THE ROLE OF DOPPLER VELOCIMETRY IN THE MANAGEMENT OF HIGH-RISK PREGNANCY

PHD SUPERVISOR:
PROF. UNIV. DR. LILIANA NOVAC

PHD STUDENT:
BOCA T. MANUELA FLORICA (STOENESCU)

CRAIOVA
2021
CONTENTS

1. INTRODUCTION

2. CURRENT STATE OF KNOWLEDGE

CHAPTER 1. PREVALENCE AND ASSOCIATED FACTORS IN HIGH RISK PREGNANCY

CHAPTER 2. THE SIGNIFICANCE OF DOPPLER ULTRASOUND IN THE ASSESSMENT OF HIGH RISK PREGNANCY

CHAPTER 3. MOMENT OF BIRTH IN A HIGH-RISK OBSTETRIC POPULATION

3. PERSONAL CONTRIBUTION

3.1. Working hypothesis and general objectives

3.2. Research methodology

3.2.1. Approaching the topic

3.2.2. Material and method

3.3. Results of clinical, ultrasound study and statistical analysis

4. DISCUSSIONS

5. GENERAL CONCLUSIONS

6. SELECTIVE REFERENCES

Keywords: high-risk pregnancy, ultrasonography, materno-fetal evolution, placental histology
**1. INTRODUCTION**

When it comes to prenatal care, pregnant women tend to be divided into low- and high-risk populations, but these groups are often difficult to differentiate. Most perinatal complications are diseases associated with placental development and it can be confirmed that Doppler in the uterine artery predicts in most cases, the onset of early onset preeclampsia and intrauterine growth restriction, improving a number of perinatal outcomes. Doppler investigation of the middle cerebral artery together with the umbilical artery could improve the prediction of the unfavorable evolution of near-term risk pregnancies.

**2. CURRENT STATE OF KNOWLEDGE**

**CHAPTER 1. PREVALENCE AND ASSOCIATED FACTORS IN HIGH RISK PREGNANCY**

**1.1. Prevalence and general characteristics of high-risk pregnancies.**

The frequency of high-risk pregnancies is between 25.6 and 63.5% (1,2), with approximately 216 maternal deaths per 100,000 births (3).

The prognosis of the outcome also depends on the type of high-risk pregnancy among pregnant women (4). The maternal mortality ratio refers to the number of maternal deaths due to pregnancy-related causes, during pregnancy or in 42 days from birth to 100,000 live births. In 2015, the ratios ranged from 3 (Finland) to 1360 (Sierra Leone) to 100,000 live births. Almost half of maternal deaths could be prevented (5).

**1.2. Risk factors for high-risk pregnancy**

Almost 50% of all maternal complications come from a high-risk group (6). Many studies around the world have shown a statistically significant association between pregnancy disease and pregnancy status, according to a study conducted by Jain in 2014 (1). Of the four million births per year in the United States, approximately 500,000 cases are placed in the high-risk pregnancy group due to maternal and fetal complications (5).
1.2.1. Maternal age. The risk of mortality is 2-5 times higher in adolescent mothers than in mothers aged 20 to 29 (4).

1.2.2. Hypertensive disorders. They represent 14% of the total incidence of maternal death (7) and it is estimated that 50,000–60,000 cases of PE are related to maternal deaths per year worldwide (8,9).

1.2.3. Diabetes mellitus. Even women whose diabetes is well controlled may have changes in metabolism, which require additional treatments and consultations for a good pregnancy (10).

1.2.4. Obesity. Gestational weight gain over 15 kg increases the risk of becoming obese later in life (11).

1.2.5. Autoimmune diseases. Certain treatments to treat autoimmune diseases can be harmful to the fetus, so a pregnant woman with an autoimmune disease will need to be well supervised throughout pregnancy (12,13).

1.2.6. Alcohol and tobacco consumption. According to an NIH study, children may experience long-term developmental problems even at a low level of prenatal alcohol exposure (14). Research has found that smoking during pregnancy leads to long-term changes in the baby's immune system and the development of the fetus can implement an increased risk of health problems (15).

CHAPTER 2.

THE SIGNIFICANCE OF DOPPLER ULTRASOUND IN THE ASSESSMENT OF HIGH-RISK PREGNANCY

Several studies have already reported reference ranges for many Doppler parameters (16,17,18), especially IP which better describes waveforms for UA, MCA and UtA, especially for high-risk pregnancies.

2.1. Uterine artery Doppler in relation to fetal outcome in high-risk pregnancy

Serial Doppler evaluation of the uterine artery in the second and third trimesters could help determine the normal development of fetal growth and appears to be a good predictor of pregnancy complications (19).

2.2. Umbilical artery Doppler in relation to fetal outcome in high-risk pregnancy
Many studies have shown a statistically significant relationship between increased feto-placental resistance, estimated by resistance index, or systolic-diastolic ratio (S/D), and subsequent development of preeclampsia or fetal growth restriction (20). This investigation is used in high-risk pregnancies to identify fetal compromise and thus reduce perinatal mortality (21,22).

2.3. Middle cerebral artery Doppler in relation to the fetal outcome in high-risk pregnancy

Doppler abnormalities in the third trimester are usually associated with perinatal complications (23). The cerebroplacental ratio as MCA-PI / UA-PI has a value, usually constant after 26 weeks, so that a cut-off of 1 is used, at which the flow rate is considered normal; values <1 are considered abnormal. A systematic review of MCA Doppler reported limited likelihood reports to predict adverse perinatal outcome (24). Doppler investigation of fetal-maternal circulation plays an important role in monitoring high-risk pregnancies associated with placental insufficiency and fetal growth restriction as well as in predicting fetal outcome (25).

CHAPTER 3.

MOMENT OF BIRTH IN A HIGH-RISK OBSTETRIC POPULATION

With medical advances in both obstetric care for high-risk pregnancies and intensive care in newborns, the survival rate of premature and critical newborns has steadily increased (26,27).

3.1. Time of birth in pregnant women with suspected premature birth

One of the major problems with the proper use of prenatal corticosteroids is that the time of birth is often unknown, about half of women hospitalized with suspected premature birth under treatment do not give birth after 7 days (28). The study of prognostic factors for preterm birth showed that fetal fibronectin, absence of fetal respiratory movements and cervical length have potential for diagnostic use (29).

3.2. Time of birth in pregnant women with preeclampsia

Although progress has been made in preeclampsia research, a reliable screening test for its prediction is still lacking. Birth is frequently induced for preeclampsia to
reduce the risk of fetal death and severe maternal morbidity (renal failure, liver failure, eclamptic seizures).

A study that focused on late preeclampsia (34-36.6 weeks of gestation) found that planned birth reduced maternal morbidity and severe hypertension, but led to increased neonatal hospitalizations for prematurity (30).

3.3. **Time of birth in pregnant women with fetal growth restriction**

An additional problem is the difficulty of distinguishing between the constitutional little fetus and the small fetus that does not meet its growth potential due to an underlying pathological condition (31). The time of birth in the case of small for gestational age fetuses (SGA) is balanced between (relative) prematurity on the one hand and prolonged malnutrition / hypoxia on the other hand. Management of late-onset fetal growth restriction is limited to adequate fetal monitoring and choice of optimal time of birth (32). Among the complicated pregnancies of SGA without Doppler abnormalities, birth at 39 weeks is safe, with no differences in perinatal outcomes between 37 and 42 weeks (33).

3. **PERSONAL CONTRIBUTION**

3.1. **WORKING HYPOTHESIS AND GENERAL OBJECTIVES**

The aim of this research is to evaluate the importance of ultrasound examination and maternal-fetal Doppler examination in order to assess fetuses from a high-risk pregnancy, in order to improve prenatal diagnosis and optimize obstetrical management. Another aim of this research was the result of finalizing the interpretation of the obtained data, namely, the elaboration of an algorithm for ultrasound monitoring of high risk pregnancies, which would allow the application of optimal obstetrical management. The ultimate goal of this study is to optimize the methods of early identification of the compromised fetus in high-risk pregnancies, streamlining the health system, the future development of medical therapies.

3.2. **RESEARCH METHODOLOGY**

3.2.1. Approaching the topic
We conducted a prospective study that included a group of 135 patients, studied between October 2016 and May 2020. The study was conducted in the Obstetrics and Gynecology Clinic of the Municipal Clinical Hospital Filantropia Craiova. Pregnant patients were distributed according to the complication that occurred in the third trimester of pregnancy, as follows: 33 pregnant women with PE; 31 pregnant women with thrombophilia; 31 pregnant women with SGA; 14 pregnant women with SGA associated with PE; 26 pregnant women with normal evolution, without risk factors, considered as the control group; 45 pregnant women with NP selected from all these categories of pregnant women with complications.

The study was conducted in full compliance with the ethical principles contained in the "Declaration of Human Rights" adopted in Helsinki, which are in accordance with the Rules for Good Practice in Clinical Trials and legal regulations in force and approved by the Ethics Commission of UMF Craiova.

3.2.2. Material and method

For a better accuracy of the collected and calculated data, we considered a series of inclusion criteria and exclusion criteria, the study being thus better delimited and focused on a certain representative group. Doppler velocimetry of the uterine artery, umbilical artery, middle cerebral artery was performed as part of routine clinical care in maternal-fetal medicine for women with high-risk pregnancies. The statistical analysis was performed within the biostatistics discipline of UMF from Craiova. Microsoft Excel (Microsoft Corp., Redmond, WA, USA) was used for data processing, together with the XLSTAT suite for MS Excel (Addinsoft SARL, Paris, France) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY), USA.

3.3. RESULTS OF CLINICAL AND ULTRASOUND STUDY AND STATISTICAL ANALYSIS

By monitoring cases until the end of pregnancy, we structured several study groups, which we analyzed statistically.

Statistical analysis of demographic data

The mean maternal age at enrollment in the study population was 30 years ± 5.53 SD for all pregnancies (range 18-41 years). Regarding the number of previous births,
we found that 45.91% of pregnant women studied (62 cases) were nulliparous. Correlating with the study groups, we found that the group with PE had the highest incidence of nulliparous (16.29%).

According to the selected risk factors, over the entire study period considered, we identified 109 risky pregnancies, to which are added the 26 cases of pregnancies with a normal evolution, but which presented one or more risk factors. According to their own information, 69.5% of the risk factors were known to pregnant women. Thus, patients knew that they had a previous diagnosis of pre-existing chronic hypertension (2%), autoimmune thyroiditis (5%), autoimmune spondylitis (3%), minor heart disease (3%), hypothyroidism (6%) and a history of gestational diabetes (4%). The evolution of the current pregnancy was marked by the presence of complications that in most cases overlapped, appearing 1, 2 or even three complications together.

We investigated the potential value and compared the MAP values in the second and third trimester to detect the risk of hypertensive pathology, taking into account a cut-off of 110, according to studies in the literature. Unfortunately, this parameter did not prove reliable for the study, as it is a predictive parameter only for PE.

In the case of high-risk pregnancy, we had a significant percentage of premature birth, less than 37 gestational weeks. In the case of PE and PE + SGA we had a percentage of 13.33% and 7.40% of premature birth, respectively. A percentage of only 2.96% of premature births was found in the case of thrombophilia, where pregnancies progressed to >37 gestational weeks. In our study we found 31 cases, 22.96% of the total cases, which had newborn with SGA, being cases with growth restriction that was not associated with PE. To these were added 14 cases of EMS associated with PE, representing a percentage of 10.37% of all cases. We also encountered 3.70% of cases with thrombophilia, which also evolved with growth restriction.

We used an Apgar score, taking into account for the neonatal evolution, the low Apgar score at 1 and / or 5 minutes which was defined as a score lower than 7, to detect the risk of neonatal complications. Depending on the associated complication, the mean Apgar score values at 1 minute in cases with PE was $7 \pm 1.58$ SD, as were
cases born with SGA, $7 \pm 1.61$ SD. In the case of PE + SGA, the mean values of the Apgar score at 1 minute were lower, $6 \pm 1.71$ SD, probably being associated with two major complications. We found a slight increase in the average values at 5 minutes compared to the average values at 1 minute, but still remaining in the risk area. The unfavorable evolution of the newborn was defined as appearing in a newborn with hospitalization in Intensive Care with / without ventilatory support, neonatal death, other complications, APGAR <7 at 1 min and 5 min.

**Ultrasound examination between 20.0-27.6 weeks of pregnancy**

In the group with PE, most cases, 78.78%, had an estimated weight of between 10 and 50 percentiles, so with an increased risk of neonatal morbidity and mortality. Also, in cases with thrombophilia, 51.61% had values <50 percentiles. Even in the control group 53.84% had a weight between 10 and 50 percentiles.

We planned to study the role of Doppler imaging of uterine arteries in predicting the outcome of high-risk pregnancies. The parameters studied in the uterine artery were: S/D ratio, pulsatility index (PI) and the presence/absence of notch, uni/bilateral. For the UtA S/D ratio, in the thrombophilia group we did not have a statistical significance in any of the 4 categories studied: PB, PE, PE + SGA, SGA. In the group with PE we did not have a statistical significance in any of the 4 categories studied. Instead, we had a high predictive value in the case of early PE and in the case of SGA, of over 70%. In the group with SGA, we did not have a statistical significance in any of the 4 categories studied. We had a high predictive value only in the case of late PE, of 100%. For the UtA pulsatility index, in the thrombophilia group, the statistical incidence of cases with early PE and PI-UtA percentages > 95, was statistically significant. Fisher's Exact Test for Count Data $p$-value = 0.0255. In the case of the presence/absence of Notch in the second trimester, in the group with thrombophilia, the statistical incidence of cases with SGA, with notch present, was statistically significant, the chi-square statistic is 7.5164. The p-value is .006114, $p < .05$. The statistical incidence of PB cases with notch present was statistically significant, the chi-square statistic is 4.71. The p-value is .029987, $p < .05$. We had a high predictive value in the case of early and late PE, of 77.78% and 100.00% respectively. In the case of Notch in the group with PE, we did not have a
statistical significance in any of the 4 categories. But we had a high predictive value in the case of PB and especially in the case of SGA, of 94.12%. Studying Notch in the cases with SGA, we did not have a statistical significance in any of the 4 categories. But we had a high positive predictive value in the case of early PE.

We tried to determine the clinical utility of the Doppler evaluation of the umbilical artery in the second trimester of pregnancy for predicting adverse pregnancy outcomes. In the case of PI-UA> 95 percentiles in cases with PB, early PE, late PE, the statistical incidence was statistically significant, p<0.05. But we had no high positive predictive value in the second trimester of pregnancy.

**Ultrasound examination between 28.0-35.6 weeks of pregnancy**

The lowest values of the average weight in grams in the studied groups, we had in the SGA group, 1508.89 gr ± 297.021 SD. A rather low weight average was also in the group with PE + SGA, 1788.975 gr ± 383.713 SD.

In the third trimester, the PI-UtA parameter> 95 percentiles was as follows: in cases with SGA, early PE, late PE, the statistical incidence was statistically insignificant (p>0.05). In cases with PB, the statistical incidence was statistically significant. The p-value is .011921. Significant at p <.05. In the case of the presence of S/D> 1.8 in the third trimester of pregnancy in cases that subsequently developed complications, we had a statistical significance only in the case of PB. We had significant PPV in all categories. We found that in the third trimester, in the case of Notch + in cases with SGA, the statistical incidence was statistically significant (p <0.05) and statistically insignificant (p>0.05) in cases with early PE, late PE and PB. We had significant PPV in all categories studied, so the persistence of a notch in the third trimester of pregnancy can predict a complication. In the third trimester, Doppler evaluation of the umbilical artery is used to monitor fetal well-being. PI-UA> 95 percentiles in cases with SGA and late PE, was statistically insignificant (p>0.05) and statistically significant (p<0.05) in the case of early PE and PB.

We correlated the aspects of an abnormal Doppler of the umbilical artery (PI-UA> 95 percentiles) with the favorable / unfavorable evolution of the newborn. In this regard, we found that the statistical incidence was statistically significant. The p-value is .000015. Significant at p <.05.
The predictive efficacy had an increased specificity, sensitivity and accuracy and a high value of PPV of 75.53%, which makes us think that the significance of the presence of PI-UA > 95 percentiles, can be predictive for the evolution of the newborn.

Statistical incidence of PI-UA > 95 percentiles vs Newborn Evolution

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PI-UA &gt;95p (number cases)</th>
<th>PI-UA &lt;95p (number cases)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable newborn evolution</td>
<td>23</td>
<td>71</td>
<td>94</td>
</tr>
<tr>
<td>Unfavorable newborn evolution</td>
<td>26</td>
<td>15</td>
<td>41</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>86</td>
<td>135</td>
</tr>
</tbody>
</table>

The chi-square statistic is 18.7279. The p-value is .000015. Significant at p < .05.

Doppler evaluation of the fetal middle cerebral arteries (MCA) is an important part of the evaluation of fetal distress or fetal hypoxia. PI-MCA below the 5th percentile was considered as an abnormal interval (values less than 0.9).

Statistical incidence of PI-MCA<5 percentiles vs Newborn Evolution

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PI-MCA &lt;5p (number cases)</th>
<th>PI-MCA&gt;5p (number cases)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable newborn evolution</td>
<td>4</td>
<td>90</td>
<td>94</td>
</tr>
<tr>
<td>Unfavorable newborn evolution</td>
<td>7</td>
<td>34</td>
<td>41</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>124</td>
<td>135</td>
</tr>
</tbody>
</table>

The chi-square statistic is 5.5488. The p-value is .018494. Significant at p < .05.

We correlated in this case as well, the aspects of an abnormal Doppler of the middle cerebral artery (PI-MCA <5 percentiles) with the favorable or unfavorable evolution of the newborn and the statistical incidence was statistically significant. The p-value is .018494. Significant at p < .05. The predictive efficacy had a high
value of PPV, of 95.74%, which makes us think that the significance of the presence of PI-MCA <5 percentiles, can be predictive for the evolution of the newborn.

**Statistical analysis of maternal lipid profile in high-risk pregnancy**

We tried to establish the lipid profile of patients and how it influences the evolution of pregnancy and the fetus. In this regard, we measured total cholesterol (CT), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C) and triglycerides (TG) in the second trimester (21-24 gestational weeks) and the third trimester (33-37 gestational weeks).

The maternal lipid profile in the second trimester showed a predictive efficacy of CT values in cases with PE associated with the presence of IGS, with a high specificity of 92.31% and a high PPV of 71.43%. The predictive efficacy of LDL values in the second trimester on the prediction of a pathology was clearly predictive in cases with PE associated with the presence of SGA, with a high specificity of 94.03% and a high PPV of 71.43%. The predictive efficacy of TG values in the second trimester on the prediction of a pathology was clearly predictive in cases with SGA, PPV of 90.32%, as well as in PE, PPV of 84.85%.

In the third trimester, the predictive efficacy of CT values on the prediction of a pathology was negative in all categories of complications studied, as well as the predictive efficacy of LDL-C. This, in contrast to the predictive efficacy of HDL-C values in the third trimester, which was positive in all categories of complications, with a high value of 93.55% in the case of late SGA. The predictive efficacy of TG values in the third trimester on the prediction of a pathology is predictive only in cases with PE + SGA, PPV of 71.43 %.

We also aimed to detect the relationship between maternal lipid profile and SGA, as well as those with adequate weight for gestational age (AGA) to reveal the impact of maternal lipid profile on birth weight. It seems that only the TG values in the third trimester influence the development of the intrauterine fetus and have a positive predictivity of 68.89%.

Histological analysis of the placenta in high-risk pregnancies analyzed the placentas from high-risk pregnancies comprising PE (23 cases) and SGA (18 cases). We specify that the lesions were not unique by pathology, but were combined, being
present several lesions on the same placenta, and this was taken into account when establishing the percentages.

The distribution of histological lesions was as follows: placental infarction (>5%) was more frequent in PE than in SGA, as well as diffuse calcifications, intervilloidal thrombosis, intervilloidal fibrinoid deposition and chorangiosis. In contrast, in the placentas from cases with SGA, the characteristic lesion was the growth of syncytial buds.

4. DISCUSSIONS

The term "high-risk pregnancy" suggests that in order to have a healthy pregnancy and a safe birth, additional supervision is needed. Pregnancy at an advanced maternal age, defined as the age of 35 or more, is associated with several complications of pregnancy, and is therefore considered a 'high-risk' pregnancy (34). In our study, the mean maternal age was 30 years ± 5.53 SD at all pregnancies (16-41 years interval). Pathological obstetric history is important to report, as some of these pathologies may be recurrent in the current pregnancy and they may be that element that includes the current pregnancy in the high-risk group. In the studied case studies we found in 20% of cases early PE and a percentage of 17.77% late PE. These cases were complicated by the occurrence of eclamptic crises in 5.18% of PE cases. HELLP syndrome was found in only 2.22% of cases.

In the case of high-risk pregnancies, we had a significant percentage of premature births, below 37 weeks, as described (35). In the case of PE and PE + SGA we had a percentage of 13.33% and 7.40% of premature birth, respectively.

Prenatal detection of SGA may play a role in preventing sequelae. There is strong evidence for this relationship in high-risk pregnancies and serial screening is recommended in this group (36). In our study we found 31 cases, 22.96% of all cases, which had a newborn with SGA at birth, being cases with growth restriction that was not associated with PE. To these were added 14 cases of SGA associated with PE, representing a percentage of 10.37% of all cases.

The unfavorable evolution of the newborn was defined as appearing in a newborn with hospitalization in Intensive Care with / without ventilatory support, neonatal
death, other complications, APGAR <7 at 1 min and 5 min. We had 4 deaths of newborns, 2 cases (1.48%) in cases with PE and 1 case each (0.74%) in the category of PE + SGA and SGA. Admission to intensive care with ventilatory support was performed in 12 cases (8.88%) of cases with PE, in 13 cases (9.62%) in newborns with SGA, in 10 cases (7.40%) in newborns with PE + SGA, the latter being the most affected category.

An accurate estimated fetal weight based on ultrasonography is important for identifying this high-risk population (37). The accuracy of estimating fetal weight is of paramount importance in prenatal care, as well as in the planning and management of labor and delivery (38). We classified the weight in percentiles, by groups: <50 percentiles, with increased risk of morbidity/mortality and > 50 percentiles. We had no cases > 90 percentile. It is noted in the PE group that the majority of cases, 78.78%, had an estimated weight between 10 and 50 percentiles. Also, in cases with thrombophilia, 51.61% had values <50 percentiles.

Uterine artery Doppler has been a useful aid in sonographic assessment of utero-placental hemodynamics. However, there are debates as to which Doppler parameter would be best for screening to best detect potentially problematic pregnancy (39). In the group with thrombophilia, PE, PE + SGA, SGA, we did not have a statistical significance in any of the 4 categories studied: PB, early PE, late PE and SGA. Mean uterine artery PI> 95th percentile, measured after 23 weeks of gestation, could be used to detect possible maternal-fetal complications in the third trimester. We also relied on this in our study. The statistical incidence of cases with preterm birth, late PE, SGA and PI-UtA percentages> 95, was statistically insignificant. The statistical incidence of cases with early PE and PI-UtA percentages> 95, was statistically significant.

As we found, the predictive value of Doppler testing on the uterine artery in selected groups of pregnant women seems to be low in the systematic analyzes of previous studies (40,41). Despite these contradictory data, conducting Doppler studies on maternal and fetal vessels to identify women at risk of pregnancy complications are important (42). Abnormal uterine waveforms or persistence of a notch after 24 weeks of gestation are associated with inadequate secondary
trophoblastic invasion of the spiral arteries (43). This study showed that the presence of a notch in the second trimester significantly increased the prevalence of PE, early and late, but also of premature birth, as shown by other studies in the literature (44,45).

Doppler ultrasound of the fetal umbilical artery, on the other hand, is often performed on the fetus, suspected of having an increased risk in pregnancy, such as growth restriction, premature birth, and stillbirth (39). In the case of the presence of PI-AU> 95 percentile in the second trimester of pregnancy in cases that subsequently developed complications, we had a statistical significance in cases with PB, early and late PE. Thus, a series of Doppler assessments of the uterine artery in the second and third trimesters could help determine the normal development of fetal growth and deserve to be a good predictor of pregnancy complications (19).

In the third trimester, the PI-UtA parameter> 95 percentiles was as follows: we had a statistical significance in the case of early PE and PB (p <0.05). The statistical incidence of notch cases in the case of SGA was statistically significant (p <0.05) and was not statistically significant (p> 0.05) in the case of early PE, late PE, PB.

Doppler assessment plays an important role in pregnancy and is recognized as a method of assessing fetal well-being (46). In this sense, we correlated the aspects of an abnormal Doppler of the umbilical artery (PI-UA> 95 percentiles) with the favorable/unfavorable evolution of the newborn. In this sense, we found that the statistical incidence was statistically significant (p <0.05). Doppler MCA measurement has been supported as an effective way to detect fetal hypoxia. In the presence of PI-MCA <5 percentiles in the third trimester of pregnancy, we did not have a statistical significance in the case of the 4 categories studied (p> 0.05), instead, we had a positive predictive value in all 4 categories studied. During pregnancy, there are multiple physiological changes that contribute to changes in the lipid profiles of healthy pregnant women (47). The predictive efficacy of CT values in the second trimester on the prediction of a pathology could be predictive in cases with PE associated with the presence of SGA, with a high specificity of 92.31% and a high PPV of 71.43%. This correlates with other studies showing that hypercholesterolemia in pregnancy has been associated with an increased risk of
spontaneous preterm birth (48). In the third trimester, the predictive effectiveness of TC values on the prediction of a pathology is negative for all categories of complications, the values being below 50%.

In a recent study, high levels of HDL-C in the 36th week of gestation increased the risk of SGA. The tendency of maternal HDL-C to change during pregnancy was associated with a lower neonatal weight (49). In our study, the predictive efficacy of HDL-C values in the third trimester is positive in all categories of complications, with a high value, 93.55% in the case of late SGA. The predictive efficacy of LDL-C values in the second trimester is clearly predictive in cases with PE associated with the presence of SGA, with a high specificity of 94.03% and a high PPV of 71.43%. The predictive efficacy of LDL-C values in the third trimester is negative in all categories studied, this being in line with other studies (50). In a recent study, women with high TG at 30 weeks of gestation had a 48% lower risk of giving birth to an SGA infant compared to women with baseline TG levels between 10 - 90th percentile (51). In our study we did not have pathological values of TG, but with an increase in TG values from the second trimester to the third trimester. It seems that the TG values in the second trimester influence the development of the intrauterine fetus with a positive predictivity of 86.67%. In the third trimester, the SGA had an incidence of abnormal TG values in the proportion of 33%, while the AGA, in a proportion of 21%. It seems that the TG values in the third trimester influence the development of the intrauterine fetus with a positive predictivity of 68.89%.

The placenta study provides information about mother and baby. The fetus, placenta and mother form a complete triad of dynamic equilibrium in reproduction, the placenta being the most accessible and evaluable component of the triad (52). In our study, there were changes present in both normal pregnancy and pregnancy with preeclampsia or SGA. But those injuries were at a higher rate in pregnancies that are accompanied by PE or SGA. This study shows that a certain type of placental lesions are frequently increased in the placentas from pregnancies with PE and SGA.

5. CONCLUZII
The age category 31-35 years presented the most common pathology. In the rest of the age groups, the pathology was dispersed in small numbers.

In the case of PE and PE + SGA we had a percentage of 13.33% and 7.40% of premature birth, respectively.

The estimation of fetal weight at the first examination, in the second trimester, showed that in the group with PE most cases, 78.78%, had an estimated weight between 10 and 50 percentiles. Also, in cases with thrombophilia, 51.61% had values <50 percentiles.

The UtA S/D report studied in the uterine artery in the second trimester, found that in the group with thrombophilia, PE, PE + SGA, SGA, we did not have a statistical significance in any of the 4 categories studied: PB, early and late PE and SGA.

PI - UtA studied in the uterine artery in the second trimester, found that in the case of PI-UtA > 95 percentiles, we had a statistical significance only in early PE.

In the case of the presence of notch in the second trimester of pregnancy in cases that subsequently developed PE, PE + SGA, SGA, we did not have a statistical significance in any of the 4 categories.

In the third trimester, the PI-UtA parameter > 95 percentile in cases that subsequently developed complications, we had a statistical significance in the case of early PE and PB.

Correlating unfavorable evolution of newborn with PI-UA > 95 percentiles we found that the statistical incidence was statistically significant (p <0.05).

Correlating unfavorable evolution of newborn with PI-MCA <5 percentiles we found that the statistical incidence was statistically significant (p <0.05).

The predictive efficacy of TC values in the second trimester could be predictive in cases with PE associated with the presence of SGA, but negative in all categories of complications in the third trimester.

The predictive efficacy of LDL-C values in the second trimester is clearly predictive in cases with PE + SGA but is negative in all categories studied in the third trimester.
The predictive efficacy of TG values in the second trimester is clearly predictive in cases with SGA and is predictive in cases with PE + SGA, PPV of 71.43%, as well as in PE, PPV of 69.70%.

The impact of the maternal lipid profile on birth weight showed that in the second trimester, only TG influences the development of the intrauterine fetus and has a positive predictivity of 86.67%.

The impact of the maternal lipid profile on birth weight showed that in the third trimester, HDL-C and TG influence the intrauterine development of the fetus, with a PPV of 89.58% and 68.89%, respectively.

This study shows that a certain type of placental histological lesions are frequently increased in placentas from pregnancies with PE and SGA: placental infarctions (over 5%), syncytial buds frequently present (specific for SGA), intervillosillary fibrinoid deposition, villous appearance angiomatous (especially in PE).

6. SELECTIVE REFERENCES


7. Safari M, Yazdanpanah B, Yazdanpanah S. High risk pregnancy and some of related factors in women who referred to Vasouj Health and Medical Centers. Scientific Journal of Hamadan Nursing & Midwifery Faculty. 2008; 16(2):18-28


18. Tarzamni MK, Nezami N, Sobhani N, Eshraghi N, Tarzamni M, Talebi Y. Nomograms of Iranian fetal middle cerebral artery Doppler waveforms and uniformity of their pattern with other populations' nomograms. BMC Pregnancy and Childbirth. 2008;8:50


