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Biochemical parameters of the retroplacental blood in preeclampsia

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ABSTRACT

BACKGROUND: The efficiency of existing methods of predicting preeclampsia is far from 100%, which dictates the need to search for new additional markers. Retroplacental blood is a unique and practically unstudied biological substrate, and its composition probably influences the course of pregnancy. This study aimed to investigate the biochemical parameters of retroplacental blood in preeclampsia.

MATERIALS AND METHODS: The study included 53 pregnant women who were divided into two groups: the first group had normal pregnancy (n=28), and the second group had severe preeclampsia (n=25). All pregnant women underwent cesarean section at delivery. Peripheral and retroplacental blood sera were examined. Sampling was performed immediately after mechanical separation of the placenta and separation of the afterbirth. Levels of alanine transaminase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), total protein, albumin, urea, creatinine, total and direct bilirubin, glucose, and uric acid were determined on a Beckman Coulter AU480 biochemical analyzer (Germany).

RESULTS: The biochemical composition of retroplacental and peripheral blood showed significant differences (p <0.05). In physiologic pregnancy, the levels of ALT, AST, LDH, urea, creatinine, direct bilirubin, and uric acid were significantly (p <0.05) higher by 1.9, 20.1, 11.4, 1.14, 1.19, 2.0, and 1.15 times, respectively, whereas glucose levels were 1.5 times lower in the retroplacental blood. In patients with severe preeclampsia, the levels of AST, LDH, creatinine, total and direct bilirubin, and uric acid were significantly (p <0.05) increased in retroplacental blood by 11.7, 11.5, 1.3, 1.2, 2.2, and 1.11 times, respectively, and glucose levels decreased 1.57 times. When comparing the biochemical composition of the peripheral blood of the first and second groups, reliable differences (p <0.05) were noted only in ALT, AST, total protein, albumin, urea, and creatinine. However, in the retroplacental blood under physiologic pregnancy and preeclampsia, significant differences (p <0.05) were found only for urea, creatinine, and uric acid levels.

CONCLUSION: The study of the biochemical composition of the retroplacental blood can provide a more complete picture of the pathogenesis of preeclampsia.

Keywords: retroplacental blood; physiologic pregnancy; preeclampsia; mother-placenta-fetus system; blood biochemical analysis.

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Биохимические показатели ретроплацентарной крови при преэклампсии

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АННОТАЦИЯ

Введение. Эффективность существующих методов прогнозирования преэклампсии далека от 100%, что диктует необходимость поиска новых дополнительных маркеров. Ретроплацентарная кровь — уникальный и практически неизученный биологический субстрат, состав которого, возможно, оказывает влияние на течение беременности.

Цель. Изучение биохимических показателей ретроплацентарной крови при преэклампсии.

Материалы и методы. В исследование включены 53 беременные, которых разделили на две группы: первая группа — с физиологической беременностью (n=28) и вторая группа — с тяжёлой преэклампсией (n=25). У всех беременных при родоразрешении использовали операцию кесарева сечения. Материалами исследования были сыворотки периферической и ретроплацентарной крови. Взятие проб производили сразу после механического отделения плаценты и выделения последа. На биохимическом анализаторе Beckman Coulter AU480 (Германия) определяли уровни показателей АЛТ, АСТ, ЛДГ, общего белка, альбумина, мочевины, креатинина, общего и прямого билирубина, глюкозы, мочевой кислоты.

Результаты. По результатам исследования биохимический состав ретроплацентарной и периферической крови имел значимые отличия (p <0,05). При физиологической беременности уровни АЛТ, АСТ, ЛДГ, мочевины, креатинина, прямого билирубина и мочевой кислоты были достоверно (p <0,05) выше в ретроплацентарной крови: в 1,9; 20,1; 11,4; 1,14; 1,19; 2; 1,15 раза соответственно, а уровень глюкозы, наоборот, ниже в 1,5 раза. У пациенток с тяжёлой преэклампсией в ретроплацентарной крови были значимо (p <0,05) повышены уровни АСТ, ЛДГ, креатинина, общего и прямого билирубина и мочевой кислоты: в 11,7; 11,5; 1,3; 1,2; 2,2; 1,11 раза соответственно, а уровень глюкозы понижен в 1,57 раза. При сравнении биохимического состава периферической крови пациенток первой и второй группы достоверные отличия (p <0,05) касались только АЛТ, АСТ, общего белка, альбумина, мочевины и креатинина. Вместе с тем в ретроплацентарной крови при физиологической беременности и преэклампсии достоверные отличия (p <0,05) выявлены только по мочевине, креатинину и мочевой кислоте.

Заключение. Таким образом, изучение биохимического состава ретроплацентарной крови может дать более полное представление о патогенезе преэклампсии.

Ключевые слова: ретроплацентарная кровь; физиологическая беременность; преэклампсия; система мать-плацента-плод; биохимический анализ крови.

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子痫前期胎盘后血液的生化指标

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摘要

论证。现有方法对子痫前期的预测效果远未达到百分之百，因此有必要寻找新的额外标记物。胎盘后血液是一种独特的生物基质，其成分可能会影响妊娠过程，但实际上尚未对其进行研究。

我们的研究旨在研究子痫前期胎盘后血液的生化参数。

材料与方法。本研究包括53名孕妇，她们被分为两组：第一组为生理性妊娠（28人），第二组为重度子痫前期（25人）。所有孕妇在分娩时都使用剖腹产手术。研究材料为外周血和胎盘后血清。在机械分离胎盘和产后分离后立即采集样本。谷丙转氨酶、谷草转氨酶、乳酸脱氢酶、总蛋白、白蛋白、尿素、肌酐、总胆红素和直接胆红素、葡萄糖、尿酸的含量由贝克曼库尔特AU480生化分析仪（德国）测定。

结果。结果显示，胎盘后血液和外周血的生化成分有显著差异（P <0.05）。在生理性妊娠中，胎盘后血液中的谷丙转氨酶、谷草转氨酶、乳酸脱氢酶、尿素、肌酐、直接胆红素和尿酸水平明显升高（p<0.05），分别为1.9、20.1、11.4、1.14、1.19、2和1.15倍，而葡萄糖水平则降低了1.5倍。在重度子痫前期患者中，胎盘后血液中的谷草转氨酶、乳酸脱氢酶、肌酐、总胆红素、直接胆红素和尿酸水平显著升高（p<0.05），分别为11.7、11.5、1.3、1.2、2.2、1.11倍，血糖水平降低了1.57倍。

在比较第一组和第二组患者外周血的生化成分时，只有谷丙转氨酶、谷草转氨酶、总蛋白、白蛋白、尿素和肌酐存在可靠的差异（p< 0.05）。同时，在生理妊娠和子痫前期的胎盘后血液中，仅尿素、肌酐和尿酸存在可靠的差异（p<0.05）。

结论。因此，通过研究胎盘后血液的生化成分，可以更好地了解子痫前期的发病机理。

关键词：胎盘后血液；生理性妊娠；子痫前期；母体-胎盘-胎儿系统；血液生化分析。

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INTRODUCTION

Preeclampsia (PE) is a complication of the pregnancy, parturition, and postpartum period. It is characterized by elevations of the systolic blood pressure (SBP) and the diastolic blood pressure (DBP) above 140 mm Hg and 90 mm Hg, respectively, after Week 20 of pregnancy, without regard to BP history, and combined with proteinuria or at least one other parameter evidencing the comorbid multiple organ dysfunction. The incidence of this disorder during pregnancy is 2–8%, and it is the major cause of the maternal (10–15%) and perinatal (20–25%) mortality [1]. The predictive efficacy of the PE in the prenatal screening (combination of the maternal characteristics with the mean BP, uterine artery pulsatility index, and serum placental growth factor) favors the PE identification through 32 and 37 weeks, and after 37 weeks in the respective 90%, 75%, and 41% of cases (level of false positive results: 10%) [2].

The ways to reduce the maternal and perinatal mortality are based on the PE prevention, timely diagnosis, and treatment. As of today, numerous predictors (up to Week 20 of pregnancy) and markers (after Week 20 of pregnancy) have been described, but none of them is deemed reliable enough to judge it the major one. This is why it is vital to search for new markers to diagnose the course of preeclampsia [3].

It is known that the retroplacental blood (RPB) is the maternal arterial blood that comes into the intervillous space from the spiral arteries and effuses at the placental stage when the placenta separates from the uterine wall. By now, this substrate is understudied. Occasional research papers of the 1970–1980's describe certain immunological indicators of the retroplacental blood but do not provide any data on its hemostatic and biochemical parameters [4].

Study aim: To identify the features of the RPB biochemical parameters in preeclampsia.

MATERIALS AND METHODS

The research is a case-control longitudinal retrospective study performed on the basis of the Center for Family Planning and Reproduction, S.S. Yudin Municipal Clinical Hospital, and the Medical Research and Education Center, Lomonosov Moscow State University, within the period from 2020 to 2021.

The study enrolled 53 pregnant women, who were divided into two groups. The first (control) group included 28 patients with physiological pregnancy, while the second one included 25 patients with severe PE. All the pregnant women underwent a cesarean section, and the afterbirth was mechanically removed immediately after the infant was extracted. The indications for the cesarean section were incompetent uterine scar or competent uterine scar combined with pelvic presentation of the fetus in the first group, and severe PE in the second group. The exclusion criteria were multiple pregnancy, severe somatic, infectious, concomitant gynecological and oncological diseases, other complications of pregnancy. All the patients signed the voluntary informed consent for participation in the study.

The materials to study were the serum of the peripheral blood (PB) from the cubital vein and the serum of the RPB from the maternal surface of placenta. Samples were taken immediately after the mechanical removal of placenta and delivery of afterbirth. From each patient, 10 mL of blood were sampled into 2 test tubes with clot activator and separation gel for biochemical blood test. To determine the ALT, AST, LDH, total protein, albumin, urea, creatinine, total and direct bilirubin, glucose, uric acid levels in the RPB and PB sera, the Beckman Coulter AU480 (Germany) biochemistry analyzer was used.

The study design involved: (1) analysis of the RPB and PB biochemical parameters in the physiological pregnancy group (n=28); (2) analysis of the RPB and PB biochemical parameters in the severe PE group (n=25); and 3) comparison of RPB and PB biochemical parameters between the two groups of patients.

The statistical analysis of the study findings was performed using the Jamovi 2.3.22 software. To check the normality of distribution, the one-sample Shapiro–Wilk test was used. To describe the normally distributed signs, the mean value and standard deviation were reported; otherwise, the median and values of the 25th and 75th percentiles were determined. When comparing the dependent variables in the main and control groups, the Wilcoxon t-test and criterion were used; when comparing the independent variables, the Mann–Whitney t-test and criterion were used. The values of all the biochemical parameters are presented by the median and 25th and 75th percentiles regardless of the distribution. The results were considered statistically valid at $p < 0.05$.

RESULTS

The mean age of the first group patients (with physiological pregnancy) was 31.8±3.9 years (25 to 42 years). In these patients, the pregnancies were without complications and terminated in scheduled cesareans at 38–40 weeks. The medical and obstetric histories of the control group pregnant women were not burdened.

All the newborns of the physiological pregnancy mothers were born full-term, in satisfactory condition, without congenital or hereditary diseases. The average body weight of the newborns was 3328±254 g (2820 to 3900 g); the average body length was 51.5±1.9 cm. The Apgar scores averaged 8 and 9 at 1 and 5 minutes, respectively.

The mean age of the second group patients (with severe PE) was 30.5±5.8 years (24 to 44 years). In this group, all the deliveries were premature (from Week 31^3 to Week 35^6) due to the worsened conditions of the mothers and/or fetuses. In addition, some pregnant women had somatic comorbidities: 7 (28%) patients had chronic arterial hypertension,

4 (16%) had chronic pyelonephritis, and 2 (8%) had chronic cystitis. In 3 (12%) women the gynecological history was burdened with the tuboperitoneal infertility.

It is known that the most common symptoms of PE are the arterial hypertension, proteinuria, and edemas [5–6]. The analysis of the baseline blood pressure before pregnancy in the second group (severe PE) women reliably identified (p <0.05) its elevation. Thus, the SBP was elevated by at least 60 mm Hg, and the DBP was elevated by at least 30 mm Hg. In the first group (physiological pregnancy) patients, the maximal blood pressure during pregnancy did not exceed 128/85 mm Hg.

Another typical criterion of the severe PE is the massive proteinuria (⩾5 g/protein/day or ⩾3 g/L/protein in 2 portions of urine sampled at 6-hour interval) and moderate proteinuria (⩾0.3 g/protein/day or ⩾0.3 g/L/protein in 2 portions of urine sampled at 6-hour interval) [1]. The main cohort patients showed massive proteinuria in 64% of cases (n=16), moderate proteinuria in 24% of cases (n=6), and 3 (12%) patients did not have protein in urine. The clinical urine test did not find protein in urine in the physiological pregnancy women (control group).

According to the latest clinical studies and recommendations, the edemas occur in most cases of the physiological pregnancy, hence, they are not recommended to be considered as an obligatory diagnostic criterion of PE [1, 7]. Nevertheless, in our study, 17 (68%) patients with severe PE had generalized edemas.

In the second group patients, the cesarean section was performed within the term from 31 weeks and 3 days to 35 weeks and 6 days.

In the second group patients, all the children were born pre-term. Nine (36%) newborns in the early neonatal period were transferred to the resuscitation and intensive care unit, followed by the second stage of developmental care. The average body weight of the newborns was 2341±558 g (1200 to 3070 g); the average body length was 46.2±3.9 cm. The Apgar scores averaged 7.55±0.65 and 8.33±0.82 at 1 and 5 minutes, respectively. The newborns did not have congenital or hereditary diseases.

The comparison between the peripheral and retroplacental blood in physiological pregnancy identified reliable differences (p <0.05) in all the parameters except for the total protein, albumin, and total bilirubin (Table 1). Noteworthy is that the AST and LDH levels in RPB were significantly higher compared with PB: 20.1- and 11.4-fold, respectively. At the same time, the total bilirubin and glucose levels in RPB were, in contrast, lower compared to the PB.

The biochemistry testing in PE has also allowed identifying a number of significant differences. In particular, the AST and LDH levels were ten-fold greater in the retroplacental blood compared to the peripheral blood, just like in the physiological pregnancy. Reliable (p <0.05) differences were also identified for certain other parameters presented in Table 2. Noteworthy is that the total protein and glucose concentrations were lower in the retroplacental blood compared with the peripheral blood.

Table 3 shows the results of comparison of the PB biochemical parameters between the main and control group patients. Significant differences (p <0.05) were observed only for the ALT, AST, total protein, albumin, urea, and creatinine. All the other parameters, except for LDH and uric acid, had practically the same median values in physiological pregnancy and severe PE.

According to the findings presented in Table 4, the biochemical compositions of the main and control groups patients RPB showed significant (p <0.05) differences only for the urea, creatinine, and ureic acid.

Table 1. Biochemical parameters of the peripheral and retroplacental blood in physiologic pregnancy

Parameter	Peripheral blood, median (Q1; Q3)	Retroplacental blood, median (Q1; Q3)	$p^{1,2}$
ALT, U/L	9 (8, 11)	17 (14, 22)	<0.001[1]
AST, U/L	17 (15, 19)	341 (296, 368)	<0.001[1]
LDH, U/L	196 (189, 205)	2227 (1907, 2758)	<0.001[1]
Total protein, g/L	51.4 (48.7, 53.7)	50.6 (46.8, 52.7)	0.967[1]
Albumin, g/L	30.4 (28.7, 31.1)	31.6 (29.9, 32.7)	0.094[2]
Urea, mmol/L	2.8 (2.0, 3.2)	3.2 (2.7, 3.7)	<0.001[1]
Creatinine, μmol/L	51 (45, 58)	61 (54, 66)	<0.001[1]
Total bilirubin, μmol/L	5.4 (3.9, 6.4)	5.1 (1.8, 7.1)	0.531[1]
Direct bilirubin, μmol/L	0.8 (0.6, 1.0)	1.6 (1.4, 2.1)	<0.001[1]
Glucose, mmol/L	4.38 (3.98, 4.82)	2.90 (2.72, 3.23)	<0.001[1]
Uric acid, μmol/L	245(224; 280)	283 (240, 297)	<0.001[1]

Note: [1] Student's t-test for paired samples; [2] Wilcoxon's criterion.

Table 2. Biochemical parameters of the peripheral and retroplacental blood in severe preeclampsia

Parameter	Peripheral blood, median (Q1; Q3)	Retroplacental blood, median (Q1; Q3)	$p^{1,2}$
ALT, U/L	27 (20, 43)	19 (17, 25)	0.160[2]
AST, U/L	32 (23, 46)	377 (324, 539)	0.002[2]
LDH, U/L	223 (196, 287)	2561 (1567, 3208)	< 0.001[1]
Total protein, g/L	61.8 (54.9, 64.0)	53.2 (51.8, 54.8)	0.064[2]
Albumin, g/L	27.0 (23.7, 29.4)	29.9 (28.4, 31.3)	0.594[2]
Urea, mmol/L	3.8 (3.2, 4.5)	4.4 (3.6, 5.2)	0.104[1]
Creatinine, μmol/L	63 (57, 71)	84 (69, 85)	0.006[1]
Total bilirubin, μmol/L	5.6 (4.0, 7.8)	6.8 (3.2, 8.6)	0.039[2]
Direct bilirubin, μmol/L	0.9 (0.7; 1.0)	2.0 (1.2, 2.1)	0.014[2]
Glucose, mmol/L	4.4 (4.2, 5.3)	2.8 (2.6; 3.1)	0.002[2]
Uric acid, μmol/L	332 (240, 388)	370 (330, 392)	0.030[1]

Note: [1] Student's t-criterion for paired samples; [2] Wilcoxon's criterion.

Table 3. Biochemical parameters of the peripheral blood in physiologic pregnancy and severe preeclampsia

Parameter	Physiological pregnancy, median (Q1; Q3)	Severe preeclampsia, median (Q1; Q3)	$p^{1,2}$
ALT, U/L	9 (8, 11)	27 (20, 43)	< 0.001[1]
AST, U/L	17 (15, 19)	32 (23, 46)	< 0.001[1]
LDH, U/L	196 (189, 205)	223 (196, 287)	0.094[2]
Total protein, g/L	51.4 (48.7, 53.7)	61.8 (54.9, 64.0)	< 0.001[1]
Albumin, g/L	30.4 (28.7, 31.1)	27.0 (23.7, 29.4)	0.018[2]
Urea, mmol/L	2.8 (2.0, 3.2)	3.8 (3.2, 4.5)	0.003[2]
Creatinine, μmol/L	51 (45, 58)	63 (57, 71)	< 0.001[2]
Total bilirubin, μmol/L	5.4 (3.9, 6.4)	5.6 (4.0, 7.8)	0.715[1]
Direct bilirubin, μmol/L	0.8 (0.6, 1.0)	0.9 (0.7; 1.0)	0.950[1]
Glucose, mmol/L	4.3 (3.9, 4.8)	4.4 (4.2, 5.3)	0.116[2]
Uric acid, μmol/L	245 (224, 280)	332 (240, 388)	0.104[2]

Note: [1] Mann–Whitney test. [2] Student's t-test for independent samples.

DISCUSSION

For long years, preeclampsia has remained an urgent challenge of the today's obstetrics. Up to today, the problems of this disease complicating the course of pregnancy and the delivery remain unsolved. Severe PE is one of the most common causes of the maternal and perinatal complications and mortality. Not being a disorder affecting a specific organ or specific system, PE is justly considered a syndrome of the multisystem dysfunction resulting in the development of the multiple organ dysfunction syndrome [8–10].

The liver is a nonspecific target organ in preeclampsia. However, it is under functional stress in physiological pregnancy due to the involvement in the fetal intrauterine development, and, hence, becomes one of the first components of the multisystem dysfunction in the severe PE. At that the liver function is believed to be unchanged at the initial manifestations of the PE, but always alters at the disease progression [8].

It is common knowledge that in the severe PE the cytolytic syndrome, whose specific feature is the moderate elevation in transaminases (ALT, AST), becomes the major one [8, 11]. This study has found that the ALT and AST levels in PB were significantly (p <0.001) greater in severe PE: 3- and 1.88-fold, respectively. The differences in RPB were insignificant (p >0.05); however, the above regularity remained: the activity of the hepatic aminotransferases was

Table 4. Biochemical parameters of the retroplacental blood in physiologic pregnancy and severe preeclampsia

Parameter	Physiological pregnancy, median (Q1; Q3)	Severe preeclampsia, median (Q1; Q3)	$p^{1,2}$
ALT, U/L	17 (14, 22)	19 (17, 25)	0.675[1]
AST, U/L	341 (296, 368)	377 (324, 539)	0.101[1]
LDH, U/L	2227 (1907, 2758)	2561 (1567, 3208)	0.993[2]
Total protein, g/L	50.6 (46.8, 52.7)	53.2 (51.8, 54.8)	0.218[2]
Albumin, g/L	31.6 (29.9, 32.7)	29.9 (28.4, 31.3)	0.281[1]
Urea, mmol/L	3.2 (2.7, 3.7)	4.4 (3.6, 5.2)	0.002[2]
Creatinine, μmol/L	61 (54, 66)	84 (69, 85)	< 0.001[2]
Total bilirubin, μmol/L	5.1 (1.8, 7.1)	6.8 (3.2, 8.6)	0.274[2]
Direct bilirubin, μmol/L	1.6 (1.4, 2.1)	2.0 (1.2, 2.1)	0.163[2]
Glucose, mmol/L	2.9 (2.7; 3.2)	2.8 (2.6; 3.1)	0.852[1]
Uric acid, μmol/L	283 (240, 297)	370 (330, 392)	0.017[2]

Note: [1] Mann–Whitney test; [2] Student's t-test for independent samples

higher in the severe PE compared with the physiological pregnancy.

At the initial stages of hepatocellular deficiency, the ALT activity is increased relative to AST, the De Ritis ratio (AST/ALT) is below 1.0. When signs of the hepatocellular deficiency appear, the AST activity is increased relative to ALT: this is due to more profound hepatocellular disease and the development of the tissue hypoxia outside the hepatobiliary system (De Ritis ratio is above 1.33) [8, 11]. Given that in this study, the AST activity in the peripheral and retroplacental blood in the main group was higher than the ALT activity (32 U/L vs 27 U/L and 377 U/L vs 19 U/L, respectively) it may be concluded that patients with pronounced hepatocellular deficiency prevail in the study. Hence, on the one hand, our laboratory findings evidence that urgent surgical delivery that prevented the progression to more pronounced involvement of the hepatocytes is the only correct management strategy in the main group patients; on the other hand, they demonstrate that earlier clinical and laboratory symptoms of the developing hepatocellular deficiency were missed at earlier stages. All these re-highlight the necessity to improve the efficacy of the severe PE prediction in the early pregnancy.

The elevated activity of the lactate dehydrogenase (LDH) complements the pattern of the hepatocellular necrosis. This enzyme exists not only in the liver but also in the myocardium, kidneys, and skeletal muscles; it is considered non-specific and evidences the development of the multiple organ tissue hypoxia [8]. The unreliability of the differences (p >0.05) in the LDH activity in the physiological pregnancy and severe PE can be explained by the small size of the patient sample; however, an upward trend in the LDH activity is obvious: 223 U/L vs 196 U/L in PB, 2561 U/L vs 2227 U/L in RPB in preeclampsia and physiological pregnancy, respectively.

The criteria of hepatocellular deficiency development in PE are the combined elevation of the cytolysis and cholestasis parameters, and a reduction in the hepatic synthetic function parameters (activity of the cholinesterase, levels of the total protein, albumin, and blood coagulation system proteins), which are considered extremely unfavorable factors [8].

Based on the results of this study, the albumin levels really decreased in the pregnant women with severe PE compared with those in the patients with physiological pregnancy (27.0 g/L vs 30.4 g/L in PB and 29.9 g/L vs 31.6 g/L in RPB). Noteworthy is the fact that the RPB total protein level was lower in both groups: this is due, most likely, to its consumption for formation of the fetal tissues.

It is known that the manifestations of cholestasis are not major in PE: the cholestatic syndrome holds higher priority position in intrahepatic cholestasis of pregnant women than in PE. The increase in the severity of the preeclampsia involves, first of all, an elevation in the total bilirubin, due, mainly, to the direct (parenchymatous) bilirubin, and to the activities of the alkaline phosphatase and gamma-glutamyl transpeptidase, and to the level of the bile acids; these reflect the damage to the hepatobiliary system [8, 11]. According to the study findings, the total and direct bilirubin levels were higher in severe PE compared with physiological pregnancy; however, the differences were insignificant (p >0.05), which fully supports this theory. Thus, the second group (severe PE) patients showed a significant (p <0.05) elevation in the total (from 5.6 to 6.8 μmol/L) and direct (from 0.9 to 2.0 μmol/L) bilirubin in RPB, which supports the generally accepted theory about the filtration capacity of placenta.

Elevated creatinine and urea are the generally accepted criterion of renal impairment, including in severe PE. We have revealed a significant (p <0.05) elevation in these parameters in the peripheral and retroplacental blood in the second group

(severe PE) patients. Besides, the above changes can be ascribed to the active proteinic metabolism in placenta, which is supported by the higher urea and creatinine levels in RPB compared with PB (p <0.05).

Another typical sign of the renal impairment in PE is the progressive elevation in the serum uric acid level, which is not only due to the deteriorated renal perfusion and ischemia as previously believed, but also by the reduced renal clearance. In recent years, there have been assumptions that the hyperuricemia in women with PE can directly contribute to the development of the vascular injury and arterial hypertension [12]. In this study, the uric acid levels were higher in the second group (severe PE) compared with the first one (332 μmol/L vs 245 μmol/L in PB and 370 μmol/L vs 283 μmol/L in RPB, respectively), which does not conflict with the typical laboratory findings in renal disease.

A higher glucose level in the PB compared with the retroplacental blood can be explained by the elevated capacity of the fetus to consume glucose [4], both in physiological pregnancy, and in severe PE.

The unique differences of the retroplacental and peripheral blood biochemical parameters found, as well as in the previous study, can be explained with regard to the current issue of the systemic to local metabolism ratio. The hypothesis that the biochemical composition of the supplied to organ blood "adapts" to the metabolic needs of this organ, is, obviously, true. These zones can be conventionally called "metabolic circulatory compartments (in contrast with the classic sense of the blood compartments: plasma, red blood cells, white blood cells, etc.). The "barrier" or "filter" (e.g., liver) determines the difference of its biochemical profile from that of the venous blood, which is the object of analysis in the clinical laboratory diagnostics [4, 13]. Hence, knowing the biochemical composition of the local placental blood flow we can get more accurate insights into the pathological processes at the boundary of the mother/placenta/fetus system compared with the examination of the systemic blood flow.

CONCLUSION

The study has demonstrated that the RPB biochemical parameters significantly differ from those of the peripheral blood. At the physiological pregnancy, the ALT, AST, LDH, urea, creatinine, direct bilirubin, and ureic acid levels were significantly (p <0.05) higher in RPB: в 1.9-; 20.1-; 11.4-; 1.14-; 1.19-; 2-; and 1.15-fold, respectively, while the glucose level was, in contrast, 1.5-fold lower. The patients with severe preeclampsia had significantly (p <0.05) elevated RPB AST, LDH, creatinine, total and direct bilirubin, and ureic acid levels: 11.7-; 11.5-; 1.3-; 1.2-; 2.2-; and 1.11-fold, respectively. The glucose values in the women of this group were 1.57-fold lower.

When comparing the PB biochemical compositions between the PE and physiological pregnancy patients, significant (p <0.05) differences were identified only for the ALT, AST, total protein, albumin, urea, and creatinine levels. In contrast, when comparing the RPB biochemical parameters between the physiological pregnancy and preeclampsia patients, significant (p <0.05) differences were identified only for the urea, creatinine, and uric acid.

Our study has demonstrated the feasibility of the further RPB studies to obtain more complete ideas of the placenta-associated diseases pathogenesis.

ADDITIONAL INFO

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Consent for publication. All study participants, prior to inclusion in the study, voluntarily signed an informed consent form for participation in the study and publication of medical data, approved as part of the study protocol by the Local Ethics Committee.

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