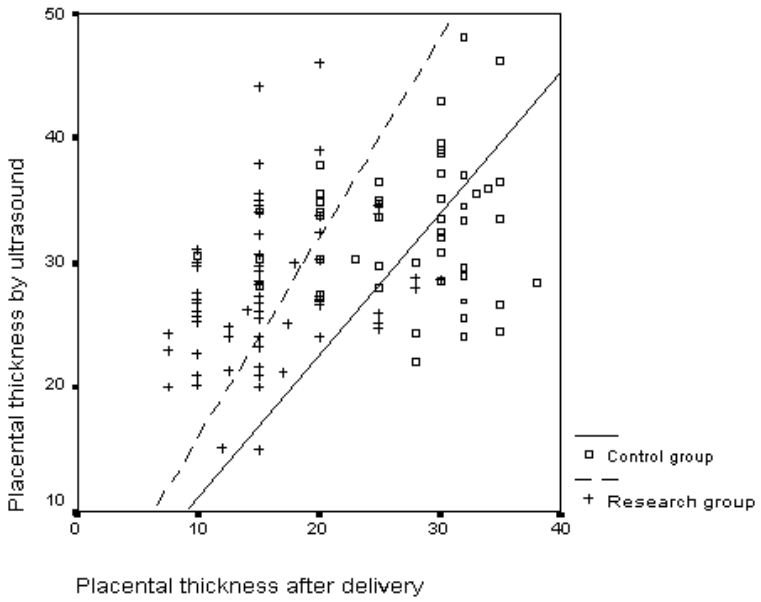

Fig. 1. Correlation between the values of placental thickness measured by ultrasound and after delivery

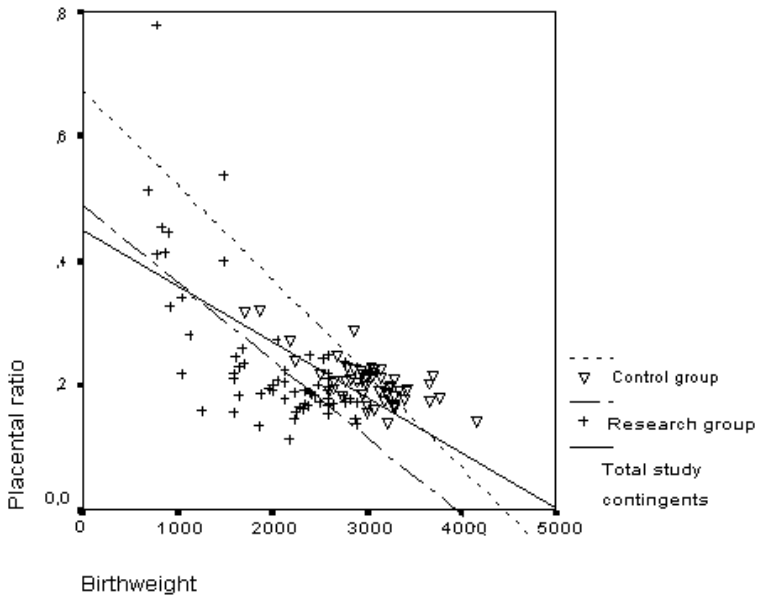

Fig. 2. Correlation between placental ratio and birth weight in the total study contingent and separately in the study groups

ficant changes were found in fetal peripheral blood flow in IUGR cases (8). Elchalal et al. (2000) determined that placental thickness during pregnancy above the 90th percentile was associated with a twofold risk of birthweight less than 2500 g as compared to the control group ($p = 0.03$, 95% CI 1.00–8.14). Thick placenta was also associated with birthweight above 4000 g. Risk for macrosomia in the thick placenta group was higher than in the control group (20.5% and 5.3%, respectively, $p < 0.05$, 95% CI 2.08–13.85). These results suggest that the sonographically thick placenta is associated with an increased perinatal risk and mortality related to higher rates of both small and large for gestational age infants at term (10).

The results of the present study suggest that placental weight is statistically significantly lower in cases of IUGR. The thesis of small fetus and small placenta has been confirmed. Contrary to other data, in cases of IUGR placentas are also thinner (Table 2). Maybe this fact reflects additional disturbance in placental adaptation and its compensatory changes in response to inadequate supply and demand.

Although placental weight in cases of IUGR is less, fetus weight loss is more considerable. The placental ratio (placental weight / fetal weight) is higher when fetus growth is affected, because maturational changes are taking place throughout gestation within the placenta in order to increase the transfer capacities (6). Leo and Tam (2000) concluded that placental size increased relatively to infant size in pregnancies complicated by anemia (Hb level less 100 g/l), but whether this phenomenon reflected actual placental hypertrophy or failure of fetal growth to keep up with placental growth remains to be determined (5). In Lithuania, Verkauskiene, Albertsson Wikland and Niklasson (2002) compared, weight of newborns and placentas in cases of IUGR. They concluded that these newborns had a low mean placental weight but a high placental ratio. Placental ratio had a strongly negative relationship with birthweight, and it was a strong indicator of impaired prenatal linear growth (4). This study found a strong negative correlation between placental ratio and birthweight. Placental ratio had a tendency to be higher in case of IUGR, but the difference wasn't statistically significant ($p = 0.48$). Maybe the difference would be larger if the control group consisted of patients without antenatal suspicion of IUGR.

The cord insertion place in the placenta had no significant influence on fetal growth. In approximately 1% of singleton pregnancies cord insertion is located away from placental mass, and only this condition, known as velamentous insertion, has been associated with IUGR (19). Patients with unexplained elevated second-trimester maternal serum human chorionic gonadotropin (hCG) concentrations are at increased risk of IUGR (OR 1.46, 95% CI 1.03–2.06) and velamentous cord insertion (OR 2.62, 95% CI 1.47–4.69). It is necessary to determine cord inser-

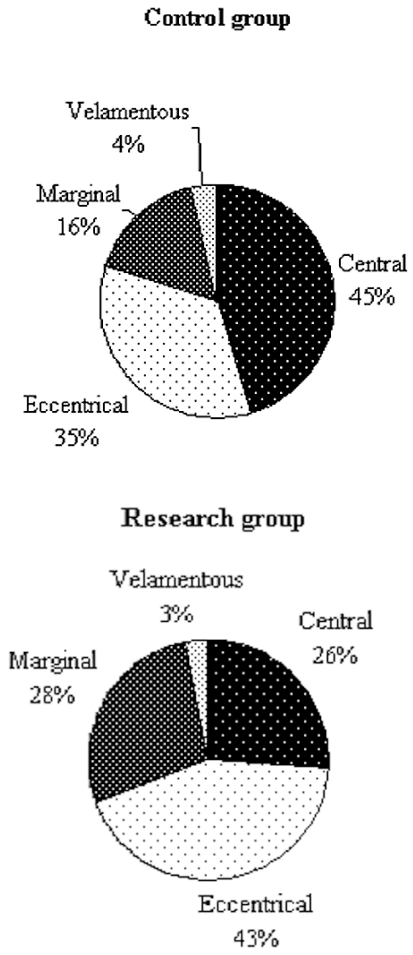

Fig. 3. Cord insertion place in control and research groups

tion by Doppler examination at risk for preeclampsia or if abnormal uterine artery velosimetry results are found (20). The present study has confirmed that cord insertion had no influence on fetal growth. Even velamentous insertion was found in both groups in equal proportion.

Routine placental histological examination didn't show significant differences between growth-restricted and normal newborns. It is common for general surgical pathologists not to recognize placental lesions, which may be of clinical significance (21). Sometimes in cases of IUGR insufficient placental capillary network (22) and enhanced necrotic cell death were found (23). Madazli et al. (2003) have concluded that the increased number of villous infarcts, cytotrophoblast proliferation and thickening of the villous trophoblastic basal membrane were significantly associated with abnormal umbilical artery Doppler velocimetry (OR 21.04, 3.8–115.9; p< 0.001). Women with abnormal uterine and umbilical artery Doppler velocimetries delivered earlier and their babies had a lower mean birth and placental weight (P < 0.001) (13). IUGR depended on the cumulative number of placental lesions. Three and more pathological placental findings had a strong association with an increased risk of IUGR (OR 14.18, 95% CI 3.41–58.99; p < 0.001) (14). Other findings such as placental lakes (24), placental surface cysts (12) or subamniotic hematomas (25, 26) had no relationship with IUGR.

The results of this study showed that the only placental lesion that can be associated with IUGR is multiple infarctions. Even in IUGR in about 1/3 of cases no histological lesions were found in routine histological examinations. Inflammatory changes had no influence on fetal growth.

Placental macroanatomic changes are related with IUGR. Antenatal and postnatal estimation of placental size and structure is important when restricted fetal growth is suspected. A decrease of placental weight is less significant than fetal weight decrease. Cord insertion has no influence on fetal growth. Thus, multiple infarctions are the main placental lesion related to IUGR found during routine histological examination. Restricted fetal growth can occur without any placental gross abnormality. Routine antenatal and postnatal estimation of placental size and structure is an important but insufficient criterion in searching for the cause of IUGR.

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PLACENTOS DYDÞIO IR MAKROSKOPINIØ PAKITIMØ ÁTAKA VAISIAUS INTRAUTERINIO AUGIMO SULËTËJIMUI ESANT DIDELËS RIZIKOS NËÐTUMUI

S a n t r a u k a

Darbo tikslas – ávertinti placentos storio, svorio, virkðtelës prisitvirtinimo vietos ir placentos makroskopiniø pakitimø ryðá su intrauteriniu vaisiaus augimu.

Darbo objektas ir metodai. 1998–2001 metais á tyrimà átraukta 121 nëðèioji, kurios vaisiui buvo átartas intrauterinio augimo sulëtëjimas (IUAS). Po gimdymo visos tiriamosios suskirstytos á dvi grupes: kontrolinæ (naujagimiø gimimo svoris tarp 10 ir 90 procentilës) ir tiriamàjà grupes (naujagimiø svoris maþesnis nei 10 procentiliø). Placentos storis iki gimdymo buvo matuotas ultragarsu. Po gimdymo placenta buvo pasverta, iðmatuotas jos storis, ávertinta virkðtelës prisitvirtinimo vieta ir atliktas rutininis histologinis tyrimas. Gimæ naujagimiai buvo pasverti ir apskaièiuotas placentinis indeksas (placentos svorio ir naujagimio svorio santykis).

Rezultatai. Tyrime dalyvavo 121 nëðèioji. Analizuoti 120 atvejø duomenys. Ir iki gimdymo, ir po gimdymo vidutinis placentos storis buvo didesnis kontrolinës grupës ($p < 0,05$). Vidutinis placentos svoris buvo statistiðkai maþesnis tiriamosios nei kontrolinës grupës moterø: atitinkamai 425 ± 111,2 g ir 608,2 ± 78,3 g. Placentinis indeksas bei virkðtelës prisitvirtinimo vieta abiejø grupiø labai nesiskyrë. Daugybiniai placentos infarktai vyravo tiriamojoje grupëje (49,2%), bet 21 atveju (33,3%) nerasta jokios ryðkesnës placentos patologijos net ir esant IUAS.

Iðvados. Sumaþëjæs placentos storis ir svoris yra susijæs su IUAS, bet pakinta maþiau nei vaisiaus svoris. Virkðtelës prisitvirtinimo vieta neturi átakos vaisiaus intrauteriniam augimui. Rutininio histologinio tyrimo duomenimis, tik daugybiniai placentos infarktai yra susijæ su nepakankamu vaisiaus augimu.

Raktaþodþiai: intrauterinio augimo sulëtëjimas, placentos storis, placentos svoris, makroskopiniai pakitimai, virkðtelës prisitvirtinimas