World Bulletin of Social Sciences (WBSS)
Available Online at: https://www.scholarexpress.net
Vol. 49, August 2025
ISSN: 2749-361X

BEYOND STANDARD RISK FACTORS: THE GENETIC AND ANAMNESTIC PROFILE OF PATIENTS WITH SEVERE PREECLAMPSIA IN THE UZBEK POPULATION

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Article history:

Received: 28th June 2025
Accepted: 26th July 2025

Abstract:

Objective: To analyze the clinical-demographic characteristics, latent risk factors, and genetic predictors of severe preeclampsia (PE) as a form of secondary thrombotic microangiopathy (TMA).

Materials and Methods: The study was conducted on a cohort of 327 patients with severe PE, accounting for 87.4% of all TMA cases in the study group, and a control group of 50 women with physiological pregnancies. The research included a detailed analysis of medical history, clinical and laboratory parameters, obstetric outcomes, and the prevalence of thrombophilia gene polymorphisms, including F5 Leiden (G1691A), F2 (G20210A), MTHFR (C677T, A1298C), and AGTR1/AGTR2.

Results: Severe PE was characterized by an earlier gestational age at delivery, lower neonatal birth weight and length, elevated liver enzymes, hemolytic anemia, and thrombocytopenia. Genetic analysis revealed a high frequency of carrier status for the mutant F5 Leiden and MTHFR C677T alleles among patients with severe PE, confirming the role of hereditary thrombophilia in the pathogenesis of this complication.

Conclusion: The identified clinical and genetic associations underscore the need for early screening of pregnant women for thrombophilias and more intensive dynamic monitoring in high-risk groups to prevent life-threatening complications.

Keywords: Preeclampsia, thrombotic microangiopathy, pregnancy, thrombophilia, F5 Leiden, MTHFR C677T, obstetric complications, placental insufficiency

INTRODUCTION

Severe preeclampsia (PE) is one of the most common and clinically significant obstetric complications, representing a multisystem disorder that develops after 20 weeks of gestation. Globally, PE remains a leading cause of maternal and perinatal morbidity and mortality **[1]**. In the context of thrombotic microangiopathies (TMAs), severe PE often acts as the primary etiological trigger for secondary TMAs in pregnant women. In our study cohort of patients with TMA, the severe PE group was the largest subgroup (n=327), corresponding to 87.4% of all TMA cases, which highlights the high relevance of this condition.

The diagnosis of severe PE in our study was established in accordance with current international clinical guidelines **[2]**. The key criteria included the onset of hypertension (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥110 mm Hg) and/or proteinuria (≥3.0 g/24 hours or ≥3+ on dipstick) after 20 weeks of gestation, combined with one or more signs of organ dysfunction, such as thrombocytopenia (<150x10⁹/L), elevated liver transaminases, renal insufficiency, or neurological symptoms. However, as our study revealed, the key clinical challenge is not the initial diagnosis of PE, but rather the assessment of the latent risk of its malignant transformation into more fulminant forms of TMA **[3]**.

MATERIALS AND METHODS

A prospective comparative study was conducted at the Center for the Development of Professional Qualifications of Medical Workers (Tashkent, Uzbekistan) from 2020 to 2025. The study included 377 patients divided into two groups. The main group consisted of 327 pregnant women with a diagnosis of severe PE, verified according to current international clinical guidelines **[2]**. The control group comprised 50 women with physiological singleton pregnancies that resulted in term deliveries without obstetric or perinatal complications.

Inclusion criteria for the main group were a gestational age >20 weeks and signs of severe PE. Exclusion criteria included primary forms of TMAs, severe extragenital pathology in a decompensated state, and patient refusal to participate. All participants provided informed consent.

A comprehensive analysis was performed, including detailed collection of clinical and anamnestic data, laboratory tests (complete blood count, biochemical

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profile, coagulation panel), Doppler ultrasonography of uteroplacental and fetal circulation, and molecular genetic testing for polymorphisms in the F5 Leiden (G1691A), F2 Prothrombin (G20210A), MTHFR (C677T, A1298C), and AGTR1/AGTR2 genes. Statistical analysis was performed using SPSS v.27.0. The Mann-Whitney U test was used for comparing quantitative data, and the χ^2 test (with Fisher's exact test where appropriate) was used for qualitative data. Differences were considered statistically significant at $p<0.05$.

RESULTS

Clinical and Demographic Characteristics: The analysis showed that patients with severe PE were comparable in age to healthy pregnant women (median age 27.0 years in both groups; $p=0.224$), which excludes age as a confounding factor. However, there were highly significant differences across all key obstetric outcomes. The gestational age at delivery in the PE group (median 36.0 [35.00-38.00] weeks) was significantly lower than in the control group (median 39.0 [38.25-40.00] weeks; $p<0.001$). This was accompanied by a critical reduction in neonatal anthropometric parameters (median birth weight 2550.0 g vs. 3410.0 g; median length 48.0 cm vs. 53.0 cm; $p<0.001$ for both).

Anamnestic Profile and Latent Predictors: An in-depth analysis revealed a significantly burdened medical history in patients with PE. The frequency of chronic hypertension in their history reached 88.4% (vs. 28.0% in controls; $p<0.001$), which is a powerful independent risk factor according to large meta-analyses **[4]**. A positive family history of thrombosis (38.5% vs. 0%; $p<0.001$), recurrent pregnancy loss (61.8% vs. 0%; $p<0.001$), and preeclampsia in previous pregnancies (50.8% vs. 0%; $p<0.001$) also acted as strong predictors, indicating that severe PE develops in patients with a pre-existing compromised somatic and obstetric status.

Genetic Profile: Patients with PE were characterized by a statistically significantly higher carrier frequency of mutant alleles in genes associated with thrombophilia and vascular tone regulation. Carrier status for the **F5 Leiden** mutation was found in 55.3% of PE patients (vs. 12.0% in controls; $p<0.001$), for **MTHFR C677T** in 63.7% (vs. 14.0% in controls; $p<0.001$), and for **AGTR2 G1675A** in 52.9% (vs. 8.0% in controls; $p<0.001$). These genetic features act as latent predictors that determine an individual's susceptibility to developing PE.

Laboratory and Instrumental Profile: There was a significant decrease in platelet count (Median 181.0 vs. 233.5 $x10^9$/L; $p<0.001$), and an increase in LDH (Median 280.0 vs. 212.0 U/L; $p<0.001$) and homocysteine levels (Median 16.0 vs. 9.49 µmol/L; $p<0.001$), reflecting systemic damage. Doppler ultrasonography revealed a significant increase in the pulsatility index in the uterine arteries (Median 1.43 vs. 0.68; $p<0.001$), indicating severe impairment of uteroplacental perfusion.

DISCUSSION AND CONCLUSION

The data obtained in this study confirm the multifactorial nature of severe PE as a clinical manifestation of TMA. The combination of identified factors indicates that the development of PE is driven by a complex interplay of hereditary predisposition, underlying vascular pathology, and obstetric history.

The F5 Leiden and MTHFR C677T mutations demonstrated the greatest clinical significance in our study, being significantly more prevalent in the main group. These polymorphisms play a key role in the mechanisms of hypercoagulation, hyperhomocysteinemia, and endothelial dysfunction, which underlie the microangiopathic damage to the uteroplacental vasculature **[5]**. Our findings are consistent with the results of large meta-analyses, which emphasize that the presence of these polymorphisms increases the risk of PE by 2- to 3-fold, especially when combined with a burdened medical history **[6]**.

The high carrier frequency of mutations in the renin-angiotensin system genes (AGTR1, AGTR2), associated with impaired vascular tone and persistent endothelial inflammation, also contributes to the worsening of placental perfusion. These genetically determined impairments, coupled with morphologically confirmed decidual vasculopathy and extensive placental thrombosis, confirm a direct link between the genetic background and the morphological manifestations of PE **[7]**.

A comparative analysis of obstetric outcomes showed marked differences in gestational age at delivery and neonatal anthropometric parameters, which correlates with data from leading international organizations such as the American College of Obstetricians and Gynecologists (ACOG) **[8]**. These organizations highlight the need for risk stratification and early initiation of preventive antithrombotic therapy in patients with thrombophilia factors.

Thus, our study demonstrates that integrating molecular genetic markers into clinical practice can facilitate the early identification of high-risk groups and the development of targeted approaches to prevent thrombotic complications. A comprehensive approach that includes the analysis of not only clinical and obstetric data but also hereditary thrombophilias is the foundation for personalized medicine in obstetrics.

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REFERENCES

1. Poon L.C., Shennan A., Hyett J.A., Kapur A., Hadar E., Divakar H., et al. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention. *International Journal of Gynecology & Obstetrics*. 2019;145(Suppl 1):1-33.
2. Magee L.A., Brown M.A., Hall D.R., Gupte S., Hennessy A., Karumanchi S.A., et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. *Hypertension*. 2022;79(4):1017-1043.
3. Gupta M., Feinberg B.B., Burwick R.M. Thrombotic microangiopathies of pregnancy: Differentiating severe preeclampsia, HELLP syndrome, and thrombotic thrombocytopenic purpura. *Pregnancy Hypertension*. 2018;12:173-178.
4. Bramham K., Parnell B., Nelson-Piercy C., Seed P.T., Poston L., Chappell L.C. Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis. *BMJ*. 2014;348:g2301.
5. Robertson L., Wu O., Langhorne P., Twaddle S., Clark P., Lowe G.D., et al. Thrombophilia in pregnancy: a systematic review. *British Journal of Haematology*. 2006;132(2):171-196.
6. Lin R., Lim K. Factor V Leiden, prothrombin G20210A, and MTHFR C677T mutations and preeclampsia: a meta-analysis. *Journal of Maternal-Fetal & Neonatal Medicine*. 2017;30(16):1930-1939.
7. Staff A.C. The two-stage placental model of preeclampsia: An update. *Journal of Reproductive Immunology*. 2019;134-135:1-10.
8. American College of Obstetricians an