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Diagnostic capabilities of the biochemical composition of amniotic fluid in assessing fetal conditions

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Abstract

Aim. To analyze the nature of changes in the biochemical parameters of amniotic fluid during fetal hypoxia.

Methods. The study was carried out in the maternity ward of the Republican Clinical Hospital named after Kuvatov (Ufa) between January 2016 and September 2018. The main group — 72 women in labor with symptoms of fetal distress, the control group — 70 women in labor without it. The biochemical composition of the amniotic fluid was measured using an analyzer. Statistical analysis was performed by using the Statistica 10.0 software. Comparison of qualitative characteristics was carried out by using Fisher's exact test when comparing quantitative data, the Mann–Whitney test. The statistical significance of the differences was set at $p < 0.05$.

Results. It was found that in fetal distress, there is a decrease in such biochemical indicators of the composition of amniotic fluid as the level of triglycerides (0.2±0.1 and 0.3±0.1 mmol/L, p=0.0036) and cholesterol (0.1±0.16 and 0.3±0.2 mmol/L, p=0.0275), gamma-glutamyl transpeptidase activity (34.5±11 and 48.7±6.8 U/L, p=0.0261), while the level the lactate (in the main group 3.5±1.2 and 3.1±0.9 mmol/L in the control group, p=0.0035), glucose (1.2±0.6 and 0.6±0.3 mmol/L, p=0.0002) and nitrogenous substances such as urea (4.5±1.1 and 3.0±1.3 mmol/L, p=0.0018) increases.

Conclusion. The biochemical composition of amniotic fluid reflects the state of the fetus at birth, and therefore the study of the amniotic fluid is a relevant and accessible method.

Keywords: amniotic fluid, fetal hypoxia, intrauterine hypoxia, biochemical analysis.

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Background. Amniotic fluid (AF), or liquor amnii (LA), is a unique biologically active environment that ensures the life of the fetus in the womb [1]. LA has many important functions. First, it creates a fluid space for free movements of the fetus and prevents compression of the umbilical cord; second, it mechanically protects the fetus and maintains a certain temperature balance and homeostasis; and lastly, it has the transport function and is involved in metabolism [2].

The source of AF formation in the first trimester of gestation is not fully investigated and is believed to be a maternal blood plasma transudate. In the later stages of pregnancy, the fetus becomes the main producer of AF. The constancy of the LA volume is ensured by maintaining a balance between transmembrane transfusion and swallowing of AF by the fetus, as well as the production of urine and alveolar fluid by the fetus; therefore, in the second and third trimesters of pregnancy, the diagnostic significance of the study of LA increases [1, 2].

In addition, LA is characterized by high metabolic rates, such as the complete change of AF in the fetal bladder that occurs in 2.9 h [3]. Therefore, the LA composition dynamically reflects the fetus condition. LA contains dissolved oxygen and carbon dioxide, electrolytes, proteins, carbohydrates, lipids, enzymes, and hormones. The microscopy of AF centrifugate reveals fetal epidermal cells, cells of sebaceous and sweat glands, and prenatal fetal hairs (*lanugo*) [4].

Fetal hypoxia (distress) occurs due to an insufficient supply of dissolved oxygen through the fetoplacental barrier, which can be both acute and chronic [5]. Lack of oxygen changes the hydrogen index (pH) of the fetal blood and induces metabolic acidosis (increased level of lactate). In addition, with oxygen starvation, the fetal body functioning reaches a new level, which is accompanied by changes in the biochemical parameters [6].

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Table 1. Biochemical parameters of amniotic fluid in puerperas in the main and control groups

Biochemical indicator of amniotic fluid in puerperas	Unit of measurement	Main group with signs of fetal hypoxia. *n* = 72	Control group without signs of fetal hypoxia. *n* = 70	p
Total protein	g/L	8.8±4.7	11.4±4.1	0.0843
Glucose	mmol/L	1.2±0.6	0.6±0.3	0.0002
Urea	mmol/L	4.5±1.1	3.0±1.3	0.0018
Creatinine	μmol/L	153±19	134±42	0.0542
Triglycerides	mmol/L	0.2±0.1	0.3±0.1	0.0036
Cholesterol	mmol/L	0.1±0.16	0.3±0.2	0.0275
γ-Glutamyl transpeptidase	U/L	34.5±11	48.7±6.8	0.0261
Alanine aminotransferase	U/L	10.8±4.5	9.9±3.8	0.2905
Aspartate aminotransferase	U/L	27.9±2.3	31.5±6.8	0.4069
C-reactive protein	mg/L	7.4±3.6	8.0±3.3	0.1453
Lactate	mmol/L	3.5±1.2	3.1±0.9	0.0035

The diagnostics of hypoxic changes helps predict and choose the most proper obstetric approach [3, 7]. Therefore, LA research is a very promising field.

This study aimed to analyze the nature of changes in the biochemical parameters of LA during fetal hypoxia.

Materials and methods. This study included women aged 18–38 years who gave birth in the period from January 2016 to September 2018 in the maternity hospital of the Kuvatov Republican Clinical Hospital (Ufa).

A total of 72 female patients were included in the study group, whose main symptom was the signs of fetal hypoxia during childbirth. Fetal hypoxia was considered a complex symptom consisting of the pathological results of cardiotocography and low Apgar scores in newborns [2, 4]. The control group included 70 women without signs of fetal distress at delivery.

Cardiotocography data were recorded on a COMEN STAR 5000E fetal monitor (China). The LA was collected by amniocentesis in order to avoid vaginal secretions entering the LA, which could distort the study results. AF was placed in sterile vacuum tubes. Before the study, LA was subjected to centrifugation (2,500–2,600 rpm) to separate impurities such as vernix caseosa, lanugo, mucus of the mother's birth canal from the liquid fraction. The LA study was performed using a biochemical analyzer, Awareness Technology (USA).

Statistical data analysis was performed using Statistica 10.0 software (StatSoft Inc, USA). We used nonparametric methods of statistical analysis, since the distribution of attributes complied with the laws of nonparametric statistics, which was confirmed by the Kolmogorov–Smirnov one-sample normality test. The qualitative characteristics were compared using Fisher's test, while the Mann–Whitney test was used to compare quantitative data. Statistical significance of differences was set at $p < 0.05$.

Results and discussion. The average age of women in the groups did not differ, which was 27.8 ± 0.86 years in the study group and 27.06 ± 0.86 years in the control group ($p = 0.136$). The average values of anthropometric indicators in women of the study and control groups were 164.18 ± 0.78 cm and 77.645 ± 1.6 kg, and 163.32 ± 0.86 cm and 72.808 ± 1.6 kg, respectively, with no statistically significant differences ($p = 0.256$).

The results of the study of biochemical parameters of LA are presented in Table 1.

LA protein is produced by the maternal organism, the placenta, and the fetus. Protein concentration increases with gestation from 1.3–1.9 g/L in the first trimester to 10–11 g/L by the end of pregnancy. The protein concentration decreases due to both a decrease in its biosynthesis by the body of the mother or fetus, the placenta, and the increased consumption or loss of protein [8]. This may be caused by insufficient intake of protein in the mother's body with food, liver and kidney damage, pathology of the placenta, increased protein loss during blood loss, infectious-inflammatory syndrome, and significant physical exertion [4].

γ-Glutamyl transpeptidase is an enzyme involved in the metabolism of amino acids. In newborns and infants aged up to 6 months, the values of this indicator are several times higher than those in adults. This is because γ-glutamyl transpeptidase is actively involved in the so-called "gluta-

thione cycle" and, consequently, in the processes of amino acid metabolism and microsomal oxidation, which is important for a growing organism [8, 9]. A lower level of γ-glutamyl transpeptidase in the study group (35.5 ± 11 U/L) compared to the control group (48.7 ± 6.8 U/L, $p = 0.0261$) indicated an impaired protein biosynthesis due to fetal hypoxia.

Nitrogenous wastes, creatinine and urea, are the end products of protein metabolism. The above nitrogenous toxins enter LA with fetal urine, and their level increases with gestational age as the fetal kidneys mature and muscle mass grows. The urea level (4.5 ± 1.1 mmol/L) in the study group was significantly higher than that in the control group, 3.0 ± 1.3 mmol/L ($p = 0.0018$). The creatinine level did not significantly change, with 153 ± 19 μmol/L in the study group and 134 ± 42 μmol/L in the control group ($p = 0.0542$). Increased excretion with the urine of the protein degradation end products, specifically urea, occurs when the tissue is damaged. The growth of creatinine and urea levels in LA occurs during acute and chronic fetal hypoxia, and with intrauterine growth retardation [1].

The glucose level in the LA of the main group was twice as high as that in the control group (1.2 ± 0.6 and 0.6 ± 0.3 mmol/L, respectively; $p = 0.0002$) because insufficient oxygenation of the fetus becomes a powerful stress factor for it. In response to stress, the body releases hormones, such as adrenaline and cortisol, which in turn increase glucose levels. However, it should be noted that some authors consider this indicator to be of little information [4].

Triglycerides and cholesterol, along with glucose and total protein, serve as energy substrates. When analyzing these indicators (Table 1), the levels of triglycerides and cholesterol in the main group (0.2 ± 0.1 and 0.1 ± 0.16 mmol/L) was slightly lower than in the control group [0.3 ± 0.1 mmol/L ($p = 0.0016$) and 0.3 ± 0.2 mmol/L ($p = 0.0275$)].

The optimal levels of triglycerides and cholesterol are important for pulmonary surfactant, which consists of 80–85% lipids [10]. A direct correlation was established between the level of triglycerides and the severity of lung damage in acute respiratory distress syndrome. This relationship may be due to the impaired function of type II alveolocytes as producers of surfactant, as well as the suppression of lipase activity [10].

Lipids, such as phospholipids, are involved in the processes of uterine contraction. Arachidonic acid is formed from phospholipids under the action of phospholipase A_2. When exposed to cyclooxygenase on arachidonic acid, biologically active lipid substances (prostaglandins) are formed, which stimulate uterine contractions [1, 2]. Consequently, childbirth under fetal hypoxia can be complicated by primary or secondary poor uterine contraction strength [2, 4].

The analysis of hepatic aminotransferases (alanine aminotransferase and aspartate aminotransferase) did not reveal statistically significant differences, so that the level of alanine aminotransferase was 10.8 ± 4.5 U/L in the study group and 9.9 ± 3.8 U/L in the control group ($p = 0.2905$), and the level of aspartate aminotransferase was 27.9 ± 2.3 U/L in the study and 31.5 ± 6.8 U/L in the control group ($p = 0.4069$).

When assessing C-reactive protein levels in LA, its high index was noted in the control and study groups compared with reference values of the blood serum (Table 1). According to other authors, C-reactive protein in LA is a very sensitive indicator, and physical activity, including contractions and strains, contributes to its growth [3].

Lactic acid (lactate) is a product of anaerobic glycolysis of pyruvate by lactate dehydrogenase. Sources of lactate are striated muscles, the brain, and erythrocytes. Endogenous formation of lactate occurs with a decrease in tissue perfusion and oxygenation with the transition to anaerobic glycolysis, lactic acid is accumulated, and pH changes toward acidification, which consequently develops metabolic acidosis [6, 11]. In this study, the lactate values were recorded to be higher in the study group than in the control group (3.5 ± 1.2 and 3.1 ± 0.9 mmol/L; $p = 0.0035$). AF during labor in diagnosing fetal distress is less traumatic and hazardous for the fetus than collecting blood from the presenting part of the fetus [6, 12].

CONCLUSIONS

1. The biochemical composition of AF indicates the state of the fetus during childbirth; therefore, the study of the AF is relevant and promising.

2. The AF composition undergoes specific changes, namely with fetal distress, significant changes are registered in some biochemical parameters of the AF compared to puerperas without signs of fetal distress, such as the decrease in triglycerides and cholesterol levels and γ-glutamyl transpeptidase activity, and an increase in lactate, glucose, and urea levels.

Author contributions. I.B.F. was the project supervisor; A.Yu.L., Yu.N.F., and L.A.F. developed the study design; A.Yu.L. and N.A.S. collected the material and performed the data analysis; A.Yu.L. and S.A.G. wrote the manuscript.

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