INTRAUTERINE GROWTH RESTRICTION – PREDICTIVE SERUM MARKERS

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INTRAUTERINE GROWTH RESTRICTION – PREDICTIVE SERUM MARKERS (Abstract) 

Aim: To determine during the first trimester of pregnancy some serum and ultrasound markers that could improve perinatal morbidity and mortality in women with intrauterine growth restriction (IUGR).

Material and methods: Prospective study of pregnant women gestational age 11 weeks and 0 days - 13 weeks and 6 days, consisting in the determination of pregnancy associated plasma protein (PAPP-A), mean platelet volume (MPV), and ultrasound appearance of placenta.

Discussion and Conclusions: This study suggests that screening by detailed history and PAPP-A and MPV determination during the first trimester of pregnancy in women at risk for IUGR makes possible the prophylactic treatment and monitoring of pregnancy according to a given protocol and thus neonatal morbidity and mortality to be reduced.

Keywords: INTRAUTERINE GROWTH RESTRICTION, PREGNANCY-ASSOCIATED PLASMA PROTEIN, MEAN PLATELET VOLUME.

Detection of IUGR risk in pregnant women in the first trimester is an important goal of research in modern obstetrics. It is known that fetuses diagnosed with IUGR are at high risk of perinatal morbidity and mortality by the complications that may occur (1,2,3).

In this context the early determination of the predictive markers for the risk of IUGR is essential. First trimester screening consists in the monitoring of pregnant women at risk according to a secondary prevention protocol and monitoring specific to each associated disorder so that the following two situations that affect fetal prognosis to be avoided:

- premature, unnecessary extraction of a healthy fetus
- delayed extraction due to fetal distress undetected on time and which can result in intrauterine fetal death

Evaluation of the predisposing/causative factors for IUGR is the first step and consists in history taking, thorough physical examination, ultrasound, and specific laboratory tests, all aimed at ultimately determining the presence or absence of the risk for IUGR (4-16)

PAPP-A is a protein secreted by the syncytiotrophoblast cells and maternal decidua, thus low PAPP-A levels are associated with abnormal placentation and fetal growth (17-22).

MPV – Increased MPV reflects en-
enhanced platelet activation, which may be caused by impaired uteroplacental circulation, and inadequate trophoblastic invasion, associated with an implicit risk of preeclampsia (PE) and IUGR (23-25)

**MATERIAL AND METHODS**

This prospective study was conducted in 70 women 11 weeks and 0 days -13 weeks and 6 days gestational age monitoring their pregnancy at the Neamt County Emergency Hospital between August 1, 2014 and September 1, 2015.

Throughout their pregnancy the women included in the study received prenatal care:
- ultrasound examinations (at 12 -13 weeks - fetal morphology, fetal development and placental appearance, at 22-24 weeks – fetal morphology, uterine artery Doppler study, at 32-34 weeks – fetal well-being study), repeated depending on fetal status and pregnancy-related disease;
- laboratory tests according to the protocol: complete blood count, MPV, blood glucose level, urea, creatinine, uric acid, transaminases, anti-toxoplasma antibodies (Ab), rubella Ab, anti-herpes Ab, cytomegalovirus (CMV), urinalysis, repeated depending on pregnancy-related disease.
- double test as part of first-trimester biochemical screening (PAPP-A and beta-human chorionic gonadotropin (B-HCG) hormone).

The study aimed to determine the PAPP-A, MPV and ultrasound placental changes, as potential predictors of the risk for IUGR.

Each participant signed and informed consent form approved by the ethics committee.

Inclusion criteria for participation in the study were:
- 11 weeks and 0 days -13 weeks and 6 days pregnant women at a craniocaudal length (LCC): 44.5 mm – 84.5 mm
- Normal fetal morphology
- Double tests with high risk for trisomy 13, 18, 21
- Fetal abnormalities diagnosed with ultrasound in the first trimester
- Genetic abnormalities confirmed by chromosomal analysis of cells obtained by chorionic villus biopsy.
- Pregnancy achieved through in vitro fertilization (IVF)
- Twin pregnancy.

PAPP-A was determined as part of first-trimester biochemical screening for aneuploidy at a LCC of 44.5 mm – 84.5 mm. Samples were processed with Brahms Kryptor immunoassay analyzer. The results were expressed as multiples of median (MoM).

The data were imported into, processed and analyzed using the SPSS version 18.0, and were statistically significant at 95% confidence level. Chi-square test was used to determine statistical significance. Frequencies and mean values for the quantitative and qualitative determinations were calculated and Pearson and Fearman tests were used to find the correlations between several variables. The difference was considered statistically significant at p <0.05.

**RESULTS**

This study was conducted in a group of 70 pregnant women monitored at the Neamt County Hospital in the interval August 1, 2014 - September 1, 2015. Pregnancies were dated by LCC at first ultrasound, LCC ranging from 44.5mm to 84.5mm.

Physical examination and history identified the following pregnancy-associated disorders and predisposing factors of IUGR: thrombophilia in 8 cases, uterine fibroma 1 case, pre-existing thrombocytopenia 1 case, iron deficiency anemia 7 cases, preexisting hypertension 11 cases, type 1 diabetes 7
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Intrauterine growth restriction (IUGR) cases, and smoking in 11 cases.

The 70 pregnant women included in this study gave birth to 41 small-for-gestational age pregnancy (SGA) and 29 normal weight babies (fig. 1). Of the 41 cases with IUGR, 30 had a first trimester PAPP-A <0.5 MoM, confirming the statistically significant correlation between maternal PAPP-A level and birth weight (p=0.016).

At the baseline ultrasound performed at 12-13 weeks gestation the ultrasound appearance of placenta was also assessed (presence of deciduous hematoma, areas of angiomatous transformation, detachment of placenta), which suggests impaired first wave of trophoblast invasion and thus a possible long-term placental insufficiency and implicitly risk of IUGR. In 25 cases such changes were identified.

Thirty of the infants had low birth weight and first trimester MPV levels > 10 fl, (fig. 2). A statistically significant correlation was found between birth weight and first trimester MPV level (p = 0.001).

Fig. 1. Distribution of cases by birth weight and PAPP-A

Fig. 2. Distribution of cases by birth weight and MPV

DISCUSSIONS

IUGR is a current problem and a research topic in modern obstetrics. In practice, IUGR has a statistical definition and is a fetal weight or fetal biometry below the 10th percentile or 2 SD below the mean for
gestational age (3, 4). According to the data in the literature, elevated PAPP-A levels are not correlated with increased risk of obstetric pathology, but it was found that a PAPP-A level below the 5th percentile is associated with increased risk of IUGR (17-22).

A study by M. Kwik in 894 women in the first trimester of pregnancy showed that serum PAPP-A levels <0.5 MoM have a sensitivity of 33% and a specificity of 89% in detecting fetuses with a weight below the 10th percentile. Low PAPP-A levels indirectly indicate abnormal placentation, that is a placental insufficiency which has effects on fetal growth (19).

In our study 30 of the pregnant women with IUGR had PAPP-A levels <0.5 MoM, suggesting a statistically significant correlation between IUGR and PAPP-A (p = 0.016).

Increased MPV reflects platelet activation caused by uteroplacental circulatory insufficiency, pathophysiological mechanism with repercussions on fetal growth. In this study it was found that 30 newborns had low birth weight and a first trimester MPV level > 10 fl, p = 0.001, data consistent with the literature (23-25).

A study by M. Kanakt-Pektas shows that MPV levels > 10 fl can predict IUGR with a sensitivity of 82.4% and specificity of 60% (24).

In our study, 41 pregnant women had PAPP-P levels <0.5 MoM and in 38 cases MPV level was >10fl, which, according to the above mentioned literature data, can be used as markers for the early prediction of IUGR.

The ultrasound appearance of impaired first wave of trophoblast invasion is described as intra- and/or periplacental pathological areas which can be considered a possible cause of placental insufficiency, thus a risk of IUGR.

CONCLUSIONS

This study shows that the early detection of serum markers PAPP-A, MPV and placental changes detected at ultrasound and the detailed medical history obtained during the first trimester of pregnancy can be used as screening markers for the detection of cases at risk for IUGR. Identifying pregnancies at risk for IUGR during the first trimester requires the use of secondary preventive measures and monitoring of these cases in order to reduce neonatal morbidity and mortality.

Acknowledgement


REFERENCES

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