Blood urea nitrogen/creatinine index is a predictor of prerenal damage in preeclampsia

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Abstract

Introduction: Preeclampsia is a disease whose etiology is not very clearly explained. The aim of this study was to investigate the importance of blood urea nitrogen (BUN)/creatinine ratio in diagnosing preeclampsia and evaluating prognosis.

Methods: The patients in this research were examined and diagnosed in the Department of Obstetrics and Gynecology, University Clinical Centre of Kosovo. Control group included 25 pregnant women with a normal blood pressure and with a gestational age of more than 20 weeks, whereas the investigation group included 25 women diagnosed with preeclampsia. The patients were not administered therapy four days before the examination. For the determination of biochemical parameters we used end point bichromatic enzymatic rate and enzymatic conductivity rate.

Results: BUN/Creatinine index in the preeclamptic group was 19±7.7, uric acid 280±70 µmol/L, lactate dehydrogenase 198±63 U/L, while the number of platelets was 195±5061 x 10^9/L. In control group BUN/Creatinine index was 12±3, lactate dehydrogenase was 165±57 U/L, uric acid 197±79 µmol/La and the platelet number was 243±61 x10^9/L. Albumin/Globulin index in the preeclamptic group was 0.8±0.12, whereas in the control group it was 0.9±0.16.

Conclusions: BUN/Creatinine ratio in pregnant women with preeclampsia was significantly increased (t=-4.14; p=0.00013) in comparison to the control group. It indicates the prerenal source of azotemia. This index can be important for the evaluation of preeclampsia severity.

Keywords: preeclampsia, BUN/Creatinine ratio, Albumin/Globulin ratio.

Introduction

Preeclampsia is a specific state of pregnant women which involves an increase of arterial blood pressure, accompanied by proteinuria, oedema or both. Eclampsia, on the other hand, is defined as a state with convulsion, coma or both in patients with preeclampsia signs (1-6). The incidence of preeclampsia is 5-7% in all pregnancies (1-6). One of the causes of preeclampsia can be considered the disbalance between prostacyclin (prostaglandin I2) and thromboxane A2, an active metabolite of arachidonic acid (1,5,6). This disbalance causes vasospasm, a central change in preeclampsia (1). Presence of brain edema at MR imaging in

patients who were presented with preeclampsia-eclampsia and neurologic symptoms is associated with abnormal red blood cell morphology and elevated LDH levels. These findings indicate microangiopathic hemolysis, which suggests endothelial damage, after 20th week of pregnancy (7). A number of biochemical and haematological parameters change in preeclampsia in comparison to the normal pregnancy (3,8-10). Therefore, laboratory evaluation of women who develop hypertension after midpregnancy is conducted and it usually includes: haemoglobin and haematocrit determination, blood smear, platelet count, urinalysis as well as the determination of serum oxaloacetic transaminase, lactic acid dehydrogenase, serum albumin, uric acid and creatinine (7, 9-13). The literature suggests that no single marker is currently adequate to predict the development of preeclampsia and that a combination of indices would be most effective (14-16). Increased plasma

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urea with normal creatinine concentrations giving rise to high ratios may be seen with any of the prerenal states (17). However, blood urea nitrogen/creatinine has been used as a crude discriminator between prerenal and postrenal azotemia (17-18). The purpose of this research was to investigate that BUN/Creatinine index is a preeclampsia predictor together with the other diagnostic parameters which would help diagnosing, treatment and prognostic evaluation of preeclamptic women.

Methods

Study Subjects
We have studied 25 pregnant women of the preeclamptic group and 25 patients of control group. Control group has resulted with no symptoms related to preeclampsia while in the preeclamptic group there were pregnant women with preeclampsia signs, hypertension, oedema and proteinuria. The patients were selected in the Obstetrical and Gynaecological Clinics of University Clinical Centre of Kosovo, whereas the sample analysis took place in the Department of Biochemistry of the Faculty of Medicine, University of Prishtina, during 2011. The women of the preeclamptic group were in the gestational age of 20 weeks, with an arterial pressure of over 140 mm Hg for the systolic and over 90 mm Hg for the diastolic. Hypertension appeared during pregnancy. Proteins in urine were over 0.5 g/L. All the patients had oedema of lower extremities while 80% had oedema of upper extremities and face as well. On the other hand, control group included pregnant women with a gestational age of over 20 weeks, normal arterial pressure (<135 /85 mmHg) and a lack of symptoms as those described in the preeclamptic group.

Detailed analysis
The blood was taken from patients with vacutainer tubes (SARSTEDT) containing the anticoagulant lithium heparin and in tubes without anticoagulants. Platelets were determined in the automatic reader (Medonic 630, Sweden). Biochemical parameters were determined in the biochemical analyzer Synchron CX7 of Beckman Coulter Company, USA. The used reagents were of Beckman Instrumental, Inc. Galway. Ireland. Urea nitrogen concentration was determined by

an enzymatic conductivity rate method; creatinine by means of the Jaffe rate method; Lactate dehydrogenase activity was measured by the enzymatic rate method. Uric acid concentration was measured by a timed-endpoint method with the enzyme uricase. Proteins in serum were measured by a timed-endpoint biuret method and albumins were determined with brome cresol purple (BCP), a timed endpoint method as well (26). We have determined proteins in urine with the end point method with pyrogallol red, a reagent of Cromatest- Linear Chemicals Company, Spain.

Statistical analysis
The statistics were made with the Vassar-Stats system. T-test was conducted and the average, correlation (r) and standard deviation were counted. These are shown in the tabular presentation. With the t-test we have compared control and preeclamptic group by including the pregnancy age, gestation age, systolic and diastolic arterial pressure as well as biochemical parameters such as urea, creatinine, proteins, albumins, LDH, uric acid, Bun/Creatinine index, A/G index and platelets. The average and standard deviations were calculated for all the parameters and indexes. The correlation between Bun/Creatinine and Albumin/Globulin, Bun/Creatinine and Uric acid, Bun/Creatinine and LDH was calculated in control group. The same correlations were calculated for the pathologic group. The differences in which the *p* value was less than 0.05 ($p <0.05$) were considered statistically significant.

Results

The patients of control group (n=25) were 28±6 years old, while the preeclamptic group (n=25) 30±6. The age of pregnancy for both groups was > 20 weeks with an average of 33 weeks gestation. The preeclamptic group's diastolic arterial blood pressure was (DATP) 115±14 mmHg, while that of control group was 75±5 mm Hg. Systolic arterial blood pressure was 115±5 mm Hg for the control group, while for the group with preeclampsia 175±13 mm Hg. Parameters like urea, creatinine, protein, albumin, uric acid, LDH (lactate dehydrogenase), the number of platelets, blood urea nitrogen/creatinine index and albumin/globulin index, have been presented in Table 1. In table 3 we have presented the difference between Blood urea ni-

TABLE 1. Some characteristics and parameters in the control and preeclamptic group

	CG	PG	T	p
N		25		
Year	28±6	30±6	-0.72	0.47
Gestational age, wk	33±4	33±4	0.09	0.928
SATP (mmHG)	115±5	175±13	-20.77	< 0.0001
DATP (mmHg)	75±5	115±14	-13.49	< 0.0001
Urea (mmol/L)	2.46±0.8	4.6±1.7	-4.92	<0.0001
Creatinine (µmol/L)	53±10	64±22	-1.62	0.11
Total protein (g/L)	65±4.6	59.4±5.8	1.69	0.09
Albumin (g/L)	31.3±2.8	27±3,6	2.2	0.03
URIC (µmo/L)	197±79	280±70	-3.39	0.0013
LDH (U/L)	165±57	198±63	-1.73	0.093
Blood urea nitrogen/creatinine index	12±3	19±7.7	-3.92	0.00027
A/G	0.9±0.16	0.8±0.12	1.28	0.2
Protein (in urine)	0.13±0.1	1.41±0.9	-6.81	<0.0001
Platelet x10⁹/L	243±61	195±50	+2.06	<0.045

trogen/Creatinine ratio in the group with a normal blood pressure and the preeclampsia group, as well as the A/G ratio between the two groups with t-test.

Discussion

Creatinine, urea and uric acid are non-protein nitrogenous metabolites that are cleared from the body by the kidney following glomerular filtration. Measurements of plasma or serum concentration of these metabolites are commonly used as indicators of kidney function and other conditions (14,17). Therefore, their determination in serum during pregnancy is of a major importance to diagnose kidney function especially at women with preeclampsia signs. This would be used to evaluate kidney function as well as the possibility of a secondary source of urea or of the nitrogen part of urea increase (Blood urea nitrogen) in plasma. The significant difference between arterial systolic and diastolic blood pressure between control group and the pregnant women with preeclampsia signs is clearly shown (t=-20 and for diastolic t= -13 , Table 2). The difference occurs in BUN/Creatinine ratio,

TABLE 2. The correlation between Blood urea nitrogen/Creatinine ratio and parameters such as uric acid, LDH and A/G ratio in both groups has been summarized.

Ratio	Number	r	p
Bun/Creatinine -Albumin/Globulin(CG)	13	0.035	0.87
Bun/Creatinine-Albumin/Globulin(PG)	22	0.420	0.04
Bun/Creatinine-uric(CG)	12	-0.162	0.59
Bun/Creatinine -uric(PG)	21	0.294	0.18
Bun/Creatinine -LDH(CG)	12	-0.021	0.95
B/C-LDH(PG)	21	-0.042	0.86

which is characterized with an increase of this ratio in the pathologic group (BUN/Creatine ratio =19±8) in comparison to control group BUN/Creatinine=12±3 (t=-3.92; p=0.00027, Table 2). This can be explained with the occurrence of microangiopathic haemolysis, which is related to the injury of endothelium in the group with preeclampsia changes (Fig. 1, 1,4,8,20-24,27- 28). As a consequence, urea synthesis in liver would be increased as well as the incapability of kidneys to excrete urea from blood with such a high concentration. This way we would have a more complete data. There is no significant difference between the A/G ratio of control group and the preeclamptic one, although a tendency for a decrease is seen in the group with preeclampsia (Table 3). The difference between albumins of CG and those of PG is statistically significant (p=0.03).This is because the protein removal in urine, in the group of preeclamptic women, is increased with an average amount of 1.41±0.9 g/L (Table 1) which brings to the decrease of albumins in serum with an average value of 27±3.6 g/L (25). The level of urea in serum at the patients of preeclamptic group is significant-

TABLE 3. T-test Blood urea nitrogen/Creatinine and A/G index between control and preeclamptic group

	Blood urea nitrogen/Creatinine-CG	Blood urea nitrogen/Creatinine -PG	A/G-CG	A/G-PG
N		25		25
Mean	12±3	19±7.7	0.9±0.16	0.8±0.12
T		-3.92		1.28
P		0.00027		0.2

*Mean of two measurements of calibrators as sample.

ly increased p<0,0001, in comparison to control group(Table 1). The comparison between creatinine in the serum of control group and of pregnant women with preeclampsia is also shown there and in this case an evident increase of creatinine at the preeclamptic group is obvious(p=0,11). The difference between the increase of blood urea nitrogen and creatinine in blood, shows a secondary source of urea related to the increase of its synthesis. As a consequence of the increase of BUN and the decrease of albumins, there exists a regressive correlation between BUN/Creatinine and A/G index at the preecplamptic group (Table 2). Also, in the preeclamptic group there was a significant decrease of platelets (Table 1) as a result of the increased rate of coagulability in this group (8,21-22, 25).

Conclusion

In this research, blood urea nitrogen/creatinine index was significantly increased in pregnant women with preeclampsia in comparison to the group of pregnant women with normal blood pressure. It indicates the prerenal source of urea. This index can be important to estimate the severity of preeclampsia.

Acknowledgments

Competing interests

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