Determination of lactate dehydrogenase in pregnancy and fetus with preeclamsia is an important parameter of fetus growth retardation

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1. Abstract

Introduction - It is known that in preeclampsia, especially in the placenta, atherosclerosis of blood vessels develops and exists. Due to damage to the blood vessels, the accumulation of amorphous material and the deposition of immunoglobulins G (IgG), immunoglobulin M (IgM) and activation of the complement, eventually obliteration of the blood vessels develops and ischemia and infarction of the placenta follows.

Recent studies have shown a close relationship between the concentration of lactate dehydrogenase and growth retardation in utero in preeclampsia (26.27). There is a correlation between the level of estriol, placental perfusion, lactate dehydrogenase and fetal growth retardation in utero (28). 5 types of lactate dehydrogenase isozymes have been detected in the placental tissue. LDH_4 and LDH_5 isoenzymes have been found in high concentrations in the placenta (29).

Some studies show that the liver of the fetus is sensitive to hypoxia, as a result of stagnation in the growth of the liver and degeneration of the tissues in the absence of the liver. These scientists have argued that the fetal liver is more sensitive to growth retardation compared to the circumference of the head and abdomen (36, 37, 38).

Aminotransferases, lactate-dehydrogenase, bilirubin (unconjugated, conjugated) are metabolites that change their concentrations depending on liver hypoxia. These scientists have found that it is important to determine between the level of aminotransferases (AST, ALT), lactate dehydrogenase, bilirubin (unconjugated and conjugated) in the blood of the fetus/newborn with growth retardation due to hypoxia (40, 41, 42, 43, 44).

The aim of the paper: The purpose of the paper is to determine and analyze the level of lactate dehydrogenase in the blood of pregnant women with normal and preeclamptic pregnancy as well as in the blood of the fetus in pregnant women with normal and preeclamptic pregnancy in predicting fetal growth retardation.

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 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.

In fetuses with physiological and preeclamptic pregnancy, ultrasonographic parameters are determined: biparietal diameter (BPD), femur length (FL). 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/ 90 mmHg.

Analysis of variables was performed using Pearson's x^2 test or Fisher's exact probability test.

Analysis of normally distributed continuous ratio features was performed using the independent simple t-test, for independent samples, while nonparametrically distributed numerical variables were analyzed using the Mann-Whitney U test for independent samples. Pearson's and Spearman's correlation coefficient was used according to the type of normality and distribution data.

Research results - With the analysis of the Mann Whitney - U test, we found that there is a statistically significant difference in the AST values in serum between pregnant women with physiological and preeclamptic pregnancy [U=521.500, z=6.717, p<0.001]. Preeclamptic pregnancies had higher serum AST values [Me=27.00 U/L (IQR=22.00 to 34.00)] compared to physiological pregnancies [Me=14.00 U/L (IQR=11.00 to 19.00)].

Analysis by means of the Mann Whitney - U test has found that there is a statistically significant difference in serum LDH values between fetuses with stunted growth and fetuses with normal development and growth [U=1203.000, z=-3.135, p=0.002]. Growth retardation (IUGR) fetuses have higher serum LDH values [Me=795.00 U/L (IQR=491.00 to 1490.00)] compared to fetuses with normal growth and development [Me=587.00U/L (IQR =376.00 to 783.00)].

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 serum of the fetus/newborn with normal growth and development (r_s=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).

Discussion - 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 (10) 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. 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.

Conclusion - On the basis of the purpose of the research, the material of the methods and the results, we found these conclusions.

Preeclamptic pregnancies had higher serum LDH values [Me=509.50 U/L (IQR=297.00 to 796.25)] compared to physiological pregnancies [Me=356.50 U/L (IQR=296.50 to 456.00)].

Growth retardation (IUGR) fetuses have higher serum LDH values [Me=795.00 U/L (IQR=491.00 to 1490.00)] compared to fetuses with normal growth and development [Me=587.00U/L (IQR =376.00 to 783.00)].

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 serum of the fetus/newborn with normal growth and development (r_s=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).

Key words - Lactate dehydrogenase, Pregnancy, Fetus, Preeclampsia, IUGR.

2. Introduction

It is known that in preeclampsia, especially in the placenta, atherosclerosis of blood vessels develops and exists. Due to damage to the blood vessels, the accumulation of amorphous material and the deposition of immunoglobulins G (IgG), immunoglobulin M (IgM) and activation of the complement, eventually obliteration of the blood vessels develops and ischemia and infarction of the placenta follows.

Recent studies have shown a close relationship between the concentration of lactate dehydrogenase and growth retardation in utero in preeclampsia (26.27). There is a correlation between the level of estriol, placental perfusion, lactate dehydrogenase and fetal growth retardation in utero (28). 5 types of lactate dehydrogenase isozymes have been detected in the placental tissue. LDH_4 and LDH_5 isoenzymes have been found in high concentrations in the placenta (29).

Some studies show that the liver of the fetus is sensitive to hypoxia, as a result of stagnation in the growth of the liver and degeneration of the tissues in the absence of the liver. These scientists have argued that the fetal liver is more sensitive to growth retardation compared to the circumference of the head and abdomen (36, 37, 38).

In fetal growth retardation, changes in the fetal ECG have also been recorded, which are manifested by an elevation of the T-wave (39). It is known that these biochemical parameters appear and are released in the blood before the degenerative morphological changes in the cells.

Aminotransferases, lactate-dehydrogenase, bilirubin (unconjugated, conjugated) are metabolites that change their concentrations depending on liver hypoxia. These scientists have found that it is important to determine between the level of aminotransferases (AST, ALT), lactate dehydrogenase, bilirubin (unconjugated and conjugated) in the blood of the fetus/newborn with growth retardation due to hypoxia (40, 41, 42, 43, 44).

The aim of the paper - The purpose of the paper is to determine and analyze the level of lactate dehydrogenase in the blood of pregnant women with normal and preeclamptic pregnancy as well as in the blood of the fetus in pregnant women with normal and preeclamptic pregnancy in predicting fetal growth retardation.

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.

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.

In fetuses with physiological and preeclamptic pregnancy, ultrasonographic parameters are determined: biparietal diameter (BPD), femur length (FL). 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/ 90 mmHg.

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

3. Ultrasonographic research methods

Measurement of biparietal diameter (BP) by ultrasonography.

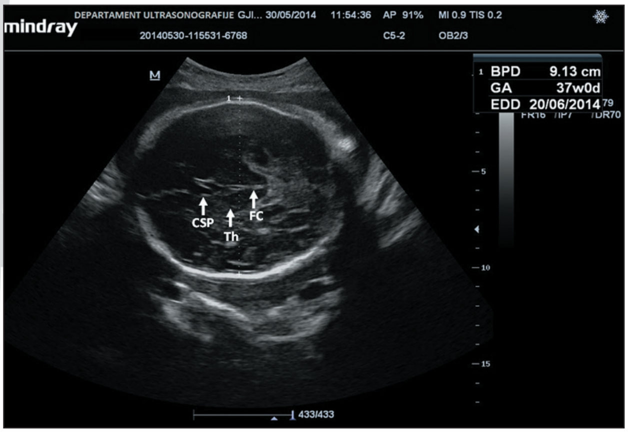


Figure 1. Measurement of biparietal diameter and showing the plan for ultrasonographic measurement of biparietal diameter. Cavum septum pellucidum (CSP), Thalamus (Th), Falcs cerebri (FC).

Femur length measurement by ultrasonography.

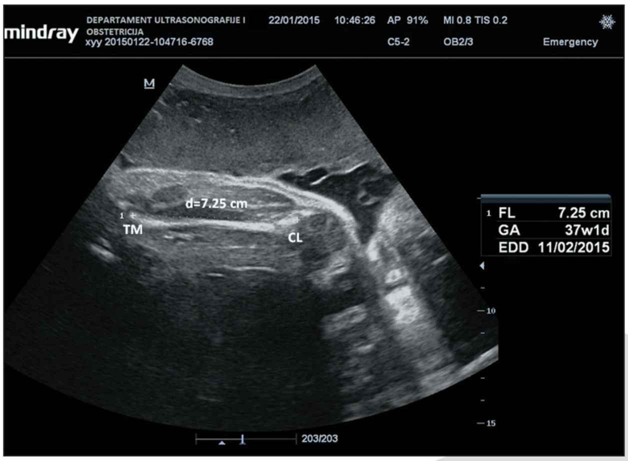


Figure 2. Presentation of femur length measurements. The femur is measured in the length of the ossified part of the femoral diaphysis in the longitudinal section. The femur is measured from the major trochanter to the lateral Condylus. Major trochanter (TM). Condylus lateralis (CL).

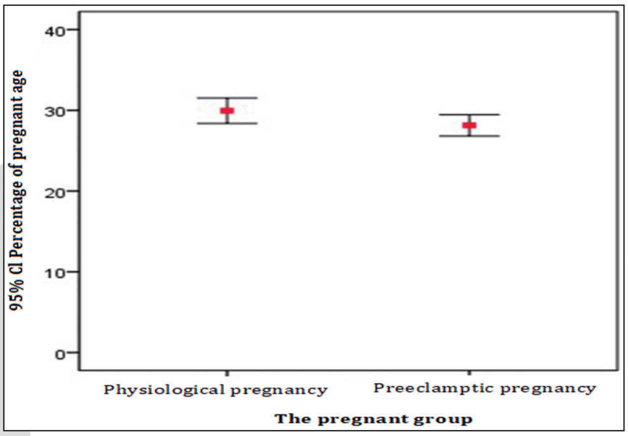
Examination of the normality of the distribution of continuous numerical changes was performed by inspection of histograms, quantile plots, and formal testing using the Kolgomorov-Smirnov test. Analysis of variables was performed using Pearson's x^2 test or Fisher's exact probability test. Analysis of normally distributed continuous ratio features was performed using the independent simple t-test, for independent samples, while non-parametrically distributed numerical variables were analyzed using the Mann-Whitney U test for independent samples. Pearson's and Spearman's correlation coefficient was used according to the type of normality and distribution data. The threshold of statistical significance was set at the conventional level of α =0.05.

4. Research results

4.1. Demographic and laboratory data of the research

1. Age of pregnant women

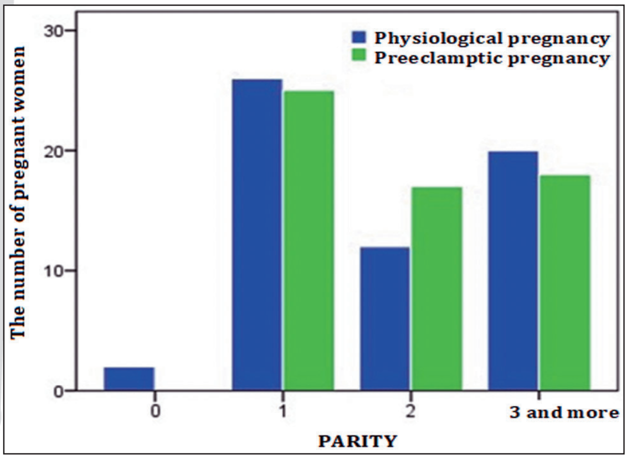
Pregnant women with physiological pregnancy were older [=29.95, SD=6.10; 95% CI (28.37, 31.53)] compared to pregnant women with preeclamptic pregnancy [=28.13, SD=5.10; 95% CI (26.82; 29.45)]. Specified age difference [1,817; 95%CI (-0.216; 3.849)] is not statistically significant [t (118) = 1.770, p=0.079].



Graph 1. Age (years) of mothers by type of pregnancy

2. Number of births (parity) according to the type of pregnant women

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



Graph 2. Correlation between parity and type of pregnancy

Table 1. Age (years) of mothers according to type of pregnancy

The pregnant group	N	Minimum	Maximum	Average value	Standard Deviation	p- value
Physiological pregnancy	60	17.00	42.00	29.95	6.10	>0.05
Preeclamptic pregnancy	60	18.00	38.00	28.13	5.10	

Table 2. 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%

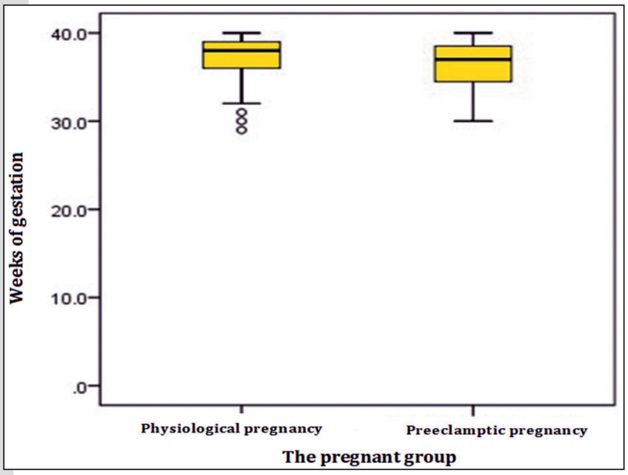
There is no statistically significant difference in parity frequency between physiological pregnancy and preeclamptic pregnancy. [χ^2 (3)=2,987, p=0,394].

3. Weeks of pregnancy of pregnant women according to the type of pregnancy

Pregnant women with preeclamptic pregnancy have lower median gestational values [Me=37.00 to 38.75)] compared to pregnant women with physiological pregnancy [Me = 38.00 (IQR = 36.00 to 39.00)].

There is a statistically significant difference.

There is no statistically significant difference in the median gestation between pregnant women with physiological and preeclamptic pregnancy [U=1455,500, z = -1.827, p = 0.068].



Graph 3. Gestational weeks according to the type of pregnancy

4. Body mass of the newborn according to the type of pregnant women

Pregnant women with preeclamptic pregnancy had newborns with a smaller body mass [Me=2220.00 g (IQR=2055.00 to 2350.00)] com-

Table 3. Weeks of gestation according to the type of pregnancy

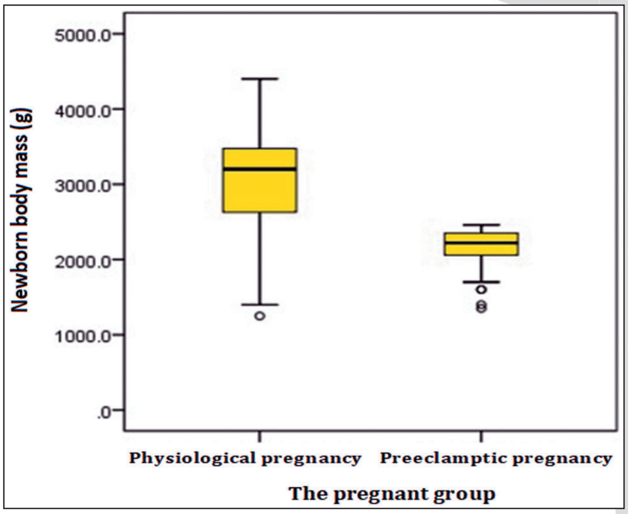
			The pregnant group	
			Physiological pregnancy	Preeclamptic pregnancy
Weeks of gestation	N		60	60
	Mean		37.03	36.32
	Std. Deviation		2.66	2.55
	Minimum		29.00	30.00
	Maximum		40.00	40.00
	Percentiles	25th	36.00	34.25
		50th (Median)	38.00	37.00
		75th	39.00	38.75
p- value			>0.05	

Table 4. Body mass (g) of the newborn according to the type of pregnancy

			The pregnant group	
			Physiological pregnancy	Preeclamptic pregnancy
Body mass of the newborn	N		60	60
	Mean		3010.00	2168.00
	Std. Deviation		670.81	261.49
	Minimum		1250.00	1350.00
	Maximum		4400.00	2460.00
	Percentiles	25th	2615.00	2055.00
		50th (Median)	3200.00	2220.00
		75th	3487.50	2350.00
p- value			<0.001	

pared to pregnant women with physiological pregnancy [Me=3200.00 g (IQR=2615.00 to 3487.50)].

There is a statistically significant difference in the median body mass among newborns in pregnant women with physiological and preeclamptic pregnancies [U=489,500, z=-6.883, p <0.001].



Graph 4. Body mass of the newborn (g) according to the type of pregnancy

5. Biparietal diameter (BPD) of fetuses in normal and preeclamptic pregnancy

IUGR fetuses have lower mean BPD values [Me=84.60 (IQR=80.00 to 86.40)] compared to fetuses with normal growth and development [Me=92.40 (IQR=82.33 to 93.50)].

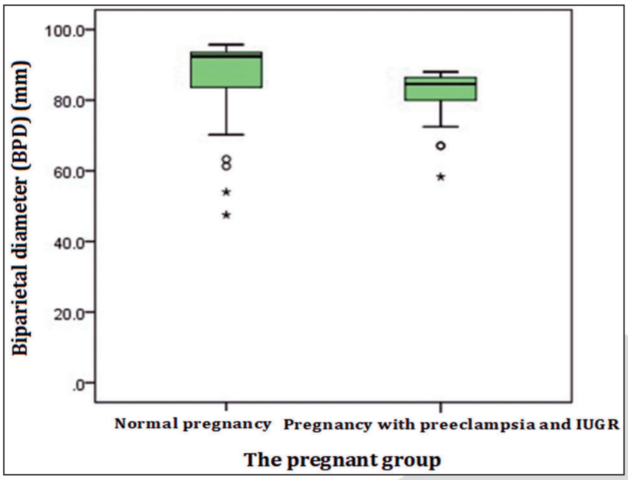
There is a statistically significant difference in the mean value of BPD between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=884.000, z=-4.817, p<0.001].

6. Correlation of gestational week and biparietal diameter (BPD) of fetus with normal growth and IUGR

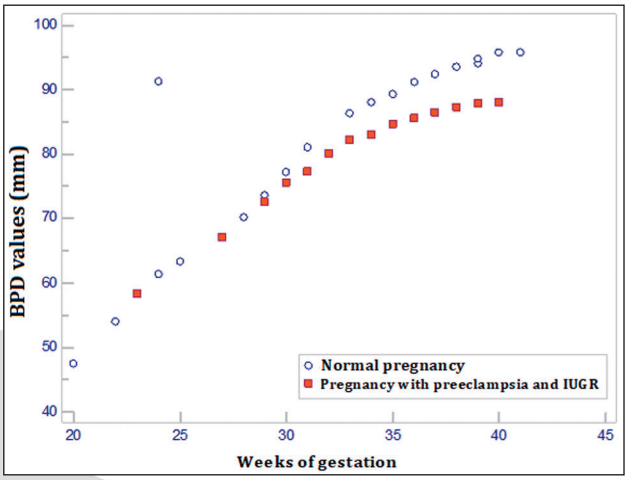
There is a statistically significant positive linear correlation between the values of gestational week and BPD in fetuses with normal development and growth (r_s=0.983; p<0.001).

Table 5. BPD values in normal and preeclamptic pregnancies with IUGR

			The pregnant group	
			Normal pregnancy	Pregnancy with preeclampsia and IUGR
Biparietal diameter (BPD) (mm)	N		60	60
	Mean		86.94	82.73
	Std. Deviation		11.24	6.03
	Minimum		47.50	58.30
	Maximum		95.70	88.00
	Percentiles	25th	82.33	80.00
		50th (Median)	92.40	84.60
		75th	93.50	86.40
p- value			<0.001	



Graph 5. BPD values in normal and preeclamptic pregnancies with IUGR.



Graph 6. Correlation between gestational weeks and fetal BPD.

There is a statistically significant positive linear correlation between gestational week and BPD values in fetuses with growth retardation (r_s=1.00; p<0.001).

7. Amniotic Fluid Index (AFI) in normal pregnancy and preeclamptic pregnancy

Growth retardation (IUGR) fetuses had lower median AFI values [Me=6.50 (IQR=4.50 to 11.00)]

Table 6. Correlation between gestational week and fetal BPD

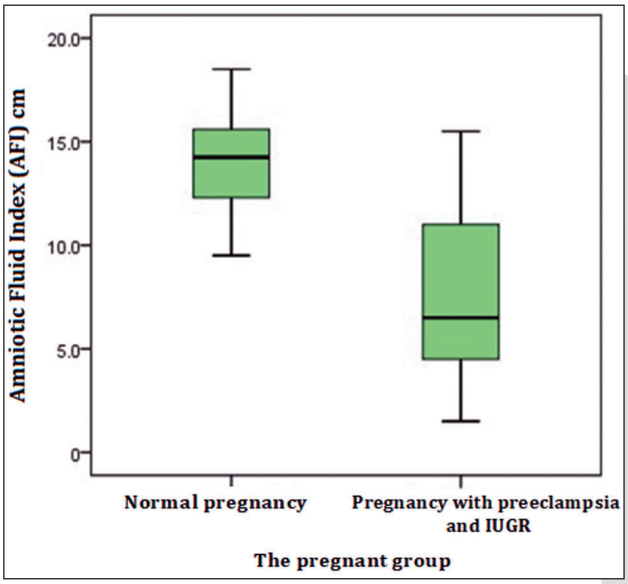
	The pregnant group			Weeks of gestation	BPD (mm)
Spearman's rho	Fetus with normal growth and development	Weeks of gestation	Correlation Coefficient	1.000	0.983**
			Sig. (2-tailed)	.	0.000
			N	60	60
		BPD (mm)	Correlation Coefficient	.983**	1.000
			Sig. (2-tailed)	0.000	.
			N	60	60
	Fetus with IUGR	Weeks of gestation	Correlation Coefficient	1.000	1.000**
			Sig. (2-tailed)	.	0.000
			N	60	60
		BPD (mm)	Correlation Coefficient	1.000**	1.000
			Sig. (2-tailed)	0.000	.
			N	60	60

Table 7. AFI values in normal and preeclamptic pregnancies with IUGR

Pregnancy with preeclampsia and IUGR			The pregnant group	
			Normal pregnancy	Pregnancy with preeclampsia and IUGR
Amniotic Fluid Index (AFI) cm	N		60	60
	Mean		14.3	7.56
	Std. Deviation		2.18	4.04
	Minimum		9.50	1.50
	Maximum		18.50	15.50
	Percentiles	25th	12.30	4.50
		50th (Median)	14.25	6.50
		75th	15.65	11.00
p- value			<0.001	

compared to fetuses with normal growth and development [Me=14.25 (IQR=12.30 to 15.65)].

There is a statistically significant difference in the AFI median values between fetuses with growth retardation (IUGR) and fetuses with normal growth and development [U=334.500, z=-7.696, p<0.001].

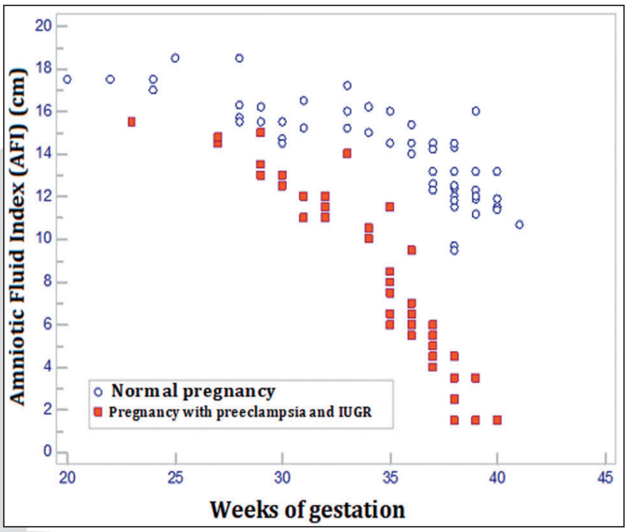


Graph 7. AFI values in normal and preeclamptic pregnancies with IUGR

8. Correlation of the week of pregnancy and the amniotic fluid index (AFI) of the fetus

There is a statistically significant negative linear correlation between the gestational week and AFI values in fetuses with normal development and growth (r_s=-0,853; p<0,001).

There is a statistically significant negative linear correlation between gestational week and AFI values in fetuses with growth retardation (r_s=-0,904; p<0,001).



Graph 8. Correlation of gestational week and AFI in the fetus

9. Lactate Dehydrogenase (LDH) in serum in physiological and preeclamptic pregnancy

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

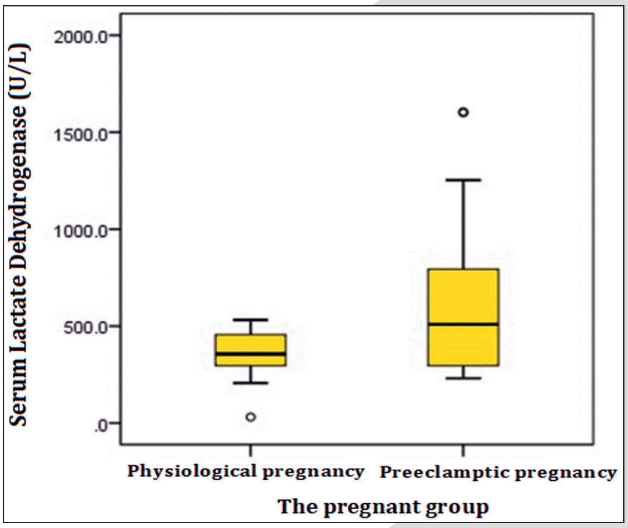
There is a statistically significant difference in the value of LDH in serum between pregnant women with physiological and preeclamptic pregnancy [U=1131,500, z = -3.509, p <0.001].

Table 8. Correlation of gestational week and AFI in the fetus

	The pregnant group			Weeks of gestation	AFI (cm)
Spearman's rho	Fetus with normal growth and development	Weeks of gestation	Correlation Coefficient	1.000	-0.853**
			Sig. (2-tailed)	.	0.000
			N	60	60
		Amniotic Fluid Index (AFI)	Correlation Coefficient	-0.853**	1.000
			Sig. (2-tailed)	0.000	.
			N	60	60
	Fetus with IUGR	Weeks of gestation	Correlation Coefficient	1.000	-0.904**
			Sig. (2-tailed)	.	0.000
			N	60	60
		Amniotic Fluid Index (AFI)	Correlation Coefficient	-0.904**	1.000
			Sig. (2-tailed)	0.000	.
			N	60	60

Table 9. Serum lactate dehydrogenase values (U/L) according to pregnancy type.

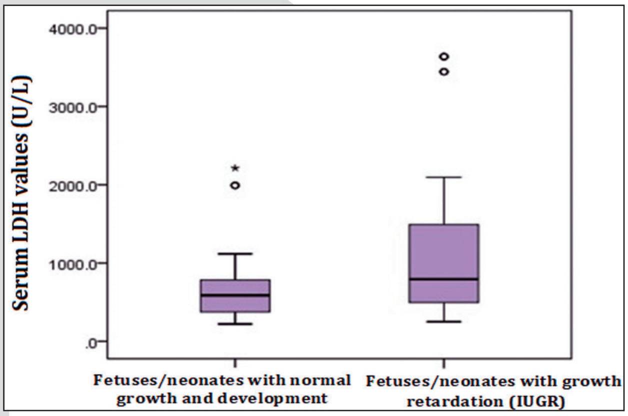
The pregnant group			The pregnant group	
			Physiological pregnancy	Preeclamptic pregnancy
Lactate dehydrogenase (U/L)	N		60	60
	Mean		364.72	590.92
	Std. Deviation		104.80	345.65
	Minimum		31.00	231.00
	Maximum		532.00	1605.00
	Percentiles	25th	296.50	297.00
		50th (Median)	356.50	509.50
		75th	456.00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



Graph 9. Serum lactate dehydrogenase (U/L) values according to pregnancy type.

10. Lactate Dehydrogenase (LDH) in fetal/ newborn serum

Fetuses/neonates with growth retardation (IUGR) have higher serum LDH values [Me=795.00 U/L (IQR=491.00 to 1490.00)] compared to fetuses/neonates with normal growth and development [Me= 587.00U/L (IQR=376.00 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].



Graph 10. Serum LDH values in fetuses/neonates with growth retardation (IUGR) and fetuses with normal growth and development.

Table 10. Serum LDH values in fetuses/newborns with growth retardation (IUGR) and fetuses/newborns with normal growth and development

			Group of fetuses/neonates	
			Fetuses/neonates 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 11. Correlation of LDH values in maternal and fetal/newborn serum

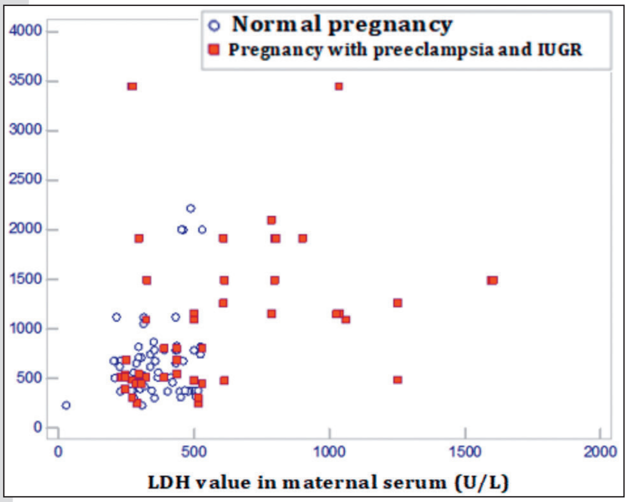
	The pregnant group			LDH (U/L) in mother	LDH (U/L) in the fetus/neonate
Spearman's rho	Normal pregnancy	Lactate dehydrogenase (U/L) in maternal serum	Correlation Coefficient	1.000	0.140
			Sig. (2-tailed)	.	0.285
			N	60	60
		Lactate dehydrogenase (U/L) in fetal serum	Correlation Coefficient	0.140	1.000
			Sig. (2-tailed)	0.285	.
			N	60	60
	Pregnancy with preec-lampsia	Lactate dehydrogenase (U/L) in maternal serum	Correlation Coefficient	1.000	0.434**
			Sig. (2-tailed)	.	0.001
			N	60	60
		Lactate dehydrogenase (U/L) in fetal serum	Correlation Coefficient	0.434**	1.000
			Sig. (2-tailed)	0.001	.
			N	60	60

11. Correlation of biochemical parameters in maternal and fetal serum

11.1. Correlation of LDH values in maternal and fetal serum

There is no statistically significant linear correlation between maternal and fetal/newborn serum LDH values in normal pregnancy (r_s=0.140; p>0.05).

There is a statistically significant positive linear correlation between maternal and fetal/newborn serum LDH values in preeclamptic pregnancy (r_s=0.434; p<0.01).



Graph 11. Correlation of maternal and fetal/newborn serum LDH values

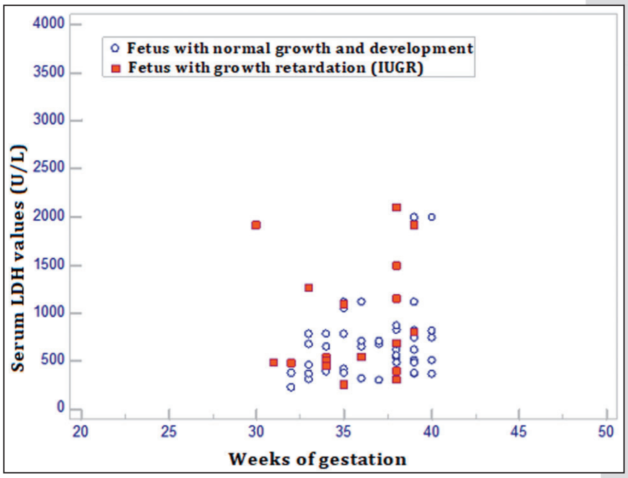
Table 12. Correlation of gestational week and LDH values in fetal/newborn serum

	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

12. Correlation between weeks of pregnancy and LDH values in fetal serum

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 between gestational week and serum LDH values in fetuses/neonates with intrauterine growth retardation (r_s=0.274; p<0.05).



Graph 12. Correlation of gestational week and fetal/newborn serum LDH values.

5. Discussion

The mechanism of increased lactate dehydrogenase in pregnancy with preeclampsia is explained by the fact of 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, in this way the ratio of prostacyclin and thromboxane is disturbed. Due to these changes, vasoconstriction and tissue hypoxia appear in the liver of pregnant women with preeclampsia. 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 (26, 27, 28). The increase in the concentration of lactate dehydrogenase, aminotransferases and some other liver metabolites can be important markers that predict 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.

With the analysis of the Mann Whitney - U test, we found that there is a statistically significant difference in the AST values in serum between pregnant women with physiological and preeclamptic pregnancy [U=521.500, z=6.717, p<0.001]. Preeclamptic pregnancies had higher serum AST values [Me=27.00 U/L (IQR=22.00 to 34.00)] compared to physiological pregnancies [Me=14.00 U/L (IQR=11.00 to 19.00)].

The study (51) found that in preeclampsia there is an increased level of lactate dehydrogenase and aspartate aminotransferase.

Analysis using the Mann Whitney - U test has found that there is a statistically significant difference in serum LDH values between physiological pregnancies and preeclamptic pregnancies [U=1131.500, z=3.509, p<0.001]. Preeclamptic pregnancies had higher serum LDH values [Me=509.50 U/L (IQR=297.00 to 796.25)] compared to physiological pregnancies [Me=356.50 U/L (IQR=296.50 to 456.00)].

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 (10) which cause degenerative changes in hepatocytes with an increase in the level of lactate dehydrogenase.

Analysis by means of the Mann Whitney - U test has found that there is a statistically significant difference in serum LDH values between fetuses with stunted growth and fetuses with normal development and growth [U=1203.000, z=-3.135, p=0.002]. Growth retardation (IUGR) fetuses have higher serum LDH values [Me=795.00 U/L (IQR=491.00 to 1490.00)] compared to fetuses with normal growth and development [Me=587.00U/L (IQR =376.00 to 783.00)].

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. 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.

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 serum of the fetus/newborn with normal growth and development (r_s=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 enzyme activity in the fetus with growth retardation is explained in this way: in the fetus with growth retardation (IUGR), the increase in the level of lactate dehydrogenase enzyme activity follows and is caused by hypoxia in the liver cells, 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. It is known that the level of lactate dehydrogenase increases in the liver due to hypoxia, which occurs in fetuses with IUGR growth retardation. The cause of the appearance of preeclampsia is the disorder of the development of the placenta, which occurs due to the lack of trophoblast invasion in the walls of the spiral arteries of the placenta. Due to the lack of extravillous trophoblast invasion into the spiral arteries of the placenta, placental ischemia follows. Due to arterioplacental insufficiency, hypoxia and fetal growth retardation develop.

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