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*Research Article*

# THE RATIO OF FETAL RIGHT LOBE LIVER AND LACTATE DEHYDROGENASE IS A PREDICTOR OF GROWTH RETARDATION IN FETUS WITH PREECLAMPTIC PREGNANCY

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**A R T I C L E I N F O**

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Fetal liver length, lactate dehydrogenase, IUGR, preeclampsia.

**A B S T R A C T**

**Introduction** - It is known that preeclampsia causes uteroplacental insufficiency, which then causes hypoxia in the fetus and its organs. As a result of placental insufficiency, fetal stagnation develops with complications in the form of intrapartum hypoxia of the fetus, perinatal morbidity, asphyxia of the fetus, as well as other postnatal complications.

**The aim of the paper** - is to analyze the importance of determining the length of the right lobe of the fetal liver and lactate-dehydrogenase in the serum of the fetus in pregnant women with preeclampsia in predicting fetal growth retardation as well as the risk of fetal well-being in pregnancy.

**Material and methods** - 120 pregnant women were included in the research, of which 60 pregnant women are with physiological pregnancy and 60 pregnant women with preeclamptic pregnancy with IUGR. In pregnant women with a physiological pregnancy, the pregnancy develops in a physiological way, with the birth of a child with a normal weight corresponding to the gestational age, normal development of the placenta, normal development of the umbilical cord and amniotic fluid. In pregnant women with preeclampsia, preeclampsia developed with the presentation of atrial pressure higher than TA = 140/90mmHg, with the presence of proteinuria higher than 0.5gr/l, as well as the determination of IUGR using the Hadlock formula. The results are calculated with these statistical methods. Examination of the normality of the distribution of continuous numerical changes was performed by inspection of histograms, quantile plots, and formal testing using the Kolgomorov-Smirnov test. Analysis of variables was performed using Pearson's $x^2$ test or Fisher's exact probability test. Analysis of features of normally distributed continuous ratio was performed using independent simple T test for independent samples, while non-parametric distributed numerical variables were analyzed using Mann-Whitney U test for independent samples. Pearson and Spearman correlation coefficients were used according to data type and normality of distribution.

**Results** - Our study with the help of the correlation coefficient according to Sperman has revealed that there is no significant difference in the linear correlation between the week of gestation and LDH values in the ser
Our study by means of the correlation coefficient according to Spearman has found that there is a statistically significant difference of the positive linear correlation between the week of gestation and LDH values of the fetus/newborn with growth retardation IUGR (rs=0.274; p> 0.05).

Mann Whitney analysis found that fetuses/newborns with growth retardation (IUGR) have higher serum LDH values [Me=795.00 to 1490.00] compared to fetuses/newborns with normal growth and development [Me =587.00 U/L (IQR=376.00 to 783.00)]. There is a significant statistical difference with the mean values of LDH in serum between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=1203.000, z=-3.135, p=0.002].

Statistical data using the Mann Whitney test in our research showed that in fetuses with growth retardation (IUGR) the median length of the fetal liver is lower [Me=0.05 (IQR=0.03 to 0.08)] compared to fetuses with normal growth and development [Me=0.09 (IQR=0.06 to 0.12)]. There is a statistically significant difference between the median

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fetal liver length ratio and serum LDH between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=973.000, z=-4.341, p< 0.001].

**Discussion** - There is a significant statistical difference with the mean values of LDH in serum between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=1203.000, z=-3.135, p=0.002]. The increase in the level of lactate dehydrogenase enzymatic activity in fetuses with growth retardation is explained in this way. In fetuses with growth retardation (IUGR), the increase in the level of enzymatic activity of lactate dehydrogenase, which follows and is caused by hypoxia in the cells of the liver, transverse muscles and kidneys. Due to hypoxia, the permeability of the cell membrane is disturbed, as LDH molecules are transferred from the tissues to the plasma.

The authors' studies (10) have found that in preeclampsia there is an increased level of lactate dehydrogenase and aspartate aminotransferase, which is consistent with our results. Our results have shown that there is an increase in the level of LDH in preeclampsia, which are consistent with the results of the authors (1, 2).

The clarification of the achieved results is based on these data that the growth retardation of the fetus due to hypoxia, which develops into preeclampsia, increases the activity of lactate dehydrogenase, which affects the glycolytic process of the breakdown of carbohydrates. In the conditions of hypoxia, damage to the liver cells follows, as well as the disorder of the permeability of the cell membrane, in some cases, the transfer of lactate dehydrogenase from the cell to the serum follows, as well as the increase in the level in the blood. The other mechanism is explained by the fact that the increase in the level of LDH follows due to stress and hypoxia of the fetus as well as due to the increase in fetal cortisol from the adrenal gland. It is assumed that the high level of fetal prolactin stimulates the synthesis of lactate dehydrogenase in the fetal liver.

There is a statistically significant difference between the median fetal liver length ratio and serum LDH between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=973.000, z=-4.341, p< 0.001]. These data are explained by the fact that the length of the right lobe of the fetal liver (FLL- Fetal Liver Length) in fetuses with growth retardation is smaller than the length of the left lobe, and on the other side of preeclampsia with fetal growth retardation, there is the phenomenon of blood redistribution so that the amount of blood supplying the right lobe is much lower. In addition, the right lobe of the liver is strengthened with deoxygenated blood because over 60% of the oxygenated blood does not pass to the liver due to the presence of the Ductus Arantii, which exceeds the liver and flows into the inferior vena cava. In adult humans, the ratio between the right lobe of the liver and the left lobe is 6:1. Due to these morphological changes (the presence of the ductus Aranti) and physiological changes (the phenomenon of blood circulation distribution that exists in IUGR) of the fetus, the amount of oxygenated blood passing through the right lobe of the liver is much lower in relation to the left lobe of the liver, for this reason there is stagnation in the growth of the right lobe of the liver.

**Conclusion** - Research has shown that the FLL/LDH ratio values in fetuses with preeclampsia are lower compared to fetuses with normal development.

Research has shown that the FLL/LDH ratio values in fetuses with preeclampsia are lower compared to fetuses with normal development. These data show that the length of the right lobe of the fetal liver in preeclampsia with IUGR is lower compared to the values of the length of the liver in fetuses with normal growth and development. As well as the LDH values of fetuses with growth retardation are higher compared to the LDH values of fetuses with normal growth and development. So the ratio FLL/LDH mathematically ( $\frac{FLL}{LDH}$ stunting in growth < $\frac{FLL}{LDH}$ normal growth) it is lower in fetuses with growth retardation compared to fetuses with normal growth. At the same time, these parameters result in significant values in the prediction of growth retardation and fetal well-being during intrauterine life. Based on the purpose of the work, the methodology and the results, we find that the ratio between the length of the fetal liver and LDH are significant indicators for the prediction of growth retardation in the fetus with preeclampsia.



## INTRODUCTION

Preeclampsia in pregnancy causes disorders in the functioning of many pregnant organs, causing disorders in the health of the pregnant woman as well as in the growth of the fetus during intrauterine life. These disorders appear due to changes in the blood vessels of the placenta, hyalinization of the placental villi, infarctions and thrombosis in the intervillous spaces which are formed due to the influence of hypertension on the blood vessels. These changes reduce the functional capacity of the placenta, which in the fetus causes stunted growth and

development. Growth retardation is associated with a high frequency of fetal morbidity and mortality.

Intrauterine stasis of the fetus causes perinatal mortality, asphyxiation of the fetus, intrapartum hypoxia, while after birth complications appear in the newborn in the form of hypoglycemia, acidemia (1), polycythemia, as well as a decrease in the amount of subcutaneous tissue.

It is known that preeclampsia causes uteroplacental insufficiency which then causes hypoxia of the fetus and its organs. Fetal hypoxia activates the phenomenon of redistribution of blood in the fetal body by reducing the blood supply to the abdominal organs, skeletal muscles, and the osteomuscular apparatus as well as to the skin, increasing blood circulation in the central nervous system, the adrenal gland and the kidney.

***Purpose of the work***

The purpose of the paper is to determine the importance of the ratio of fetal liver length and lactate-dehydrogenase in fetal serum in pregnant women with preeclampsia in predicting fetal growth retardation as well as the risk of fetal well-being in pregnancy.

## MATERIAL AND METHODS

120 pregnant women were included in the study, of which 60 pregnant women are with physiological pregnancy and 60 pregnant women are with preeclampsia and IUGR.

In the study, the group of pregnant women with physiological pregnancy included pregnant women whose pregnancy developed in a physiological way with the birth of a child with a normal weight corresponding to the gestational age, normal development of the placenta, umbilical cord and amniotic membranes.

The selection of the group of pregnant women with preeclampsia is formed based on the determination of the method of the last menstruation, Hadlolck's formula, based on the presence of proteinuria (>0.5 g/l) as well as high blood pressure above TA = 140/ 90mmHg.

In pregnant women with physiological and preeclamptic pregnancies, blood is taken from the cubital vein, while in fetuses/neonates with physiological and preeclamptic pregnancies, blood is taken from the umbilical vein to determine the laboratory parameters: lactate-dehydrogenase and cholesterol.

Pregnant women with diabetes mellitus, anemia in pregnancy, lupus erythematosus, autoimmune diseases, hepatitis (A, B, C, D and E), pregnant women with cardiovascular and renal diseases, as well as pregnant women with fetal abnormalities were excluded from the study.

Examination of the normality of the distribution of continuous numerical changes was calculated by inspection of histograms, quantile plots and formal testing using the Kolgomorov-Smirnov test. Analysis of variables was performed using Pearson's $x^2$ test or Fisher's exact probability test. Analysis of normally distributed continuous features was performed using the simple independent t test for independent samples, while nonparametric distributed numerical variables were analyzed using the Mann-Whitney U test. For independent samples, the correlation coefficient of Pearson and Spearman was used according to the type of data and normality of distribution. The threshold of statistical significance was set at the conventional level of $\alpha$=0.05. In fetuses with physiological and preeclamptic pregnancies, the ultrasonographic parameters are determined: biparietal diameter (BPD), femur length (FL), amniotic fluid index (AFI) as well as the gradation of the placenta according to Grannum and the length of the fetal liver (FLL Fetal Liver Lengh).

In the figure, we have presented the technique of measuring the amniotic-fluid index (AFI) at the gestational age.

Measurement of amniotic fluid index by means of ultrasonography.

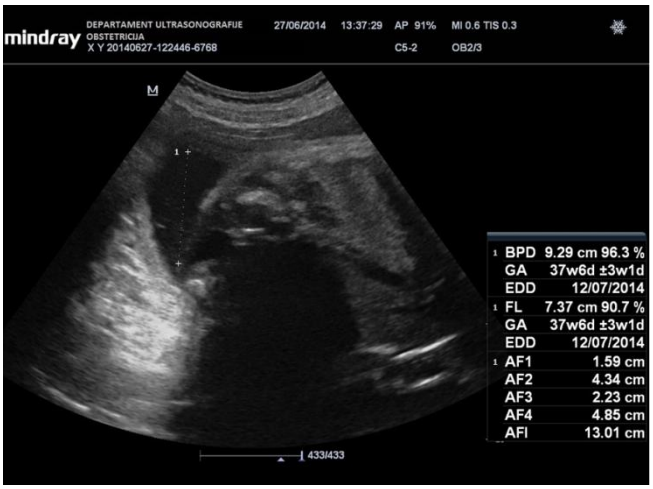



**Figure 1**. Presentation of AFI measurements. Measurement of the maximum depth of the amniotic fluid pocket (without the presence of small parts of the fetus) in four quadrants. AFI represents the numerical sum in four quadrants of amniotic fluid. Gestational age 37 weeks and 6 days (37w6d).

In the figure, we have shown the measurement of the length of the right lobe of the fetal liver in relation to the gestational age. Ultrasonographic measurement of the length of the right lobe of the fetal liver (FLL).

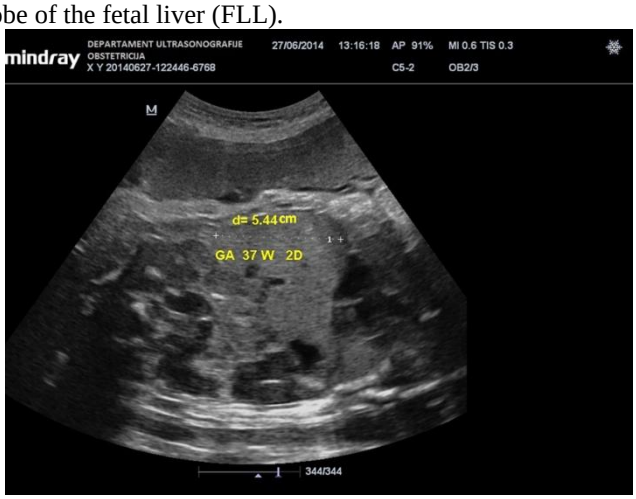



**Figure 2** Display of the measurement of the length of the right lobe of the fetal liver (FLL - Fetal Liver Length).

The length of the right lobe of the fetal liver was measured in the paramedian incision passing through the right lobe of the liver. It is measured from the right hemidiaphragm to the tip of the right lobe. The length of the right lobe of the fetal liver is d=5.44 cm. Gestational age is (GA 7w6d).

## RESEARCH RESULTS

### 1. Demographic and clinical characteristics of pregnant women

#### *1. 1 Number of births (parity)*

From the total number of pregnant women with physiological pregnancy (n=60), most of them had one birth (43.3%), from 3 or more births (33.3%), 2 births (20%) and no birth (3.3%). From the total number of pregnant women with preeclamptic pregnancy (n=60), most of them had one birth (41.7%), from 3 or more births (30.0%), 2 births (28.3%) and none without birth (0.0 %).

The number of pregnant women

There is no statistically significant difference in the frequency of parity between physiological pregnancy and preeclamptic pregnancy [$\chi^2$ (3)=2,987, p=0,394].

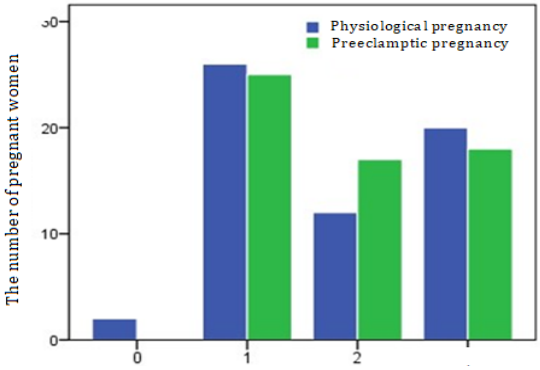



**Table 1** Correlation between parity and type of pregnancy

| | | | The pregnant group | | Total |
|---|---|---|---|---|---|
| | | | Physiological pregnancy | Preeclamptic pregnancy | |
| **Parity** | 0 | Number | 2 | 0 | 2 |
| | | % of the pregnant group | 3.3% | 0.0% | 1.7% |
| | 1 | Number | 26 | 25 | 51 |
| | | % of the pregnant group | 43.3% | 41.7% | 42.5% |
| | 2 | Number | 12 | 17 | 29 |
| | | % of the pregnant group | 20.0% | 28.3% | 24.2% |
| | **3 and more** | Number | 20 | 18 | 38 |
| | | % of the pregnant group | 33.3% | 30.0% | 31.7% |
| Total | | Number | 60 | 60 | 120 |
| | | % of the pregnant group | 100.0% | 100.0% | 100.0% |

**Table 2 -** Correlation between miscarriage and type of pregnancy

| | | | The pregnant group | | Total |
|---|---|---|---|---|---|
| | | | Physiological pregnancy | Preeclamptic pregnancy | |
| Number of abortions | 0 | Number | 48 | 45 | 93 |
| | | % of the pregnant group | 80.0% | 75.0% | 77.5% |
| | 1 | Number | 8 | 8 | 16 |
| | | % of the pregnant group | 13.3% | 13.3% | 13.3% |
| | **2 and more** | Number | 4 | 7 | 11 |
| | | % of the pregnant group | 6.7% | 11.7% | 9.2% |
| Total | | Number | 60 | 60 | 120 |
| | | % of the pregnant group | 100.0% | 100.0% | 100.0% |

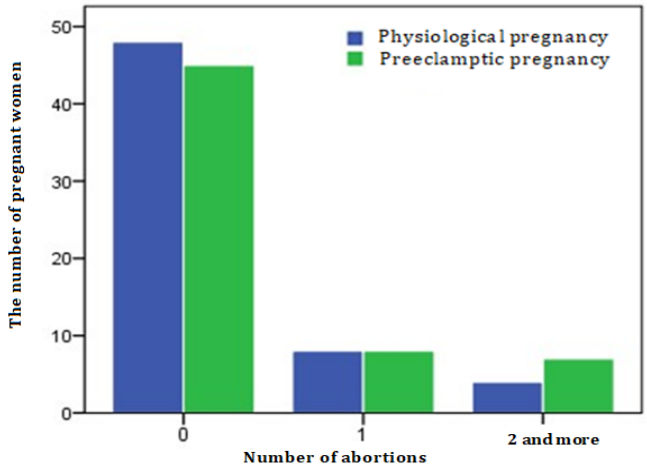
**Table 3** Lactate dehydrogenase values in the serum (U / L) according to the type of pregnancy.

| | | | **The pregnant group** | |
|---|---|---|---|---|
| | | | Physiological pregnancy | Preeclamptic pregnancy |
| Lactate dehydrogenase (U/L) | N | | 60 | 60 |
| | Mean | | 364.72 | 590.92 |
| | Std. Deviation | | 104.80 | 345.65 |
| | Minimum | | 31.00 | 231.00 |
| | Maximum | | 532.00 | 1605.00 |
| | Percentiles | 25th | 296.50 | 297.00 |
| | | 50th (Median) | 356.50 | 509.50 |
| | | 75th | 456.00 | 796.25 |
| | p- value | | <0.001 | |

### *1.2 Number of abortions*

Of the total number of pregnant women with physiological pregnancy (n=60), most of them were without abortion (80.0%), followed by one abortion (13.3%) and 2 or more abortions (6.7%). Of the total number of pregnant women with preeclamptic pregnancy (n=60), the majority were without abortion (75.0%), followed by one abortion (13.3%) and 2 or more abortions (11.7%).

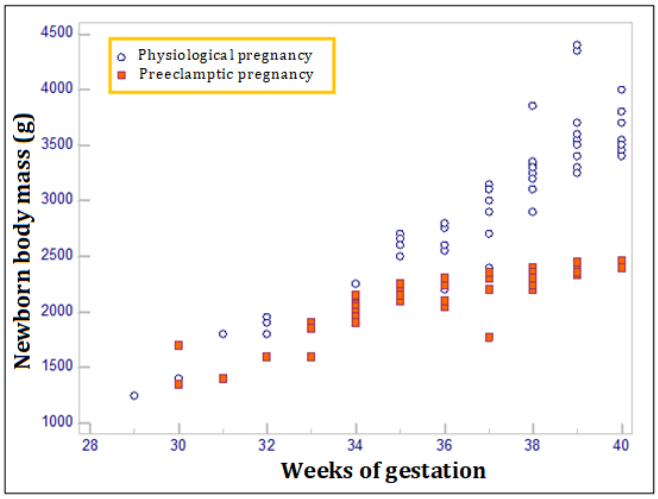
There is no statistically significant difference in the frequency of abortions between the groups of pregnant women with physiological pregnancy and preeclamptic pregnancy [$\chi^2(2)=0.915$, p=0.633].




**Graph 2** Correlation between abortion and type of pregnancy

### 2. Correlation between the gestational week and the body mass of the newborn with physiological and preeclamptic pregnancy

There is a statistically significant linear correlation between gestational week and body mass of newborns with physiological pregnancy ($r_s$=0.926; P<0.001) and preeclamptic pregnancy ($r_s$=0.916; P<0.001).




**Graph 3** Correlation between the weeks of gestation and the body mass of the newborn.

### 3. Lactate Dehydrogenase (LDH) in serum

Preeclamptic pregnant women have higher serum LDH values [Me = 509.50 to 796.25)] compared to normal pregnancy women [Me = 356.50 U/L (IQR = 296.50 to 456.00)].

There is a statistically significant difference in the value of LDH in serum between pregnant women with physiological and preeclamptic pregnancy [U=1131,500, z = -3.509, p <0.001].

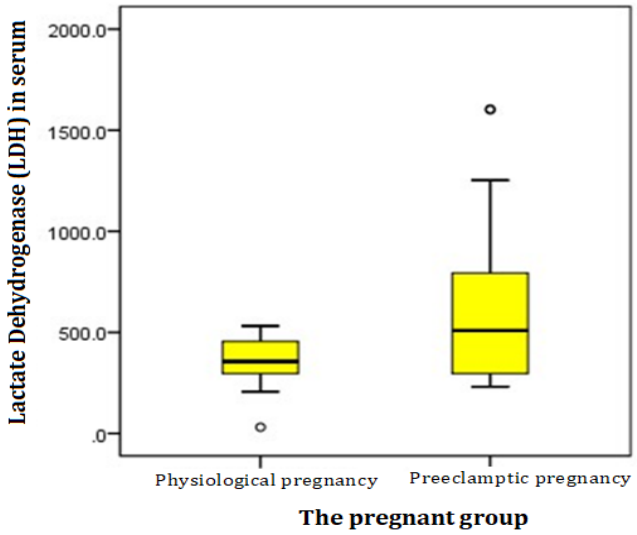
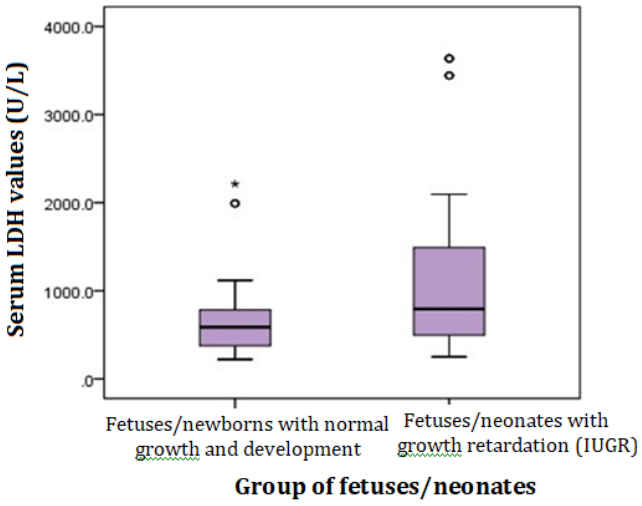



**Chart 4** Serum lactate dehydrogenase values (U/L) according to pregnancy type.

### 4. Lactate Dehydrogenase (LDH) in fetal/newborn serum

Fetuses/newborns with growth retardation (IUGR) have higher serum LDH values [Me=795.00 to 1490.00] compared to fetuses/newborns with normal growth and development [Me=587.00 U/L (IQR=376.00 up to 783.00)].

There is a statistically significant difference in the mean serum LDH values between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=1203.000, z=-3.135, p=0.002].



between gestational week and serum LDH values in

**Table 4** Serum LDH values in fetuses/newborns with growth retardation (IUGR) and Fetuses / newborns with normal growth and development

| | | | Group of fetuses/neonates | |
|---|---|---|---|---|
| | | | Fetuses/newborns with normal growth and development | Fetuses/neonates with growth retardation (IUGR) |
| Lactate dehydrogenase (U/L) | N | | 60 | 60 |
| | Mean | | 678.02 | 1179.95 |
| | Std. Deviation | | 431.16 | 944.82 |
| | Minimum | | 222.00 | 251.00 |
| | Maximum | | 2213.00 | 3639.00 |
| | Percentiles | 25th | 376.00 | 491.50 |
| | | 50th (Median) | 587.00 | 795.00 |
| | | 75th | 783.00 | 1490.00 |
| | p- value | | <0.01 | |

**Table 5** Correlation of gestational week and LDH values in fetal/newborn serum.

| | The pregnant group | | | Weeks of gestation | Serum LDH (U/L) |
|---|---|---|---|---|---|
| Spearman's rho | Fetus with normal growth and development | Weeks of gestation | Correlation Coefficient | 1.000 | 0.242 |
| | | | Sig. (2-tailed) | . | 0.062 |
| | | | N | 60 | 60 |
| | | Serum LDH (U/L) | Correlation Coefficient | 0.242 | 1.000 |
| | | | Sig. (2-tailed) | 0.062 | . |
| | | | N | 60 | 60 |
| | Fetus with IUGR | Weeks of gestation | Correlation Coefficient | 1.000 | 0.247* |
| | | | Sig. (2-tailed) | . | 0.034 |
| | | | N | 60 | 60 |
| | | Serum LDH (U/L) | Correlation Coefficient | 0.274* | 1.000 |
| | | | Sig. (2-tailed) | 0.034 | . |
| | | | N | 60 | 60 |

**Table 6** The ratio between the length of the fetal liver and the LDH value in the fetal serum in normal and preeclamptic pregnancies with IUGR.

| | | | The pregnant group | |
|---|---|---|---|---|
| | | | Normal pregnancy | Pregnancy with preeclampsia and IUGR |
| FLL/LDH ratio | N | | 60 | 60 |
| | Mean | | 0.10 | 0.06 |
| | Std. Deviation | | 0.05 | 0.04 |
| | Minimum | | 0.02 | 0.01 |
| | Maximum | | 0.25 | 0.17 |
| | Percentiles | 25th | 0.06 | 0.03 |
| | | 50th (Median) | 0.09 | 0.05 |
| | | 75th | 0.12 | 0.08 |
| | p- value | | <0.001 | |

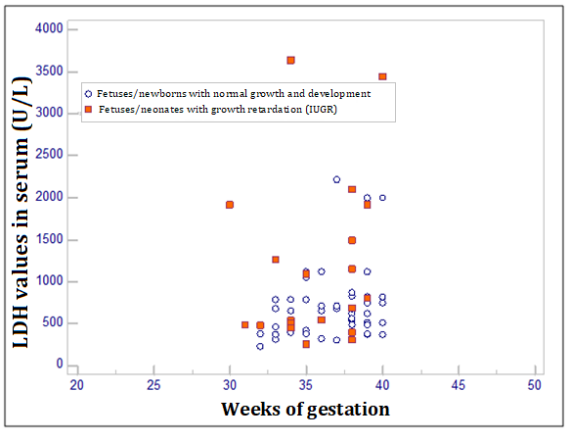
**Chart 5** - Serum LDH values in fetuses/newborns with growth retardation (IUGR) and fetuses with normal growth and development

**5. Correlation between gestational weeks and fetal serum LDH values**

There is no statistically significant linear correlation between gestational week and serum LDH values in fetuses/newborns with normal growth and development ($r_s$=0.242; p>0.05). There is a statistically significant positive linear correlation fetuses with growth retardation in intrauterine life ($r_s$=0.274; p<0.05).

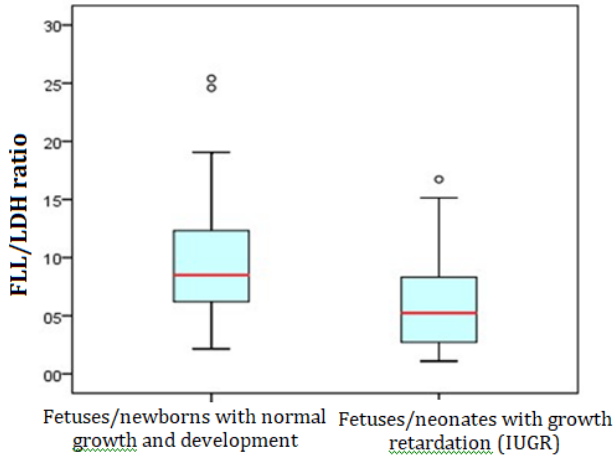
**5.1. The ratio between the length of the right lobe of the fetal liver and LDH values in the fetus**

In fetuses with growth retardation (IUGR) the median fetal liver length is lower [Me=0.05 (IQR=0.03 to 0.08)] compared to fetuses with normal growth and development [Me=0.09 (IQR=0.06 to 0.12)].




**Graph 6** Correlation of the week of pregnancy and LDH values in the serum of the fetus/newborn.

There is a statistically significant difference between the median of the ratio of the length of the right lobe of the fetal liver and serum LDH between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=973.000, z=- 4.341, p<0.001].




**Graph 7** The ratio between the length of the right lobe of the fetal liver and the LDH value in the fetal serum in normal and preeclamptic pregnancies with IUGR.

## DISCUSSION

Pregnancy with preeclampsia is associated with endothelial cell damage and the release of these biochemical mediators (fibronectin, laminin). The release of cell degradation products stimulate the coagulation processes as well as the aggregation of platelets in the capillary walls. Due to these disorders in the degeneration of cells, the ratio of prostacyclin and thromboxane is disturbed, vasoconstriction of blood vessels and hypoxia of tissues in the organs of the pregnant woman and fetus appear. Vasoconstriction in preeclampsia causes ischemia in the liver and kidneys, especially in severe cases of preeclampsia. It is known that in preeclampsia there is also fetal growth retardation (IUGR). In severe cases of preeclampsia, an increase in the activity of the hepatitis enzymes LDH, AST and ALT follows. There are data that lactate dehydrogenase and aminotransferases are increased in preeclampsia (2, 3, 4). Increased concentration of lactate dehydrogenase, aminotransferases and some other liver metabolites can be important markers predicting fetal growth retardation. The determination of lactate dehydrogenase, aminotransferase and cholesterol in pregnant women and newborns with growth retardation enable the differentiation and risk of perinatal complications due to hypoxia. The ratio of FLL and aminotransferases in the blood of a fetus with growth retardation (IUGR) is an important parameter for predicting fetal growth retardation (5). Changes in the pathohistology of the placenta appear in the form of infarctions, fibrin deposits and atherosclerosis in the blood vessels associated with IUGR in preeclampsia (6, 7).

Data in the literature show that there is a close correlation between uteroplacental ultrasonographic parameters and fetal growth retardation (8). The increase in lactate dehydrogenase values is explained by the action of oxidative stress and the disorder of the synthesis of nitrogen monoxide, prostacyclin, coagulation factors, endothelin components, neuropeptides (9) which cause degenerative changes in hepatocytes with an increase in the level of lactate dehydrogenase. In fetal growth retardation due to hypoxia, which develops into preeclampsia, the activity of lactate dehydrogenase increases, which affects the glycolytic process of carbohydrate breakdown.

Under conditions of hypoxia, damage to the liver cells (hepatocytes) follows, as well as a disruption of the permeability of the cell membrane, in some cases, the transfer of lactate dehydrogenase from the cell to the serum follows, as well as an increase in the level in the blood. The other mechanism is explained by the fact that the increase in the level of LDH follows due to stress and hypoxia of the fetus, which follows with the increase in fetal cortisol from the adrenal gland. It is assumed that the high level of fetal prolactin stimulates the synthesis of lactate dehydrogenase in the fetal liver.

Our study with the help of the correlation coefficient according to Spearman has revealed that there is no significant difference in the linear correlation between the week of gestation and LDH values in the serum of the fetus/newborn with normal growth and development (rs=0.242; p >0.05). Our study by means of the correlation coefficient according to Spearman has found that there is a statistically significant difference of the positive linear correlation between the week of gestation and LDH values of the fetus/newborn with growth retardation IUGR (rs=0.274; p> 0.05). The increase in the level of lactate dehydrogenase enzymatic activity in fetuses with growth retardation is explained in this way. In fetuses with growth retardation (IUGR), the increase in the level of lactate dehydrogenase enzymatic activity follows and is caused by hypoxia in the cells of the liver, transverse muscles and kidneys. Due to hypoxia, the permeability of the cell membrane is disturbed, as LDH molecules are transferred from the tissues to the plasma. The authors' studies (10) have found that in preeclampsia there is an increased level of lactate dehydrogenase and aspartate aminotransferase, which is consistent with our results. Our results have shown that there is an increase in the level of LDH in preeclampsia, which are consistent with the results of the authors (1, 2). Mann Whitney analysis found that fetuses/newborns with growth retardation (IUGR) have higher serum LDH values [Me=795.00 to 1490.00] compared to fetuses/newborns with normal growth and development [Me =587.00 U/L (IQR=376.00 to 783.00)]. There is a significant statistical difference with the median values of serum LDH between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=1203.000, z=-3.135, p=0.002]. Our results are consistent

with the authors' results (1, 2, 4). Other authors (10, 11) have also achieved similar results.

The clarification of the achieved results is based on these data that the growth retardation of the fetus due to hypoxia, which develops into preeclampsia, increases the activity of lactate dehydrogenase, which affects the glycolytic process of the breakdown of carbohydrates. In the conditions of hypoxia, damage to the liver cells follows, as well as the disruption of the permeability of the cell membrane, in some cases, the transfer of lactate dehydrogenase from the cell to the serum, as well as an increase in the level in the blood, follows. The other mechanism is explained by the fact that the increase in the level of LDH follows due to stress and hypoxia of the fetus as well as due to the increase in fetal cortisol from the adrenal gland. It is assumed that the high level of fetal prolactin stimulates the synthesis of lactate dehydrogenase in the fetal liver.

Statistical data using the Mann Whitney test in our research showed that in fetuses with growth retardation (IUGR) the median length of the fetal liver is lower [Me=0.05 (IQR=0.03 to 0.08)] compared to fetuses with normal growth and development [Me=0.09 (IQR=0.06 to 0.12)]. There is a statistically significant difference between the median of the ratio of the length of the right lobe of the fetal liver and serum LDH between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=973.000, z=-4.341, p<0.001].

These data are explained by the fact that the length of the right lobe of the fetal liver (FLL- Fetal Liver Length) in fetuses with stunted growth is smaller than the length of the left lobe, and on the other hand in preeclampsia with stunted growth growth of the fetus, there is a phenomenon of blood redistribution so that the amount of blood supplying the right lobe is much lower. In addition, the right lobe of the liver is supplied with deoxygenated blood because over 60% of the oxygenated blood does not pass to the liver due to the presence of the Ductus Arantii which exceeds the liver and flows into the inferior vena cava. In adult people, the size ratio between the right lobe of the liver and the left lobe is in the ratio 6:1. Due to these morphological changes (the presence of the ductus Aranti) and physiological changes (the phenomenon of blood circulation distribution that exists in IUGR) of the fetus, the amount of oxygenated blood passing through the right lobe of the liver is much lower in relation to the left lobe of the liver, for this reason there is stagnation in the growth of the right lobe of the liver. Researches (12, 13, 14,) show that the left lobe of the liver is supplied with higher amounts of oxygenated blood compared to the right lobe. The authors have argued that the Hepato-Cephalic index is an important predictor for the detection of growth retardation in cases with preeclampsia as a result of uteroplacental insufficiency due to hypoxia (15).

The morphological and physiological changes in the blood circulation in the fetus as well as the appearance of changes in the blood circulation in preeclampsia and the fetus with growth retardation cause a reduced supply of oxygen and nutrients (glucose, amino acids, fatty acids and minerals) in the liver, especially in the right lobe of the liver, which is manifested by growth retardation.

## CONCLUSION

Research has shown that the FLL/LDH ratio values in fetuses with preeclampsia are lower compared to fetuses with normal development. These data show that the length of the right lobe of the fetal liver in preeclampsia with IUGR is lower compared to the liver length values in fetuses with normal growth and development, as well as LDH values in stunted fetuses. in growth, they have higher values compared to the LDH values of fetuses with normal growth and development. So the ratio FLL/LDH mathematically ($\frac{FLL}{LDH}$ stunting in growth$<\frac{FLL}{LDH}$ normal growth) is lower in fetuses with stunted growth compared to fetuses with normal growth. At the same time, these parameters result in significant values in the prediction of fetal growth retardation and fetal well-being during intrauterine life.

Based on the purpose of the work, the methodology and the results, we find that the ratio between the length of the fetal liver and LDH are significant indicators for the prediction of growth retardation in the fetus with preeclampsia.

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