

Evaluation of fetal condition in uncomplicated pregnancies at 40 weeks and beyond by calculation of amniotic fluid indexes and Doppler in the middle cerebral artery: an original research.

Running head: Examination of fetal condition at 40 weeks and more.

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Abstract

Objective. The aim of our data is to reveal the method of prognosis abnormal perinatal outcome, using combination US and Doppler results in uncomplicated pregnancies at 40 weeks and beyond.

Design. 1020 uncomplicated pregnant women at 40 weeks and beyond were examined 48 hours before delivery. We analyzed fetus's condition during labor and just after.

Setting. According these dates all women were divided into 3 groups after amniotic index(AI) and pulsatility indices(PI) in the middle cerebral artery(MCA).

Population. 260 women were included in the study because they met the inclusion criteria.

Methods. All women were divided into 3 groups (group 1 - $PI > 0.835$, any value of AI, group 2 - $AI > 85$, $PI \leq 0.835$, group 3 - $AI \leq 85$ and $PI \leq 0.835$). We analyzed fetus's condition during labor and just after delivery (Apgar score ≤ 7 and > 7 on the 1st minute).

Result. We've got trigger level for pulsatility index (PI) as 0.835, if we had PI less than that threshold cases of emergency cesarean section increases in 2,12 times, if PI less than 0,835 in combination with Amniotic Index(AI) 85 and less in 5,28 times. If $PI \leq 0,835$ risk of newborns having Apgar 7 and less increases in 1,18, but in combination with $AI \leq 85$ in 4,72 times.

Conclusion. In results we found out the following data: low PI in the MCA may be parameter which can prognoses fetus distress. Combination of PI reduce with low AI increases its specific and can use in practical ways to avoid hypoxic brain damage during labor..

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Tweetable abstract

Combination of low Pulsatility indexes (PI) in the Middle Cerebral Artery and AI can be an indicator of fetal distress in uncomplicated pregnancy 40 weeks and beyond.

Key words: Amniotic fluid index, fetal distress, Doppler, pulsatility index, middle cerebral artery.

Introduction

Currently, on the pages of periodicals from different sources time and the way of delivery after detecting signs of placental insufficiency and intrauterus growth restriction (IUGR) is actively discussed, including multicenter studies in major centers in Europe, Canada and the United States (1-2).

The question of the timing and methods of timely delivery of a normal pregnancy that has reached the term of 40 weeks of pregnancy or more remains poorly understood. While practicing obstetricians meet with this dilemma several times a day.

According to various sources, the rate of post-term pregnancy varies from 0.8-4% to 8-10% (3). Difference depends on the frequency of labor induction and methods for determining gestational age. The reasons for over-pregnancy are not clear, but there is a link between the frequency of over-pregnancy and the following factors: genetic (4), male sex of the fetus(5), high body mass index of the patient before pregnancy (6).

It is a well-known fact that during pregnancy lasting more than 40 weeks of gestational age (more than 280 days), there are involutive changes in the placenta and at the same time moderate fetal hypooxygenation. According to some authors, a decrease in the excretion of placental and fetal steroids in the daily urine of a pregnant woman indicates an antenatal violation of the functional state of the fetus (7).

This is manifested in the following: changes in the placenta during ultrasound (petrification), oligohydramnion, lack of growth in the biometric parameters of the fetus during dynamic research, clearer contours of the head, large size of the fetus, reduced motor activity (8).

Doppler has a great practical value for the detection of chronic fetal distress, which contributes to the prenatal identification of groups of newborns subject to careful monitoring and treatment. The Doppler study of fetal blood flow makes it possible to diagnose intrauterine hypoxia somewhat earlier than cardiotocography.

Evaluation of the blood flow indexes in the middle cerebral artery gives better results in the diagnosis of intrauterine hypoxia than with a similar assessment in the umbilical artery(9).

Currently, it is known that in a state of chronic hypoxia, the so-called brain-sparing effect occurs in the fetus, when the cardiac output with the maximum oxygenated blood is directed to the fetal brain (10).

Fetal circulation has its own characteristics, where a larger amount of blood released by the right ventricle of the fetal heart goes through the ductus arteriosus shunt to the descending aorta, while the left ventricle mainly supplies the brain and body.

In placental insufficiency, which occurs in intrauterus growth restriction syndrome and can occur among fetuses in more than 40 weeks of pregnancy, increased resistance of placental vessels increases the overall systemic resistance of blood flow in the fetus (11).

At the same time, dilation of fetal brain arteries reduces the load on the left ventricle. As a result, blood is redistributed towards the left ventricle, which provides increased cerebral circulation (12).

There are many studies to identify a decrease in the resistance index in the middle cerebral middle artery (CMA) in the phenomenon of intrauterus growth restriction (IUGR) (13-22).

According to histomorphological studies, nerve tissue is most sensitive to hypoxia (23, 24). A lot of researchers in experiments on animals (primates, lambs, pigs) have found that a decrease in the perfusion capacity of the placenta and chronic hypoxia almost immediately lead to the centralization of blood circulation with a redistribution of blood flow to vital organs such as the brain, heart and adrenal glands ("brain sparing effect"). This pattern was also confirmed in humans (23, 25-29).

In this regard, the Doppler study of cerebral circulation in complicated pregnancy is of particular clinical importance for assessing the functional state of the fetus (29).

Materials and methods.

In our study we used the same criteria for the diagnosis of chronic fetal hypoxia based on Doppler in the brain vessels as in the cases of IUGR, i.e. identification of a group of high-risk pregnant women to choose the method of delivery and follow-up in childbirth based on Doppler in the cerebral middle artery.

The most convincing signs of fetal hypoxia are a decrease in heart rate variability and the appearance of long-term deep deceleration in CTG, but this is more consistent with cases of critical blood flow in the umbilical artery and fetal aorta.

Currently, there are no sufficient grounds and convincing data to consider the use of Doppler as a screening method in the cases of uncomplicated pregnancies, but it is undeniable that the Doppler study of utero-placental and fetal blood flow has an important diagnostic and prognostic value in the group of pregnant women at high perinatal risk.

In our study, we analyzed the amount of amniotic fluid using the amniotic index measurement method and evaluated Doppler in the middle cerebral artery, measured no later than 48 hours before delivery, for the period from 2014 to 2017 at the maternity hospital No. 9 in St. Petersburg. After that, we evaluated the relationship of these indicators with the percentage of cesarean sections performed due to fetal distress and the condition of the newborn evaluated by Apgar score at 1 and 5 minutes after birth.

The study included 260 patients aged 18 years to 41 years with a gestation period of 40 weeks and above. The study excluded pregnant women with severe somatic pathology (chronic diseases, anemia II-III, bronchial asthma, diabetes mellitus, destructive diseases of the spine, etc.), as well as with pregnancy complications (preeclampsia, eclampsia, IUGR, HELLP-syndrome) who have indications for planned cesarean section. Patients with multiple pregnancies, breech position were also excluded from the analysis. When assessing the outcome of labor, cases of operative delivery were taken into account only because of fetal distress, detected by abnormal cardiotocography (CTG).

Ultrasound and Doppler studies were performed on ultrasound devices Voluson E6, Voluson S6 and Medison QZ V-20 with convex probes with a frequency of 3.5 MHz and 5.0 MHz no more than 48 hours before delivery. The study of blood flow in the middle cerebral artery was carried out using color Doppler by increasing the image of the fetal head. The middle cerebral artery (MCA) was displayed, and the calipers of the spectral Doppler were located just above the vessel's departure from the Vilisian circle. The resistance indexes in the MCA and Umbilical artery (UA) were measured several times (3-5) and the best, i.e. the highest indices for the MCA and the lowest for UA, were taken into the final results.

The frequency filter was set at 60 Hz, the angle of insolation did not exceed 30°, the width of the control volume was selected so the diameter of the vessel (Figure 1). Registration and assessment of the blood flow profile was performed in conditions of motor rest and apnea in the fetus, with a rhythmic and normal heart

rate corresponding to the gestational period. Preference was given to automatic estimation of blood flow rates. We used a standard pulsation index (PI) in the MCA.

To analyze the dates of pregnant women, the system was used STATISTICA for Windows (version 10 lic. BXXR310F964808FA-V).

Results

We had the following characteristics of the analyzed indicators in 260 women in labor (table 1).

The age of women ranged from 18 to 41 years and averaged 29.69 ± 4.50 years. The weight of fetuses after birth was in the range from 2400 to 4880 gram, the average value was 3543.73 ± 420.46 . The average height of the fetus was 52.42 ± 1.97 (from 47 to 59 cm).

All newborns were evaluated for their physical development. The condition of the newborn was determined based on a clinical assessment on the Apgar scale at birth.

At 1 minute, the score was from 1 to 8 points (its average value was 7.70 ± 0.73), at 5 minutes, from 0 to 9 points (average 8.69 ± 0.76). The amniotic index in the study group of patients ranged from 0 to 270 mm (mean value 88.54 ± 49.88)

Natural childbirth occurred in 145 women (55.8%) and ended in cesarean section in 115 women (44.2%).

In patients with natural delivery, the AI was in the range of $9 \div 240$, the average value was 87.70 ± 45.34 , the median was 74, in women with caesarean section, the AI was in the range of $0 \div 270$, the average value was 89.60 ± 55.26 , the median was 80. There were no significant differences in AI in these groups, although the range of AI values is somewhat wider in the group of women who gave birth by caesarean section.

During the analysis of available clinical results, the method of constructing classification trees while taking into account both PI in the CMA and AI revealed their threshold values associated with the risk of fetal distress. We've got $PI = 0.835$ and $AI = 85$.

An example of a decrease in PI in the CMA below the threshold level is shown in figure 2.

We found that $PI > 0.835$ is the norm, and $PI \leq 0.835$ is a decrease in this indicator. For $AI > 85$ – the prognosis of the fetus is more favorable, for $AI \leq 85$ – less favorable. Subsequent analysis allowed us to form 3 groups based on the levels of AI and PI.

Group 1 - PI norm (> 0.835), any value of AI-favorable group

Group 2-AI > 85 , PI reduced (≤ 0.835) - group with increased risk of distress

Group 3-reduced both AI (≤ 85) and PI (≤ 0.835) - a group with a significant risk of fetal distress.

We had 212 people (81.54%) in the favorable group, 26 people (10%) in the group with an increased risk of fetal distress and 22 people (8.46%) in the group with a significant risk of fetal distress

Table 2 shows the frequency of birth outcomes and Apgar levels in the formed groups and the results of their comparison.

Clearly, the increase in the percentage of fetal distress in childbirth is shown in figures 3-5.

We calculated an increase in the risk (OR) of fetal distress characteristics during transition in groups 2 and 3 compared to group 1. The risk of cesarean section increases in group 2 by 2.12 times, and in group 3 compared to group 1 by 5.28 times.

The risk of reducing Apgar at 1 minute less than 8 points in the 2nd group is insignificant, is only 1.18, and in the 3rd increases to 4.72. The risk of reducing Apgar at 5 minutes less than 9 points in the 2nd group is insignificant, is only 1.15, and in the 3rd increases to 5.52.

Discussion and conclusions.

In our study, the values of resistance to blood flow in the fetal cerebral arteries were significantly lower in the group of women whose delivery was complicated by decompensation of the placental blood flow, which required emergency delivery by caesarean section. In addition, in the course of our study, there were 2 cases of death of a newborn. In one case, a Doppler study was performed on an outpatient basis at gestation of 40 weeks and 6 days, and the PI value in the CMA was 0.54. An emergency caesarean section was performed, as a result of which a child was born with an Apgar score of 1 point, and revival measures were ineffective. Cause of death at autopsy: asphyxia resulting from an acute violation of the utero-placental blood flow. In the second case, a pregnant woman complained of worsening fetal movement at 38 weeks, Doppler analysis revealed a decrease in blood flow resistance indices: PI in the CMA was 0.63, cardiotocography revealed deep deceleration, and therefore an emergency caesarean section was performed. As a result, a live boy of 3150 g was born with an Apgar score of 4/5 points, despite the resuscitation measures, the child died in 2 hours after birth. Pathological diagnosis: intranatal asphyxia, massive aspiration of meconial amniotic fluid. The last case was not included in the study because the pregnancy was less than 40 weeks gestational age, in addition, the pregnant woman had a history of previous deliveries by caesarean section. According to our data, PI in the cerebral middle artery is a more important predictor of fetal distress, since if it is normal (>0.835), the value of AI does not play a role. The prognosis is slightly worse if the PI is reduced (≤ 0.835), and the AI is normal. According to our data, the most unfavorable situation occurs when both the Amniotic index and PI decrease simultaneously.

We've registered a patent for invention in Russian Federation of our diagnostic method of fetus's condition in uncomplicated pregnant women (patent for invention # 2735926).

And we made a special algorithm for clinicians which can help prevent poor outcome during labor in the age of pregnancy 40 weeks and more (figure 6).

Similar conclusions were reached by Carroll and Bruner [30], who studied resistance indices in the umbilical artery in pregnant women with a reduced amount of the amniotic index. The authors concluded that a change in PI in the umbilical artery towards an increase significantly worsens the prognosis of labor and the condition of the newborn after birth.

The Mexican researchers Romero-Gutiérrez G. et al [31] in their attempts to predict the outcome of labor based on ultrasound and Doppler data, studied 130 patients at 30-41 weeks of gestation. As a result of their work, the authors concluded that dopplerometry in the umbilical artery shows a higher specificity and sensitivity in predicting a favorable outcome of labor than the measurement of the amniotic index of amniotic fluid. In a systematic review, Vollgraff Heidweiller-Schreurs CA et al [32] reviewed 4,693 articles (including 128 studies involving 47,748 women) on the possibility of predicting an unfavorable outcome of labor based on the assessment of dopplerometry in SMA and the Cerebro-placental ratio (CPR) in the fetus. The authors of this review claim that CPR and dopplerometry in SMA is superior to the assessment of blood flow in AP as a

method for predicting emergency delivery and the worst condition of the newborn immediately after delivery. However, it remains unclear for which groups this pattern can be used.

In our study, the predictive significance of PI in SMA based on the method of constructing classification trees was obtained higher (in relative units) compared to AI. Thus, we propose to introduce a routine Doppler examination in the fetal SMA at more than 40 weeks of gestation into the practice of maternity hospitals and outpatient clinics, and if PI is detected in the SMA below the threshold value (<0.835), send it to the hospital in a timely manner to determine further delivery tactics, or timely delivery. When choosing delivery tactics in favor of natural childbirth, conduct constant monitoring of the fetus' condition and, if signs of improvement in the fetus' condition are detected, perform an emergency caesarean section in a timely manner.

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Contribution to authorship:

Semenova E.R.- took part in conception of investigation, carrying out examinations and collect results, analyzing results and writing up this work.

Ruhliada N.N.- took part in conception and edition of writing this work.

Klicenko O.A. - statistical analysis of the obtained data.

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Reference

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Table 1. Characteristics of the study group.

Indicator	Mean	Min ÷Max	Me (LQ;UQ)
Age	29,69±4,50	18÷41	29 (27; 33)
Weight of newborn	3543,73±420,46	2400÷4880	3500 (3250; 3810)
Length	52,42±1,97	47÷59	52 (51; 54)
Apgar on 1 st min	7,70±0,73	1÷8	8 (8; 8)
Apgar on 5 th min	8,69±0,76	0÷9	9 (9; 9)
Amniotic index	88,54±49,88	0÷270	75,5 (50;120)

Table 2. Birth outcomes and Apgar levels in the formed groups

Outcome	1 group		2 group		3 group		Total	P
	Num.	%	Num.	%	Num.	%		
Vaginal delivery	129	60,85%	11	42,31%	5	22,73%	145	<0,001
Cesarean section	83	39,15%	15	57,69%	17	77,27%	115	
Total	212	81,54%	26	10,00%	22	8,46%	260	
Apgar on 1 st min								
8 and more	169	79,72%	20	76,92%	10	45,45%	199	<0,01
7 and less	43	20,28%	6	23,08%	12	54,55%	61	
Total	212	81,54%	26	10,00%	22	8,46%	260	
Apgar on 5 st min								
9 and more	168	79,25%	20	76,92%	9	40,91%	197	<0,01
7 and less	44	20,75%	6	23,08%	13	59,09%	63	
Total	212	81,54%	26	10,00%	22	8,46%	260	

Figure 1. Example of measuring blood flow rates in the middle cerebral artery.

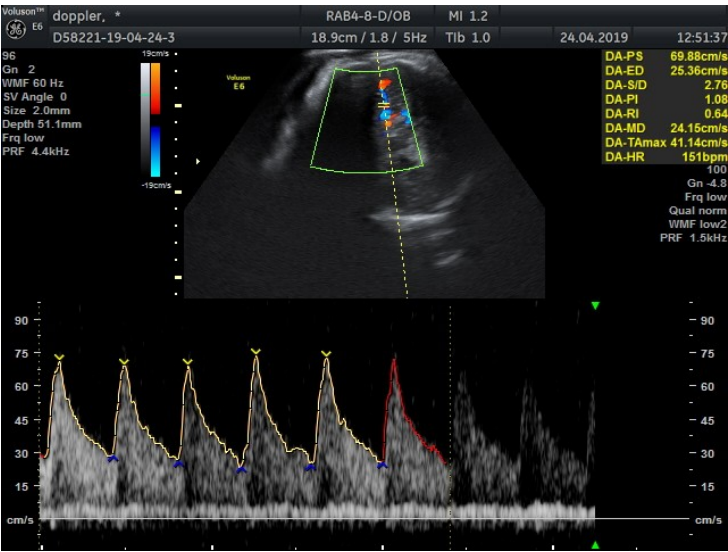


Figure 2. Indicators of fetal blood flow indices below the threshold level.

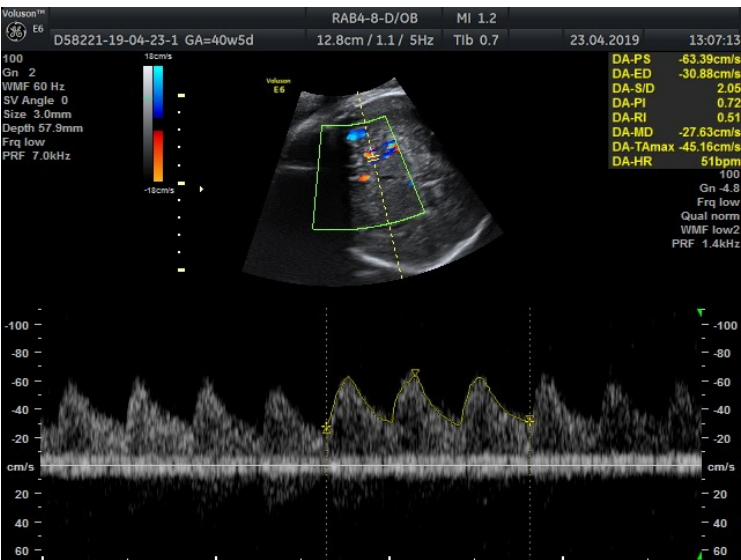


Figure 3. The outcomes of labor in groups by levels of PI and AI.

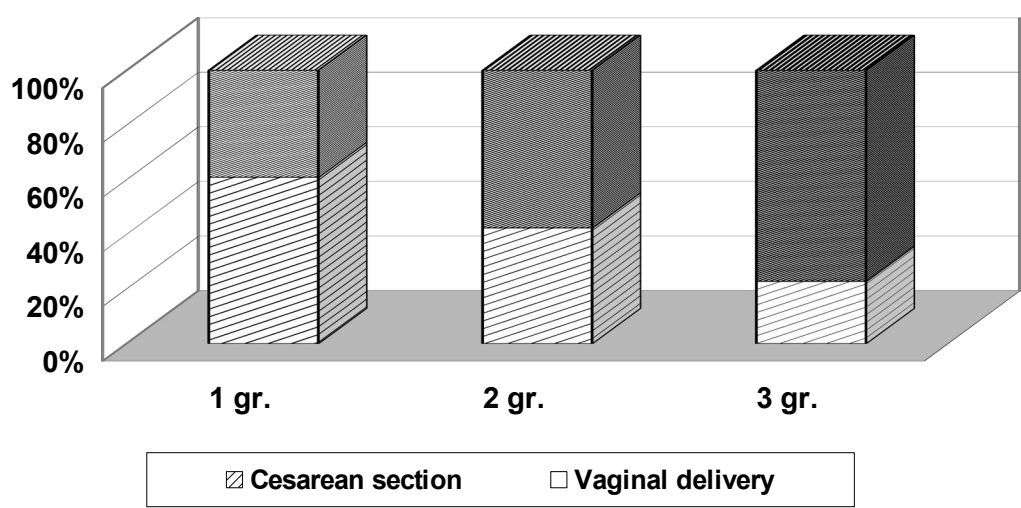


Figure 4. Apgar at 1 minute in groups of PI and AI levels



Figure 5.. Apgar at 5 minutes in groups of PI and AI levels.

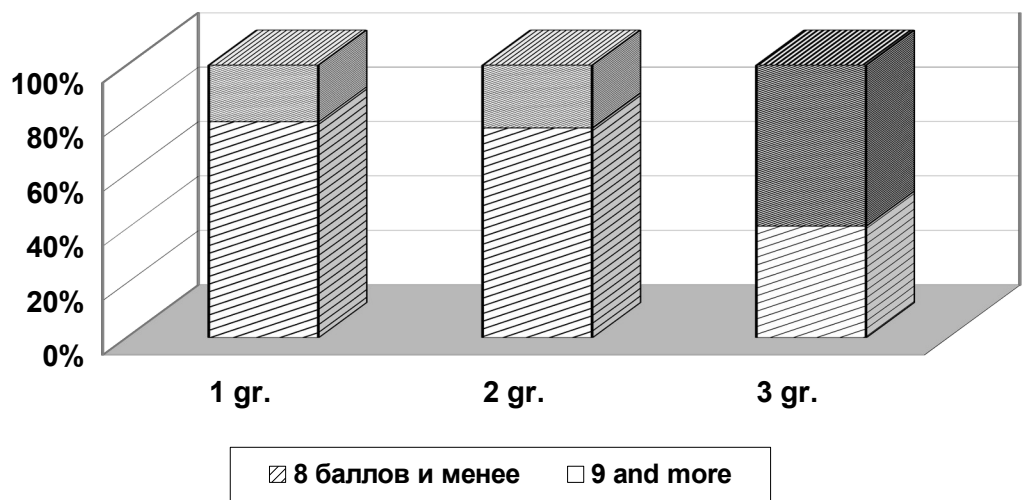


Figure 6. Algorithm of examination and rout of labor in uncomplicated pregnancy in 40 weeks and more.

