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HEMOSTATIC SYSTEM IMBALANCE IN THE PRE-ECLAMPSIA MODEL IN RATS

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Background. *Preeclampsia (PE) is a multisystem disorder in pregnancy, that results from placental ischemia, oxidative stress-induced placental damage and placental factors dissemination that cause systemic endothelial dysfunction. Patients with preeclampsia often develop a severe prothrombotic state, the mechanisms of which are not fully elucidated.* ***Objectives.*** *The aim of this study was to assess the informativeness of hemostatic system parameters that characterize the degree of coagulation pathway activation and anticoagulant pathway capacity capacity in experimental preeclampsia model in rats for predicting the development of thrombotic complications in PE.* ***Methods.*** *Wistar females rats were used in the study. To induce a preeclampsia-like syndrome, N(ω)-nitro-L-arginine methyl ester (L-NAME), at a concentration of 0.3 g/l in the drinking water was administered ad libitum from the 8th to the 14th day of gestation. On gestational day 21 the rats were anesthetized and blood samples were collected. Urinary and serum concentrations of creatinine, urea, and uric acid were determined using a fully automated Chemistry Analyzer and commercially available kits. Fibrinogen, soluble fibrin monomeric complexes and protein C concentrations, prothrombin time and antithrombin III activity in the blood plasma were estimated with a standard spectrophotometric methods.* ***Results.*** *Increased plasma fibrinogen, significant shortening of plasma clotting time, decrease in both protein C and AT III and increase in SFMCs plasma levels were detected in rats with experimentally L-NAME induced preeclampsia, indicating not only activation of the coagulation system but also disruption of the balance between procoagulant and anticoagulant pathways.* ***Conclusions.*** *L-NAME-induced PE in rats resulted in a pronounced imbalance of the hemostatic system and reproduced key pathophysiological features of PE, including excessive procoagulant shift, intravascular thrombin generation and impairment of anticoagulant mechanisms, making this model a valuable tool for studying mechanisms of disease progression. Analysis of hemostasis parameters in this model, indicates that soluble fibrin, protein C and antithrombin III are the most informative markers for assessing the risk of intravascular coagulation during preeclampsia.*

K e y w o r d s: preeclampsia, L-NAME induced preeclampsia model, coagulation, thrombosis, soluble fibrin, fibrinogen, protein C, antithrombin III.

Preeclampsia (PE) is a multisystem disorder specific to pregnancy, resulting from placental ischemia, oxidative stress-induced placental damage, and the dissemination of placental factors that cause systemic endothelial dysfunction [1-3]. It is well known that patients with PE often develop a severe prothrombotic state, which increases the risk of venous thromboembolism during late pregnancy and the early postpartum period [4, 5].

The mechanisms underlying the increased risk of thrombosis remain incompletely elucidated. Increased expression of procoagulant factors, endothelial dysfunction, reduced anticoagulant activity, and enhanced platelet activity are known to be associated with a prothrombotic tendency [6-8].

To identify mechanisms that may potentially contribute to the pathogenesis of PE, numerous experimental models using laboratory animals have been developed [9, 10]. Preclinical *in vivo* models play an important role in understanding the pathophysiology of PE and serve as a valuable tool for developing new therapeutic approaches for this condition [11, 12].

Experimental preeclampsia is induced by surgical [13], pharmacological [14, 15], immunological [16], and genetic [17, 18] manipulations. The use of experimental models enables assessment of the informativeness of laboratory diagnostic tests for the timely detection of hypercoagulation and prevention of a prothrombotic state, as well as for identifying subtle long-term effects of PE on the cardiovascular system.

In our study, PE was simulated using N(ω)-nitro-L-arginine methyl ester (L-NAME), an antagonist of nitric oxide synthase. Inhibition of NOS leads to endothelial dysfunction, which is believed to underlie the pathophysiology of PE and is directly linked to hemostasis abnormalities [19].

The aim of this study was to assess the informativeness of hemostatic system parameters that characterize the degree of activation of the coagulation pathway and the capacity of the anticoagulant pathway of hemostasis for predicting the development of thrombotic complications in PE.

Materials and Methods

All experimental procedures involving animals were conducted in accordance with internationally recognized bioethical standards and principles of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 1986) and in accordance with institutional guidelines for the care and use of laboratory animals, with the approval of the Local ethics committee (Protocol 01/03/20, date 16.03.2020).

Materials. Chromogenic substrates S2238 (H-D-Phe-Pip-Arg-pNA), and S2236 (p-Glu-Pro-Arg-pNa) were purchased from BIOPHEN (Neuville-sur-Oise), sodium citrate, phosphate-buffered saline (PBS) tablets (pH 7.2, sodium chloride, 0.15 M) were purchased from Sigma-Aldrich (St. Louis, USA). PT-reagent, control donors' blood plasma, and test-systems for determining Protein C and antithrombin III levels were purchased from Siemens-Biomed (Marburg, Germany). The thrombin-like enzyme was purified from *Agkistrodon halys halys* venom according to the method described in [20].

Modelling of preeclampsia. Wistar rats were used in the study: females weighing 180-220 g (2 months old) and males weighing 200-240 g (3 months old). The animals were housed in polycarbonate cages under controlled environmental conditions (temperature 22-24°C, relative humidity 40-70%, and a 12 h light/dark cycle) and had free access to a standard pelleted diet (Research Limited Liability Company “F.U.D.”, Tetiiv, Ukraine).

During the acclimatization period and prior to mating and pregnancy, five female rats were housed per cage; similarly, five male rats were housed per cage during acclimatization and before mating. For mating, females in estrus were co-housed overnight with males in individual cages at a ratio of 1 male to 1 female. The zero day of pregnancy was determined by vaginal cytology and defined as the day of sperm detection in the vaginal smear. After confirmation of pregnancy, females were housed individually, with cage labels indicating the gestational day and experimental group.

To induce a preeclampsia-like syndrome, L-NAME was administered ad libitum in the drinking water at a concentration of 0.3 g/l from gestational day 8 to day 14. The average daily consumption of the L-NAME solution was 30 ml, corresponding to an approximate L-NAME dose of 9 mg per rat per day. Body weight of pregnant females was measured once weekly in the morning throughout gestation and immediately prior to euthanasia. Changes in body weight were assessed relative to the first day of pregnancy and compared between the experimental and control groups.

Blood pressure in the tail artery was measured on gestational day 19, after that females were placed in Tecniplast metabolic cages for overnight urine collection. On gestational day 21 females were anesthetized with thiopental (LLC “Brovapharma”, Ukraine), and blood samples were collected by cardiac puncture. Animals were then euthanized by cervical dislocation.

The complete experimental timeline and detailed procedures are presented in Fig. 1.

Pressure measurement. Blood pressure in the tail artery was measured on gestational day 19 using the Sphygmomanometer S-2 system (HSE, Germany), which enables non-invasive determination of systolic arterial pressure. To minimize movement, animals were placed in plastic restrainers and trans-

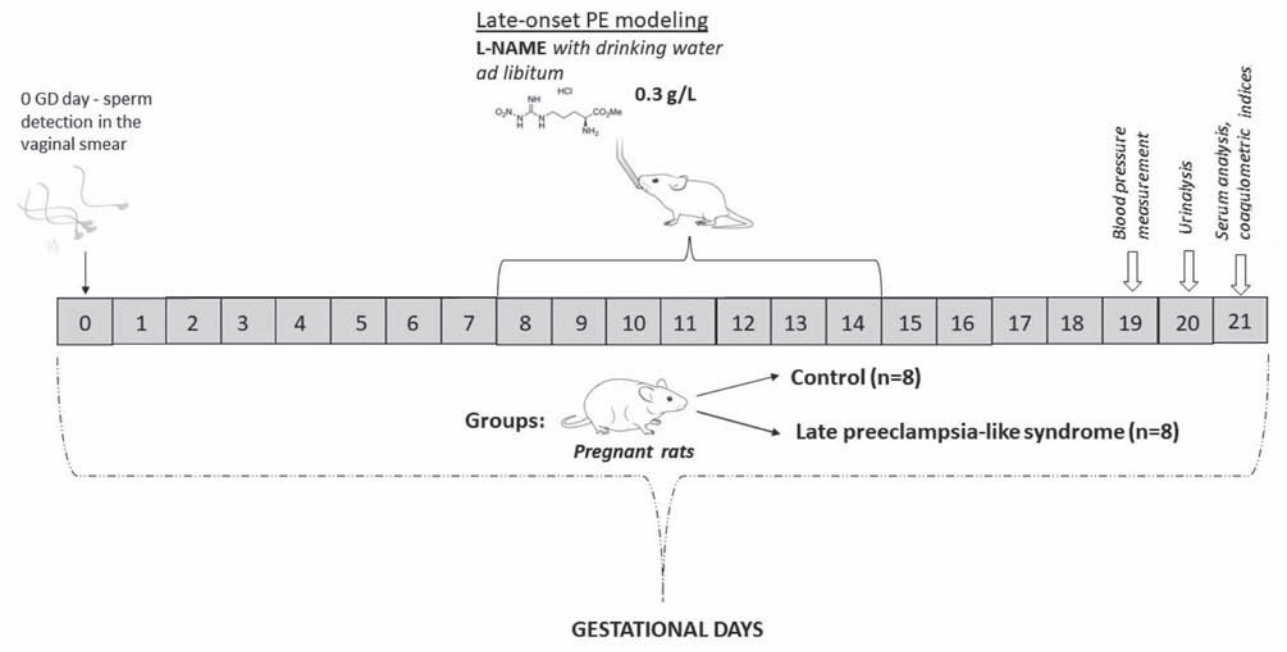

Fig. 1. Experimental design and timeline of the study. Icons were adapted from the SciDraw repository (Creative Commons Attribution license)

ferred to a temperature-controlled chamber maintained at 34°C. After a 20-min habituation period, the restrainers were positioned on a dedicated stand, and a rubber occlusion cuff equipped with an ultrasonic transducer was placed around the tail to detect arterial pulsations.

The acquired signals were digitized using a PowerLab 4/30 analog-to-digital converter (AD Instruments, Australia) and analyzed with Chart 5 software (AD Instruments, Australia).

Urine analysis. On gestational day 19, females were placed in Tecniplast metabolic cages for overnight urine collection.

Urinary concentrations of creatinine, urea, and uric acid were measured using a fully automated Prestige 24i Chemistry Analyzer (Tokyo Boeki Medisys Inc., Tokyo, Japan) with commercially available kits (Futura System Group, Italy).

Serum analysis. Serum concentrations of creatinine, urea, and uric acid were determined using a fully automated biochemical analyzer Prestige 24i Chemistry Analyzer (Tokyo Boeki Medisys Inc., Tokyo, Japan) with commercially available kits (Futura System Group, Italy).

Fibrinogen concentration. Fibrinogen concentration in the blood plasma was determined by the modified spectrophotometric method. Blood plasma preparation was performed according to [21]. Blood plasma (0.2 ml) and PBS (1.7 ml) were mixed in a glass tube. Coagulation was initiated by the addition of 0.1 ml of thrombin-like enzyme from the venom of Aghistrodon halys halys (1 NIH/ml) that allowed to avoid fibrin cross-linking. Mixture was incubated during 30 min at 37°C. The fibrin clot was removed and re-solved in 5 ml of 1.5% acetic acid. The concentration of protein was measured using spectrophotometer POP (Optizen, Korea) at 280 nm (ε = 1.5) [22].

Prothrombin time. Prothrombin time (PT) was measured as follows: clotting was initiated by mixing 0.1 ml of blood plasma with 0.1 ml of 0.025 M $CaCl_2$ and 0.1 ml of thromboplastin reagent, time of clotting was monitored. Thromboplastin acts through tissue factor pathway of coagulation and activates only carboxylated and uncleaved forms of prothrombin. Time of clotting was evaluated using coagulometer CT2410 (Solar, Belarus). Results were expressed as the prothrombin index (PI), calculated as the ratio of the clotting time of plasma from the control animal, to that of the animal experimental animal expressed as a percentage:

$$PI\ (\%) = PT_{control}/PT_{experimental} \times 100\ (\%).$$

Soluble fibrin monomeric complexes (SFMCs). For the SFMCs measurement in the glass tube to the 0.25 ml of studied blood plasma sample was mixed

with equal volume of 0.1 M KH_2PO_4 buffer pH 7.5. Then 0.4 ml of 1 M KH_2PO_4 buffer pH 7.5 was added to the whole volume after gentle mixing. Samples were incubated during 30 min at ambient temperature. After incubation, the accumulation of saturated SFMCs was estimated semi-quantitatively in the range of concentrations 0.007-0.14 mg/ml. For the calibration we used samples of blood plasma with monomeric fibrin desAB added at final concentrations from 0.007 to 0.14 mg/ml prepared according to the method [23, 24].

Protein C level. PC level was determined using the activator of PC (Siemens, Germany). The generation of activated PC was measured by chromogenic substrate assay using specific chromogenic substrate S2236 (p-Glu-Pro-Arg-pNa). The analysis was performed in 0.05 M Tris-HCl buffer pH 7.4, at 37°C. Chromogenic substrate concentration was 30 mM. The generation of para-nitroaniline was measured at 405 nm on a microtiter plate reader Multiscan EX (Thermo Fisher Scientific, Waltham, USA). Results were presented as ratio of PC level in the blood plasma of studied animal to PC level in the blood plasma of healthy control animal [25].

Antithrombin level. The activity of antithrombin III (ATIII) is determined based on its ability to neutralize thrombin in the presence of heparin. The overabundance of thrombin was inhibited by the ATIII-heparin complex proportionally to the ATIII in blood plasma. The analysis was performed according the recommendations of manufacturer. Remaining activity of thrombin was measured using chromogenic thrombin-specific substrate S2238 (H-D-Phe-Pip-Arg-pNA). The generation of colorful p-nitroaniline (pNa) was monitored at 405 nm using ThermoMultiscan (ThermoFisher, USA). The amount of ATIII was determined using the calibration curve [26].

Statistics. Statistical data analysis was performed using the Wilcoxon-Mann-Whitney (WMW) test and Student's *t*-test. All blood coagulation assays were replicated thrice. Results are presented as means ± standard deviation. Data were considered significant when $P < 0.05$ [27].

Results

Model characterization. Injection of L-NAME led to numerous pathophysiological changes in pregnant rats compared with the control group, including a significant increase in systolic blood pressure and enhanced urinary excretion of protein, uric acid, and creatinine. Contrary to clinical observations in human preeclampsia, where serum uric acid levels are typically elevated, we observed a decrease in serum uric acid accompanied by increased urinary excretion. This may reflect preserved or enhanced renal filtration and reduced tubular reabsorption of urate in the L-NAME-induced model, particularly at the studied gestational stage. These findings suggest that while the model successfully reproduces key features of preeclampsia, including hypertension and proteinuria, it may differ in renal handling of metabolites (Table 1).

Taken together, the functional and biochemical alterations observed in pregnant rats following administration of L-NAME confirm the successful induction of a preeclampsia-like state. L-NAME treatment resulted in arterial hypertension, proteinuria, and altered uric acid handling, while serum creatinine levels remained unchanged, suggesting preserved glomerular filtration. These findings are consistent with key features of preeclampsia, particularly endothelial dysfunction and renal involvement at the functional level.

Hemostasis system parameters. To characterize the state of the blood coagulation system, the concentrations of fibrinogen, soluble fibrin-monomer complexes (SFMCs), protein C, antithrombin III, as well as plasma clotting time in the prothrombin time test, were measured.

A significant increase in the prothrombin index (i.e., a shortening of plasma clotting time in the prothrombin time test) was observed in rats with experimentally induced preeclampsia. Overall, the trend toward accelerated clot formation under preeclamptic conditions is expected and indicates an increased risk of intravascular thrombosis (Fig. 2).

In the studies conducted, no increase in fibrinogen concentration was observed in rats with normal pregnancy. However, a trend toward elevated fibrinogen levels was noted under PE (Fig. 3, *A*). Experimentally induced PE was also associated with a statistically significant increase in SFMCs (Fig. 3, *B*), indicating intravascular thrombin generation. Together with the trend toward higher fibrinogen levels and the shortening of plasma clotting time in the prothrombin time test, these findings point to an enhanced risk of intravascular thrombosis.

To evaluate the anticoagulant branch of hemostasis, the levels of protein C and antithrombin III were measured. Plasma protein C levels were significantly decreased in rats with experimentally induced

Table 1. Basic parameters of rats with preeclampsia induced by L-NAME injection. Systolic blood pressure was measured on the 19st day of pregnancy; protein content, uric acid, and creatinine in urine were measured on the 20th day of pregnancy; body weight, protein content, uric acid, and creatinine in blood plasma were measured on the 21st day of pregnancy

Parameters	Control (intact)	Late-onset PE (l-NAME)
Systolic blood pressure	112.44 ± 5.81	139.75 ± 5.01*
Body weight	268.0 ±7.4	265.0 ± 4.7
Urine:		
Total protein, mg/dl	18.04 ± 0.84	33.47 ± 7.71*
Uric acid, μmol/l	290.80 ± 35.88	501.64 ± 63.46*
Creatinine, mmol/l	3685.06 ± 566.48	4057.07 ± 500.92
Serum:		
Urea, mmol/l	8.05 (6.95; 8.45)	3.80 (3.70; 4.60)*
Uric acid, μmol/l	90.0 (71.0; 115.0)	59.00 (52.50; 68.50)*
Creatinine, mmol/l	17.57 ± 1.89	18.08 ± 1.40

Notes. 1) Data are presented as mean ± SEM for normally distributed variables and as Mediana (First Quartile; Third Quartile) for non-normally distributed variables. 2) *Differences were considered statistically significant at $P \leq 0.05$

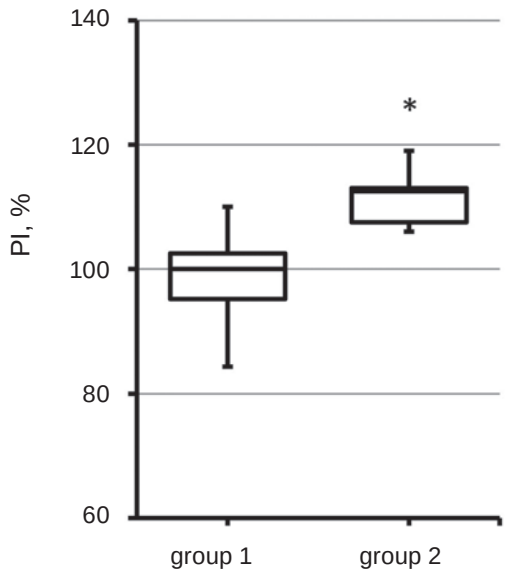

*Fig. 2. The prothrombin index (PI) of the plasma of healthy pregnant female rats (group 1) and in pregnant rats with experimentally induced preeclampsia (group 2) on day 21 of pregnancy was measured. *Differences were considered statistically significant at $P \leq 0.05$*

PE (Fig. 4, *A*), confirming the generation of active thrombin, which consumes anticoagulant protein C.

Furthermore, a significant decrease in antithrombin III activity was observed in rats with experimental preeclampsia. Antithrombin III proved to be the most sensitive marker, clearly indicating a hemostatic imbalance under experimental preeclamptic conditions.

In general, we detected a substantial increase in the procoagulant potential of the blood coagulation system in pregnant rats with modelled PE.

Discussion

The present study aimed to evaluate the informativeness of hemostatic parameters for predicting thrombotic complications in experimental preeclampsia induced by L-NAME. The obtained findings confirm that this model reproduces key features of preeclampsia, including arterial hypertension and proteinuria [5, 10], thereby supporting its applicability for investigating endothelial dysfunction–associated hemostatic disturbances.

A notable finding of the present study was the decrease in serum uric acid levels accompanied by increased urinary excretion at gestational day 20-21. This pattern contrasts with clinical observations in human preeclampsia, where hyperuricemia is a well-established marker associated with disease severity and adverse outcomes, primarily attributed to reduced renal clearance and increased tubular reabsorption of urate [28, 29]. However, this discrepancy does not undermine the validity of the model and can be explained by several pathophysiological considerations.

First, the L-NAME-induced model predominantly reflects nitric oxide deficiency–driven en-

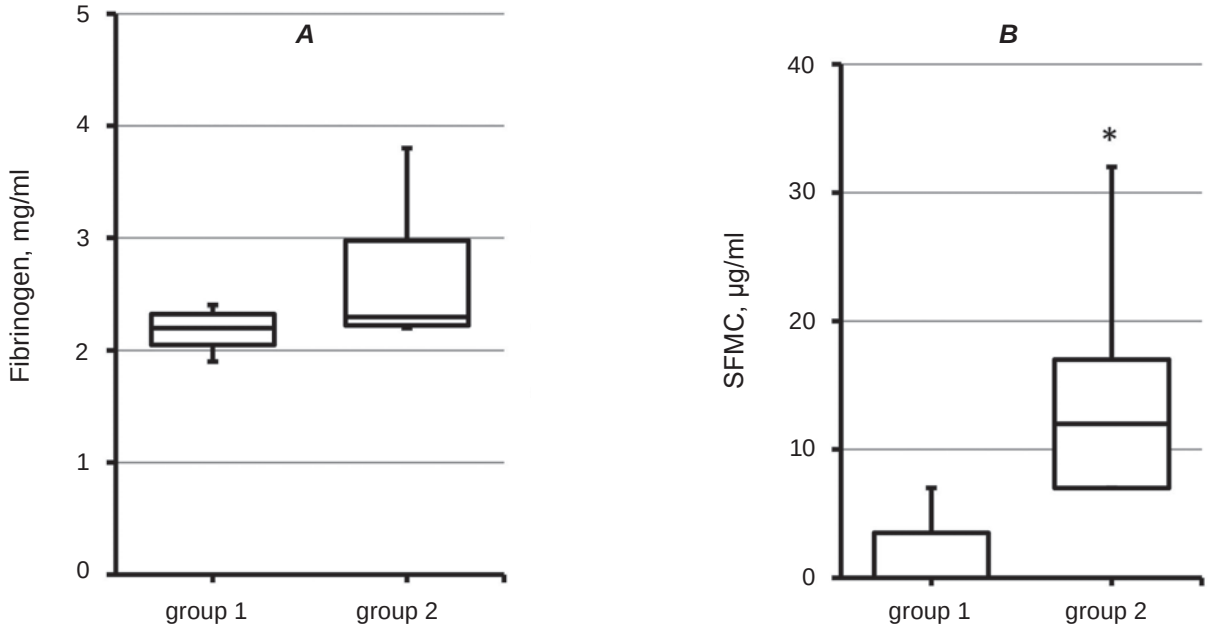

*Fig. 3. The concentration of fibrinogen (**A**) and soluble fibrin monomeric complexes (**B**) in the plasma of healthy pregnant female rats (group 1) and in pregnant rats with experimentally induced preeclampsia (group 2) on day 21 of pregnancy was measured. *Differences were considered statistically significant at $P \leq 0.05$*

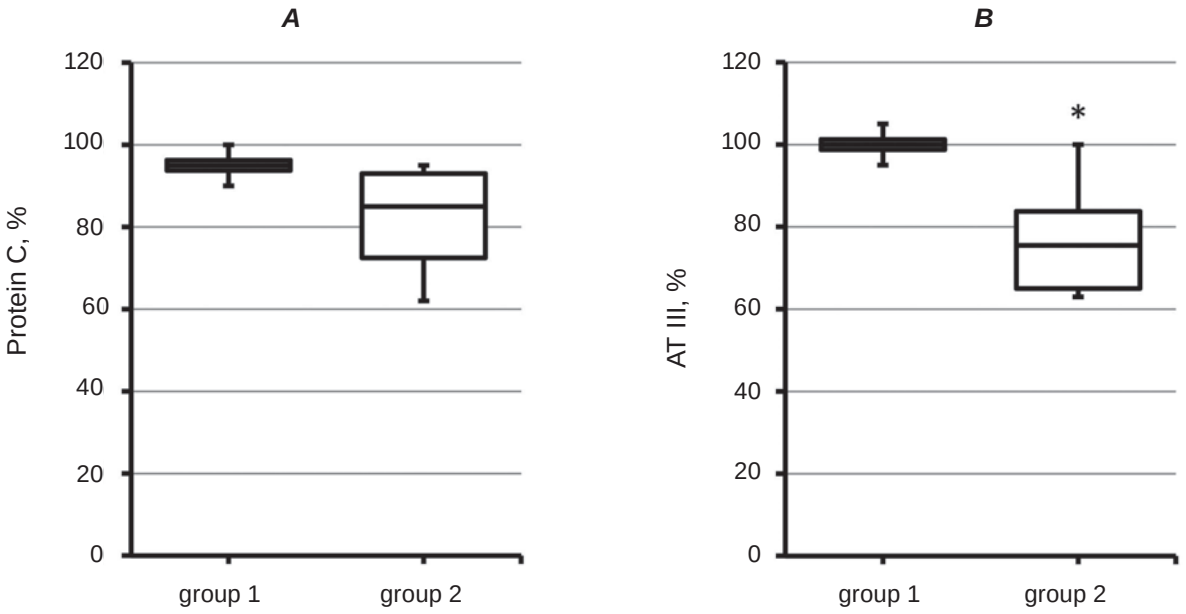

*Fig. 4. The level of antithrombin III (**A**) and protein C (**B**) in the plasma of healthy pregnant female rats (group 1) and in pregnant rats with experimentally induced preeclampsia (group 2) on day 21 of pregnancy was measured. * Differences were considered statistically significant at $P \leq 0.05$*

dothelial dysfunction rather than advanced renal impairment. Inhibition of nitric oxide synthase results in systemic vasoconstriction, increased peripheral resistance, and hypertension, but does not consistently lead to a reduction in glomerular filtration rate (GFR), particularly at earlier stages of disease development [30, 31]. In line with this, the absence of significant changes in serum creatinine

observed in our study suggests preserved glomerular filtration. Therefore, the reduction in serum uric acid is unlikely to be driven by impaired renal clearance.

Second, the combination of decreased serum uric acid and increased urinary excretion strongly indicates altered tubular handling of urate. In contrast to human preeclampsia, where enhanced proximal tubular reabsorption contributes to hyperuricemia, nitric oxide deficiency may differentially regulate renal urate transporters, such as URAT1 and GLUT9, leading to reduced reabsorption or increased secretion [32, 33]. This interpretation is further supported by the concomitant decrease in serum urea levels, which, in the absence of creatinine elevation, may reflect hemodilution or pregnancy-associated metabolic adaptations rather than renal dysfunction.

Third, species-specific differences in uric acid metabolism may contribute to the observed findings. Rodents differ from humans in both urate production and renal transport mechanisms, including the presence of urate oxidase and differences in transporter expression, which limits the direct translational interpretation of uric acid dynamics [34, 35]. Consequently, uric acid should be interpreted with caution as a biomarker in preclinical models of preeclampsia.

Importantly, despite differences in uric acid metabolism, the model demonstrated clear evidence of endothelial dysfunction, as reflected by the development of hypertension and proteinuria–hallmark features of preeclampsia that are closely linked to hemostatic imbalance and prothrombotic risk [5, 10]. These findings support the suitability of this model for studying coagulation abnormalities, even in the absence of classical hyperuricemia.

Investigation of the hemostatic system in rats with L-NAME-induced PE showed increased plasma fibrinogen and a shortened prothrombin time, suggesting an elevated procoagulant potential. A shift of the hemostatic balance toward hypercoagulability during pregnancy is considered evolutionarily advantageous to reduce bleeding, but it may also increase the risk of venous thromboembolism [8, 36]. However, disruption of the dynamic balance between procoagulant, anticoagulant, and fibrinolytic pathways can lead to excessive activation of the coagulation cascade, potentially resulting in thrombosis.

Therefore, to assess the risk of thrombus formation in PE, our study focused on identifying imbalances between procoagulant and anticoagulant potential and determining markers of coagulation system activation [37-39].

Shortening of clotting time observed in the L-NAME-induced PE model correlates with hemostatic changes described in PE-complicated pregnancy. During pregnancy, plasma levels of factor X may increase by 10-20% [40], thereby enhancing thrombin generation via the coagulation cascade.

A more specific indicator of thrombin generation is the accumulation of soluble fibrin-monomer complexes (SFMCs), whose plasma levels reflect thrombin activity and serve as reliable markers of thrombophilia. In our study, a significant increase in SFMCs was detected in the plasma of rats with induced PE, indicating intravascular generation of active thrombin. This finding reflects not only activation of the coagulation system but also disruption of the balance between procoagulant and anticoagulant pathways [41, 42].

This concept is supported by direct measurements of protein C and antithrombin III (AT III) levels. The protein C system is particularly sensitive under pathological conditions, as physiological anticoagulants are consumed more rapidly than they are generated. Accordingly, rats with PE exhibited a significant decrease in both protein C and AT III levels, a disturbance also reported in pregnant women with PE [43].

Overall, the imbalance between procoagulant factors and physiological anticoagulants observed in this model mirrors clinical PE and indicates dysregulation of hemostatic control, increasing the risk of transition from hypercoagulability to a prothrombotic state. Thus, the L-NAME *in vivo* model reproduces key pathophysiological features of PE, including excessive procoagulant shift, intravascular thrombin generation, and impairment of anticoagulant mechanisms.

Conclusions. L-NAME-induced PE in rats results in a pronounced imbalance of the hemostatic system, making this model a valuable tool for studying mechanisms of disease progression, evaluating diagnostic markers, and testing therapeutic approaches. Analysis of blood coagulation parameters in this model, compared with those reported in pregnant women with preeclampsia, indicates that soluble fibrin and protein C (or antithrombin III) are the most informative markers for assessing the risk of intravascular coagulation during preeclampsia.

Limitations of the study. This study focuses on changes in the blood coagulation system in a rat model of L-NAME–induced PE. Although the observed alterations reliably reflect key pathophysiological features of PE in pregnant women, direct

comparison between the animal model and the human condition is not possible. Therefore, the findings should be interpreted in terms of shared trends rather than exact correspondence. The model is intended to facilitate extrapolation of underlying mechanisms and to support the identification of potential preventive and therapeutic approaches, rather than to reproduce all aspects of human preeclampsia.

Author contributions. Conceptualization, S.Z. and T.M.; methodology, I.U.; investigation, O.G. and N.B.; data curation, G. Sh.; writing – original draft preparation, G.Sh. and L.B.; writing – review and editing, A.P.; formal analysis, statistical analysis – I.U.

Conflict of interest. The authors have completed the Unified Conflicts of Interest form at http:// ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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ДИСБАЛАНС ГЕМОСТАТИЧНОЇ СИСТЕМИ НА МОДЕЛІ ПРЕЕКЛАМПСІЇ У ЩУРІВ

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Вступ. Прееклампсія (ПЕ) – це мультисистемне захворювання вагітності, що виникає внаслідок ішемії плаценти, пошкодження плаценти, індукованого оксидативним стресом, та поширення плацентарних факторів, що спричиняють системну ендотеліальну дисфункцію. У пацієнток із прееклампсією часто розвивається тяжкий протромботичний стан, механізми якого до кінця не з’ясовані. **Мета.** Метою цього дослідження була оцінка інформативності параметрів гемостатичної системи, що характеризують ступінь активації коагуляційних шляхів та пропускну здатність антикоагулянтних шляхів, в експериментальній моделі прееклампсії у щурів для прогнозування розвитку тромботичних ускладнень при ПЕ. **Методи.** У дослідженні використовували самок щурів лінії Вістар. Для індукції прееклампсіоподібного синдрому N(ω)-нітро-L-аргініну метиловий естер (L-NAME) у концентрації 0,3 г/л у питній воді вводили *ad libitum* з 8-го по 14-й день вагітності. На 21-й день вагітності щурів анестезували та збирали зразки крові. Концентрації креатиніну, сечовини та сечової кислоти в сечі та сироватці крові визначали за допомогою автоматизованого хімічного аналізатора та комерційно доступних наборів. Концентрації фібриногену, розчинних мономерних комплексів фібрину та протеїну С, протромбінового часу та активності антитромбіну III у плазмі крові оцінювали стандартними спектрофотометричними методами. **Результати.** У щурів з експериментально індукованою L-NAME прееклампсією було виявлено підвищення рівня фібриногену в плазмі, значне скорочення часу згортання плазми, зниження рівня як протеїну С, так і АТ III, а також підвищення рівня SFMC у плазмі, що свідчить не лише про активацію системи згортання крові, але й про порушення балансу між прокоагулянтними та антикоагулянтними шляхами. **Висновки.** Індукована L-NAME прееклампсія у щурів призвела до вираженого дисбалансу гемостатичної системи та відтворила ключові патофізіологічні особливості прееклампсії, включаючи надмірне прокоагулянтне зміщення, внутрішньосудинне утворення тромбіну та порушення антикоагулянтних механізмів, що робить цю модель цінним інструментом для вивчення механізмів прогресування захворювання. Аналіз параметрів гемостазу в цій моделі показує, що розчинний фібрин, протеїн С та антитромбін III є найбільш інформативними маркерами для оцінки ризику внутрішньосудинного згортання крові під час прееклампсії.

Ключові слова: прееклампсія, L-NAME індукована прееклампсія, коагуляція, тромбоз, розчинний фібрин, фібриноген, протеїн С, антитромбін III.

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