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Elevated Liver Enzymes in Cases of Preeclampsia and Intrauterine Growth Restriction

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ABSTRACT

Aim: The aim of this study was to evaluate biochemical parameters in serum of women with preeclampsia and IUGR. **Material and methods:** A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women *(n=60)* and IUGR group included pregnant women with preeclampsia and IUGR (n=60). Outcome measures were following values of biochemical parameters in serum of mother and fetuses: aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), bilirubin (indirect and direct) and cholesterol. A blood for analysis was drawn from the cubital vein of mothers and the umbilical vein of the fetuses during delivery period. **Results:** The mean of maternal age was 30.0±6.1 years in women with preeclampsia and IUGR and 28.1±5.1 years in healthy pregnant women, $p > 0.05$. The most of women with preeclampsia and IUGR had grade III of placental maturation (48.3%). There is a significant association between the placental maturation and the diagnosis, $p < 0.001$. There was a statistically significant difference in body mass of newborns between IUGR and non IUGR groups, $p < 0.001$. There was a significant statistically difference in serum value of AST, ALT, LDH and total cholesterol between women with preeclampsia and IUGR and healthy pregnant women *(all $p < 0.001$)*. **Conclusion:** Measurement of AST, ALT, LDH, and total cholesterol in serum of pregnant women and newborns with IUGR allows the differentiation and threatening risk of perinatal complications due to hypoxia.

Key words: Preeclampsia, intrauterine growth restriction, liver of fetus, biochemical parameters

1. INTRODUCTION

Preeclampsia affects 3-5% of pregnancies and is traditionally diagnosed by the combined presentation of high blood pressure and proteinuria. New definitions also include maternal organ dysfunction, such as renal insufficiency, liver involvement, neurological or hematological complications, uteroplacental dysfunction, or Intrauterine Growth Restriction (IUGR) (1, 2). IUGR is the term used to describe a fetus that has not reached its growth potential because of fetal, placental, or maternal factors. It is defined as an estimated fetal weight <10th percentile. Clinically, most infants with IUGR are identified because they are born small for gestational age (SGA) which is defined as a weight less than a specified percentile (usually the 10th percentile) (3). The risk of mortality and morbidity is increased in infants with IUGR because of the compromised growth and reduced energy reserves that increase the vulnerability of these infants during the stressful perinatal period with the transition from intrauterine to extrauterine life. Identification of IUGR infants is important because these infants are at increased risk of perinatal morbidity and mortality and affects approximately 7–15% of worldwide pregnancies (3, 4). Defining the population of growth restricted fetuses at high risk of adverse out-

come, accurately identifying these fetuses in utero, and determining interventions to improve outcome remains a challenge. Clinical assessment is a reasonable screening tool for IUGR in low risk pregnancies, as there is no high quality evidence that alternative approaches, such as routine ultrasound examination, improve outcome over clinical assessment alone (5, 6). Clinical assessment is based on assessment of past and present risk factors, physical examination, and ultrasound studies. The aim of this study was to evaluate biochemical parameters of liver of women with preeclampsia and IUGR and fetuses with IUGR.

2. MATERIALS AND METHODS

A clinical prospective study was conducted and included 120 pregnant women divided in two groups: non IUGR group included healthy pregnant women (n=60) and IUGR group included pregnant women with preeclampsia and IUGR (n=60). Preeclampsia was determined with method of Last Menstrual Period (LMP), Hadlock's formula on the basis of presence of proteinuria (> 0.5 g/L) and high blood pressure (TA = 140/90 mmHg) (7). Antenatal diagnosis of IUGR was based on sonographic evaluation of the fetus, placenta, and amniotic fluid. Sonography was carried out by probe 3.5 Mhz type MINDRAY DC 7. Outcome measures were following values of biochemical parameters in serum of mother and fetuses: aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), bilirubin (indirect and direct) and cholesterol. A blood for analysis was drawn from the cubital vein of mothers and the umbilical vein of the fetuses during delivery period. Results are expressed as mean value and standard deviation in case of normal distributed continue variables, as median and interquartile range (IQR) in case of non-normal distributed continue variables. The inspection of histograms and quantile diagrams and the Kolmogorov–Smirnov test with a Lilliefors significance level were used for testing normality of distribution of continuous numerical variables. In case of categorical variables, counts and percentages were reported. Categorical data were analyzed with Pearson's Chi-Square test or Fisher's Exact test. Statistical analysis comparing the two groups was performed with Independent Sample T-test for continuous normal distributed variables and Mann-Whitney U-test for continuous non-normal distributed variables. Pearson's and Spearman's correlation coefficient was used to describe the strength and direction of the linear relationship between variables. A p-value <0.05 was considered as significant. Statistical analy-

Variables	IUGR (n=60)	non IUGR (n=60)	p-value
Age (yrs)	30.0±6.1	28.1±5.1	0.079
Week of gestation	37 (32 to 38)	38 (36 to 39)	0.068
Stage of placental maturation (%)			
0	3.3	13.3	<0.001
I	16.7	38.3	
II	31.7	38.3	
III	48.3	10.1	
Number of abortion (%)			
0	80.0	75.0	0.633
1	13.3	13.3	
≥2	6.7	11.7	
Number of deliveries (%)			
0	3.3	0.0	0.394
1	43.3	41.7	
2	20.0	28.3	
≥3	33.3	30.0	

Table 1. Characteristics of pregnant woman in both groups

Variables	IUGR (n=60)	non IUGR (n=60)	p-value
Pregnant women			
AST (U/L)	27.0 (22.0 to 34.0)	14.0 (11.0 to 19.0)	<0.001
ALT (U/L)	20.5 (15.0 to 25.8)	11.5 (10.0 to 13.0)	<0.001
LDH (U/L)	509.5 (297.0 to 796.3)	356.5 (296.5 to 456.0)	<0.001
Indirect bilirubin (mmol/L)	14.4 (12.8 to 15.4)	12.6 (10.5 to 15.0)	0.052
Direct bilirubin (mmol/L)	0.0 (0.0 to 3.3)	0.0 (0.0 to 4.4)	0.115
Total cholesterol (U/L)	6.4 (5.7 to 7.4)	5.5 (4.7 to 6.3)	<0.001
Fetuses			
AST (U/L)	24.0 (21.0 to 31.0)	22.5 (12.3 to 30.1)	0.014
ALT (U/L)	14.0 (12.0 to 18.0)	10.0 (9.0 to 13.0)	<0.001
LDH (U/L)	795.0 (491.0 to 1 490.0)	587.0 (376.0 to 783.0)	0.002
Indirect bilirubin (mmol/L)	32.4 (26.4 to 39.0)	27.0 (22.6 to 32.6)	0.054
Direct bilirubin (mmol/L)	16.6 (6.8 to 23.1)	10.4 (6.9 to 13.3)	0.042
Total cholesterol (U/L)	1.6 (1.2 to 1.8)	1.2 (0.7 to 1.5)	<0.001

Table 2. Laboratory findings in mother and fetuses with/without IUGR. Note: Continuous variables are expressed as median with interquartile range (IQR, 25th to 75th percentiles), statistics by Mann-Whitney. Definition of abbreviations, IUGR = Intrauterine growth restriction; AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; LDH = Lactate dehydrogenase

sis was performed by using the Statistical Package for the Social Sciences (SPSS Release 19.0; SPSS Inc., Chicago, Illinois,United States of America) software.

3. RESULTS

The mean of maternal age was 30.0±6.1 years in women with preeclampsia and IUGR and 28.1±5.1 years in healthy pregnant women. There is no statistically significant difference in maternal age distribution between two groups ($p > 0.05$). The most of women with preeclampsia and IUGR had grade III of placental maturation (48.3%). There is a significant association between the placental maturation and the diagnosis [$\chi2(3)=24.216$; $p<0.001$]. There is no a significant difference in frequency of previous abortion ($\chi2(2)=0.915$, $p=0.633$) and deliveries ($\chi2(3) = 2.987$, $p=0.394$) between these two groups (Table 1).

There was a significant statistically difference in serum value of AST (U = 521.500, z = -6.717, p < 0.001), ALT (U = 554.000, z =-6.560, p< 0.001), LDH (U =1 131.500, z = -3.509, p<0.001) and total cholesterol (U=1 065.000, z =-3.856, p< 0.001) between women with preeclampsia and IUGR and healthy pregnant women.

There was a significant statistically difference in serum value of AST (U=1 333.000, z =-2.454, p<0.05), ALT (U =908.000, z=-4.698, p<0.001), LDH (U=1 203.000, z =-3.135, p< 0.01), direct bilirubin (U=1 412.500, z = -2.037, p< 0.05) and total cholesterol (U=939.500, z = -4.526, p<0.001) between fetuses with IUGR and non IUGR (Table 2).

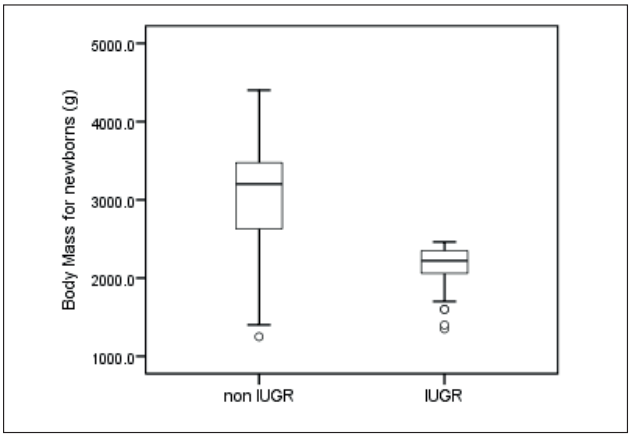

Figure 1. Body mass for newborns in women with preeclampsia and IUZR and women with physiological pregnancy

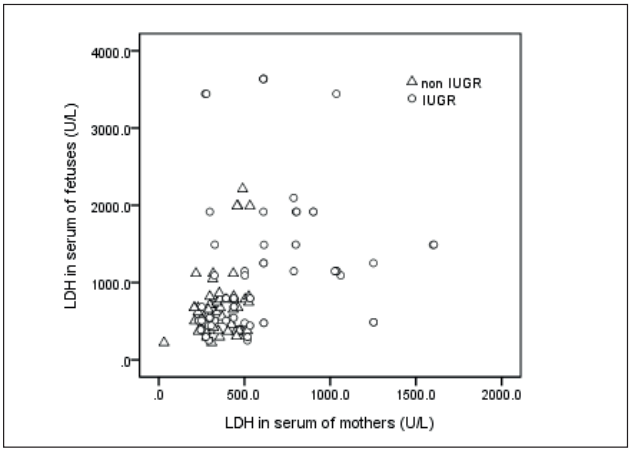

Figure 2. Correlation between values of LDH in serum of fetuses and mothers for IUGR and non IUGR group

Median of body mass of newborns in IUGR group was 2 220 g (IQR = 2 055 to 2 350) and 3 200 g (IQR = 2 615 to 3 487.5) in non IUGR group. There was a statistically significant difference, U=1 065.500, z =-3.856, p< 0.001.

There was a positive correlation in values of lactate dehydrogenase between serum of mother and fetuses in IUGR group, rs=0 .434, p< 0.01.

4. DISCUSSION

In this prospective study, we evaluated biochemical parameters in serum of women with preeclampsia and IUGR. In our study, women with preeclampsia have statistically significant higher values of AST, ALT, LDH and total cholesterol compared with healthy pregnant women. There are evidences that the lactate dehydrogenase and aminotransferase are increased in preeclampsia (8, 9, 10, 11). Elevated serum level of AST in preeclampsia is explained by the effect of hypoxia on the liver in preeclamptic pregnancy. Disruption of endothelium leads to a reduction of prostacyclin level and increase of thromboxane level. The ratio PgI2/TxA2 is increased in favor of thromboxane, which causes vasoconstriction of blood vessels of the liver. Due to the effects of hypoxia in the liver will cause necrosis and degeneration of hepatocytes and thus would increase AST levels. In preeclampsia there is releasing of different mediators from liver and blood vessel endothelium (fibronectin, thrombomodulin, endothelin-l, thromboxane), which causes vasoconstriction and liver hypoxia. Hypoxia increases the level of ALT, respectively (12). In meta-analysis of Cassandra N et al., 64 original article were included and examined the association between total cholesterol levels during pregnancy and preeclampsia. This meta-analysis showed that maternal serum total cholesterol, non-HDL-C, and triglyceride levels during pregnancy are elevated during the first/second and third trimesters in women who subsequently develop preeclampsia compared with women who remain normotensive during pregnancy (13). In our study, newborns in IUGR group had lower body mass (2 220 g) compared with newborns in non IUGR group (3 200 g), p<0.001. There is negative linear correlation between level of LDH in serum of mother and body mass of newborns, rs =- 0.231, p = 0.011. In the study of Jaiswar SP et al., the mean gestational age at the time of delivery was significantly less in patients with increasing LDH levels (p=0.025) This indicates increase in preterm deliveries in patients with higher LDH levels (11). In the study of Shu HE et al., preeclamptic women with small-for-gestational-age (SGA) infants had significantly higher LDH concentrations than those in the appropriate-for-gestational-age (AGA) group (14). In fetuses with IUGR there is increased levels of the value of lactate dehydrogenase in serum due to the effects of hypoxia in a cell of the liver, skeletal muscles and kidneys. A hypoxia disrupts the cells membrane which lead to that LDH molecules pass from tissue into plasma. The LDH-A gene in the endothelial cells of the placenta within the fetal microvascu-

lature is increased in pre-eclampsia, probably as a result of hypoxia (15).

5. CONCLUSION

Measurement of aminotransferases, lactate dehydrogenase and cholesterol levels in serum of pregnant women and newborns with IUGR allows the differentiation and threatening risk of perinatal complications due to hypoxia.

- **Author's contribution:** All authors contributed in all phases of preparing this article. Final proof reading was made by first author.
- **Conflict of interest: none declared.**

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