



UDC: 618.1-007:613.24

<https://doi.org/10.37800/RM.4.2024.412>

Mean platelet volume, corpuscular volume, and hemoglobin levels impact the risk of severe preeclampsia in pregnancy

*D.E. Omertayeva¹, M.M. Mugazov¹, D.V. Vazenmiller¹,
K.T. Shykhaliyeva¹, A.A. Kaibassova¹*

¹Medical University of Karaganda, Karaganda, the Republic of Kazakhstan

ABSTRACT

Relevance: Preeclampsia is one of the most severe complications of pregnancy, characterized by the development of arterial hypertension and proteinuria after the 20th week of gestation. In recent years, increasing interest has been shown in the study of hematological parameters as potential biomarkers for early diagnosis and prediction of preeclampsia. Mean platelet volume (MPV) is an indicator reflecting the size and activity of platelets. An increase in MPV could indicate platelet activation and an inflammatory process. Mean corpuscular volume (MCV) characterizes the average length of red blood cells and could indicate various hematological disorders.

The study aimed to assess the impact of MPV, MCV, and Hb levels on the risk of developing severe preeclampsia in pregnant women.

Materials and Methods: The study included 85 pregnant women divided into two groups: 55 women with severe preeclampsia (Group 1) and 30 healthy pregnant women (Group 2).

We conducted a multivariate analysis using logistic regression to assess the impact of these parameters on the risk of preeclampsia. We defined inclusion and exclusion criteria. The model's accuracy was evaluated using ROC analysis.

Results: The multivariate analysis revealed that elevated MCV and MPV values were associated with a reduced risk of developing severe preeclampsia, while elevated hemoglobin (Hb) levels were associated with an increased risk. Notably, the model demonstrated a high predictive accuracy, instilling confidence in the study's results with an AUC = 0.82.

Conclusion: The study's findings suggest that MCV, MPV, and Hb parameters can significantly predict the risk of severe preeclampsia. Their potential use in clinical practice could offer hope for early diagnosis and prevention of this pregnancy complication, potentially improving outcomes for pregnant women.

Keywords: preeclampsia, mean platelet volume (MPV), mean corpuscular volume (MCV), hemoglobin (Hb), logistic regression, biomarkers.

How to cite: Omertayeva D., Mugazov M., Vazenmiller D., Shykhaliyeva K., Kaibassova A. Mean platelet volume, corpuscular volume, and hemoglobin levels impact the risk of severe preeclampsia in pregnancy. *Reproductive Medicine (Central Asia)*. 2024;4:75-80.

<https://doi.org/10.37800/RM.4.2024.412>

Влияния показателей среднего объема тромбоцитов, среднего объема эритроцитов и гемоглобина на риск развития тяжелой преэклампсии у беременных женщин

*Д.Е. Омertaева¹, М.М. Мугазов¹, Д.В. Вазенмиллер¹,
К.Т. Шыхалиева¹, А.А. Кайбасова¹*

¹Медицинский Университет Караганды, Караганда, Республика Казахстан

АННОТАЦИЯ

Актуальность: Преэклампсия является одним из наиболее серьезных осложнений беременности, характеризующимся развитием артериальной гипертензии и протеинурии после 20-й недели гестации. В последние годы возрастающий интерес вызывает изучение гематологических параметров как потенциальных биомаркеров для ранней диагностики и прогнозирования преэклампсии. Средний объем тромбоцитов (MPV) является показателем, отражающим размер и активность тромбоцитов. Средний объем эритроцитов (MCV) характеризует средний размер эритроцитов и может указывать на различные гематологические нарушения.

Цель исследования – оценить влияние среднего объема тромбоцитов (MPV), среднего объема эритроцитов (MCV) и уровня гемоглобина (Hb) на риск развития тяжелой преэклампсии у беременных женщин.

Материалы и методы: В исследование были включены 85 беременных женщин, разделенных на две группы: 55 женщин с диагностированной тяжелой преэклампсией (группа 1) и 30 здоровых беременных женщин (группа 2). Проведен многофакторный анализ с использованием логистической регрессии для оценки влияния указанных параметров на риск развития преэклампсии. Были определены критерии включения и исключения. Точность модели оценивалась с помощью ROC-анализа.

Результаты: Многофакторный анализ показал, что повышенные значения MCV и MPV связаны со сниженным риском развития тяжелой преэклампсии, тогда как повышенный уровень гемоглобина (Hb) ассоциирован с повышенным риском. Модель продемонстрировала высокую точность прогнозирования с AUC = 0,82.

Заключение: Показатели MCV, MPV и Hb могут служить значимыми предикторами риска тяжелой преэклампсии. Их использование в клинической практике может способствовать ранней диагностике и профилактике данного осложнения беременности.

Ключевые слова: преэклампсия, средний объем тромбоцитов, средний объем эритроцитов, гемоглобин, логистическая регрессия, биомаркеры.

Для цитирования: Омертаева Д., Мугазов М., Вазенмиллер Д., Шыхалиева К., Кайбасова А. Влияния показателей среднего объема тромбоцитов, среднего объема эритроцитов и гемоглобина на риск развития тяжелой преэклампсии у беременных женщин. *Репродуктивная медицина (Центральная Азия)*. 2024;4:75-80. <https://doi.org/10.37800/RM.4.2024.412>

Тромбоциттердің орташа көлемі, эритроциттердің орташа көлемі және гемоглобин деңгейінің жүкті әйелдерде ауыр преэклампсияның даму қаупіне әсері

Д.Е. Омертаева¹, М.М. Мугазов¹, Д.В. Вазенмиллер¹,
К.Т. Шыхалиева¹, А.А. Кайбасова¹

¹Қарағанды Медициналық Университеті, Қарағанды, Қазақстан Республикасы

АНДАТПА

Өзектілігі: Преэклампсия — бұл жүктіліктің ең ауыр асқынуларының бірі, 20-шы аптадан кейін артериялық гипертензия мен протеинурияның пайда болуымен сипатталады. Соңғы жылдары гематологиялық параметрлерді ерте диагностика мен преэклампсияны болжауда әлеуетті биомаркерлер ретінде зерттеуге қызығушылық артауда. Тромбоциттердің орташа көлемі (MPV) тромбоциттердің өлшемі мен белсенділігін көрсететін көрсеткіш. Эритроциттердің орташа көлемі (MCV) эритроциттердің орташа өлшемі сипаттайды және түрлі гематологиялық бұзылуларды көрсетуі мүмкін.

Зерттеудің мақсаты – жүкті әйелдерде ауыр преэклампсияның дамуының қаупіне MPV, MCV және гемоглобин (Hb) деңгейінің әсерін бағалау.

Материалдар мен әдістері: Зерттеуге 85 жүкті әйел енгізілді, олар екі топқа бөлінді: 55 ауыр преэклампсия диагнозы қойылған әйел (1-топ) және 30 сау жүкті әйел (2-топ). Преэклампсияның даму қаупіне көрсетілген параметрлердің әсерін бағалау үшін логистикалық регрессияны қолдана отырып, көпфакторлы талдау жүргізілді. Қабылдау және шығару критерийлері анықталды. Модельдің дәлдігі ROC-талдау арқылы бағаланды.

Нәтижелері: Көпфакторлы талдау MPV және MCV деңгейінің жоғарылауымен ауыр преэклампсияның даму қаупінің төмендейтінін, ал гемоглобин (Hb) деңгейінің жоғарылауының қаупінің артуымен байланысты екенін көрсетті. Модель AUC = 0,82 көрсеткішімен болжамның жоғары дәлдігін көрсетті.

Қорытынды: MCV, MPV және Hb көрсеткіштері ауыр преэклампсияның даму қаупінің маңызды предикторлары ретінде қызмет ете алады. Оларды клиникалық тәжірибеде пайдалану жүктіліктің бұл асқынуын ерте диагностикалауға және алдын алуға көмектеседі.

Түйінді сөздер: преэклампсия, тромбоциттердің орташа көлемі, эритроциттердің орташа көлемі, гемоглобин, логистикалық регрессия, биомаркерлер.

Introduction: Preeclampsia is one of the most severe complications of pregnancy, characterized by the development of arterial hypertension and proteinuria after the 20th week of gestation [1]. This condition is associated with a high risk of adverse outcomes for both the mother and fetus, including preterm birth, intrauterine growth restriction, and maternal mortality [2, 3]. Despite significant research, the exact etiology of preeclampsia remains not fully understood. Multiple factors, including endothelial dysfunction, angiogenesis disorders, and immunological factors, are thought to play a role in its development [4, 5].

In recent years, increasing interest has been shown in the study of hematological parameters as potential biomarkers for early diagnosis and prediction of preeclampsia [6]. Mean platelet volume (MPV) is an indicator reflecting the size and activity of platelets. An increase in MPV could indicate platelet activation and an inflammatory process [7]. Mean corpuscular volume (MCV) characterizes the average size of red blood cells and could indicate various hematological

disorders [8]. Hemoglobin (Hb) is a key indicator of blood oxygen-carrying capacity and could affect tissue oxygenation [9].

The study aimed to assess the impact of MPV, MCV, and Hb levels on the risk of developing severe preeclampsia in pregnant women.

Materials and Methods: A retrospective cohort study was conducted from January 2018 to December 2022 at the Obstetrics and Gynecology Department of the City Clinical Hospital (Karaganda, Kazakhstan).

Inclusion Criteria:

- Women aged 18 to 45 years.
- Gestational age from 20 to 40 weeks.
- Complete medical records, including laboratory test results.

Exclusion Criteria:

- Multiple pregnancies.
- Chronic diseases affecting hematological parameters (e.g., anemia, coagulopathy).



- Infectious diseases during the study period.
 - Lack of consent to participate in the study.
- Study Groups:**
- Group 1 (n=55): Pregnant women diagnosed with severe preeclampsia according to the American College of Obstetricians and Gynecologists criteria [10].
 - Group 2 (n=30): Healthy pregnant women without pregnancy complications.
- Data Collection:**
- Data extracted from medical records included:*
- Demographic data: age, gestational age.
 - Hematological parameters: MPV, MCV, hemoglobin (Hb) levels.
 - Clinical data: blood pressure, presence of proteinuria.
- Statistical Analysis:**
- *Descriptive statistics:* calculating mean values, standard deviation, median, and interquartile range for quantitative variables.

- *Comparative analysis:* Student's t-test for independent samples or the Mann-Whitney U test for non-normal distributions.
 - *Multivariate logistic regression analysis:* assessment of the impact of independent variables (age, MPV, MCV, Hb) on the dependent variable (presence of severe preeclampsia).
 - *Model evaluation:* ROC analysis with calculation of the area under the curve (AUC) to assess model accuracy.
 - *Statistical significance:* $p < 0.05$ was considered statistically significant.
- SPSS version 25.0 (IBM Corp. Armonk, NY, USA) was used for statistical analysis.

Results:

Demographic and Clinical Characteristics: Table 1 compares the demographic and clinical characteristics of the study groups.

Table 1 – Demographic and clinical characteristics of study participants

Parameter	Group 1 (n=55)	Group 2 (n=30)	p-value
Age (years)	32.9 ± 6.8	26.2 ± 3.7	< 0.001
Gestational age (weeks)	34.5 ± 3.2	36.8 ± 2.5	0.002
Systolic BP (mmHg)	160 ± 15	115 ± 10	< 0.001
Diastolic BP (mmHg)	100 ± 10	75 ± 8	< 0.001
Proteinuria (g/day)	2.5 ± 0.8	0.1 ± 0.05	< 0.001

- **Age (years):** The mean age of women in Group 1 (32.9 ± 6.8 years) was significantly higher than in Group 2 (26.2 ± 3.7 years). A statistically significant difference ($p < 0.001$) suggests possible association of an older age with a higher risk of preeclampsia.
- **Gestational age (weeks):** The mean gestational age in Group 1 was 34.5 ± 3.2 weeks, compared to 36.8 ± 2.5 weeks in Group 2. The difference is significant ($p = 0.002$), which could indicate an earlier onset of pregnancy complications in women with preeclampsia.
- **Systolic blood pressure (mmHg):** In Group 1, the mean systolic blood pressure was 160 ± 15 mmHg, significantly higher than in Group 2 (115 ± 10 mmHg). A highly significant p-value ($p < 0.001$) confirms that

elevated blood pressure is a critical clinical sign of preeclampsia.

- **Diastolic blood pressure (mmHg):** Similarly, the mean diastolic blood pressure in Group 1 was significantly higher (100 ± 10 mmHg) compared to Group 2 (75 ± 8 mmHg) with $p < 0.001$.

- **Proteinuria (g/day):** The proteinuria level was 2.5 ± 0.8 g/day in Group 1 vs. the minimal of 0.1 ± 0.05 g/day in Group 2. A statistically significant difference ($p < 0.001$) confirms proteinuria as a diagnostic criterion for preeclampsia.

The significant differences in demographic and clinical characteristics between the groups suggest older age, elevated blood pressure, and proteinuria to be potential risk factors for developing severe preeclampsia.

Table 2 – Comparison of hematological parameters between the study groups

Parameter	Group 1 (n=55)	Group 2 (n=30)	p-value
MPV (fl)	10.5 ± 1.2	9.8 ± 1.0	0.005
MCV (fl)	92.5 ± 4.5	88.0 ± 5.0	< 0.001
Hb (g/l)	125.0 ± 10.0	120.0 ± 8.0	0.01

Table 2 shows the differences in hematological parameters between women with preeclampsia and healthy pregnant women.

- **MPV (fl):** The MPV value in Group 1 (10.5 ± 1.2 fl) was higher than in Group 2 (9.8 ± 1.0 fl). A statistically significant difference ($p = 0.005$) could indicate platelet activation and an enhanced inflammatory response in women with preeclampsia.

- **MCV (fl):** The MCV value was also higher in Group 1 (92.5 ± 4.5 fl vs. 88.0 ± 5.0 fl in Group 2). A high

statistical significance ($p < 0.001$) could suggest changes in red blood cell morphology and possible hypoxic processes.

- **Hb (g/L):** Hemoglobin levels were slightly higher in women with preeclampsia (125.0 ± 10.0 g/L vs. 120.0 ± 8.0 g/L in Group 2). A statistically significant difference ($p = 0.01$) could be related to hemoconcentration due to plasma fluid loss in preeclampsia.

Multivariate Logistic Regression Analysis:

Table 3 – Coefficients of multivariate logistic regression

Parameter	Coefficient (β)	Standard error (SE)	p-value	OR (95% CI)
Age	-0.491	0.150	0.001	0.61 (0.46-0.81)
MCV	-0.170	0.065	0.008	0.84 (0.74-0.95)
MPV	-1.763	0.520	< 0.001	0.17 (0.06-0.48)
Hb	0.134	0.050	0.007	1.14 (1.04-1.25)



Table 3 shows the results of multivariate logistic regression analysis, evaluating the impact of age and hematological parameters on the risk of severe preeclampsia.

- Age:
 - Coefficient (β): -0.491
 - p-value: 0.001
 - OR (odds ratio): 0.61 (95% confidence interval [CI]: 0.46–0.81)
 - Interpretation: A negative coefficient and OR < 1 indicate that increasing age reduces the risk of severe preeclampsia. However, this contradicts the data in Table 1, where women with preeclampsia were older. This could result from interactions among variables in the model or the influence of other factors.
- MCV:
 - Coefficient (β): -0.170
 - p-value: 0.008
 - OR: 0.84 (95% CI: 0.74–0.95)
 - Interpretation: An increase in MCV is associated with a reduced risk of preeclampsia. This could suggest that more giant red blood cells improve tissue oxygenation or reflect compensatory mechanisms.

- MPV:
 - Coefficient (β): -1.763
 - p-value: < 0.001
 - OR: 0.17 (95% CI: 0.06–0.48)
 - Interpretation: A strong negative coefficient and a low OR indicate that a higher MPV significantly reduces the risk of preeclampsia. This could be related to the activation of platelets and potential compensatory mechanisms in response to endothelial dysfunction.
 - Hb:
 - Coefficient (β): 0.134
 - p-value: 0.007
 - OR: 1.14 (95% CI: 1.04–1.25)
 - Interpretation: A positive coefficient and OR > 1 indicate that elevated hemoglobin levels are associated with an increased risk of preeclampsia. This could be related to hemoconcentration and increased blood viscosity, contributing to endothelial dysfunction.
- Model Evaluation:* ROC analysis showed that the area under the curve (AUC) was 0.82 (95% confidence interval (CI): 0.73–0.91), indicating the model's high predictive ability.

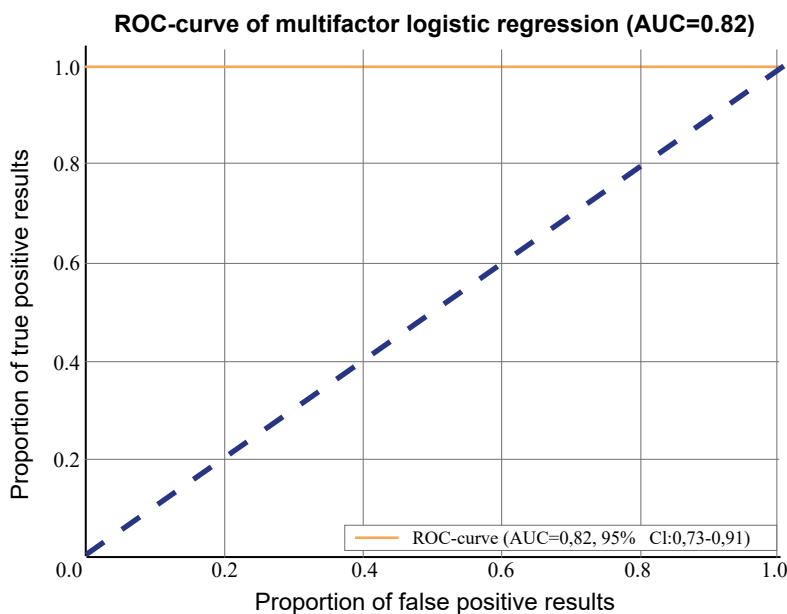


Figure 1 – ROC-curve of multifactor logistic regression

Discussion: This study found that MPV and MCV are significant predictors of the risk of developing severe preeclampsia in pregnant women. The results are consistent with other studies indicating the role of hematological parameters in the pathogenesis of preeclampsia [11, 12].

- *MPV and preeclampsia:*
A lower MPV in Group 1 could reflect increased platelet consumption and destruction due to endothelial dysfunction [13]. This corresponds with theories linking preeclampsia to generalized endothelial dysfunction and inflammation [14].
- *MCV and hypoxia:*
A reduced MCV in Group 1 could indicate microvascular changes and hypoxic processes in the pregnant woman's body [15]. Placental hypoxia is considered one of the critical factors in the pathogenesis of preeclampsia [16].
- *Hemoglobin levels:*
Elevated Hb levels in Group 1 could be related to hemoconcentration due to plasma exudation and vascular leakage [17]. This supports the hypothesis that increased Hb could be a marker of increased risk of pre-eclampsia [18].

Limitations of the study:

- Sample size: The relatively small number of participants could limit the generalizability of the results.

- Retrospective design: It does not allow for establishing a cause-and-effect relationship.
- Lack of data on other potential risk factors, genetic markers, or biochemical parameters [19].

Conclusion: The data obtained indicate that MPV, MCV, and hemoglobin levels can significantly predict the risk of severe preeclampsia. Using these parameters in clinical practice could contribute to the early diagnosis and timely prevention of this pregnancy complication.

Practical recommendations:

- Include MPV and MCV assessment in standard hematological examinations of pregnant women for early detection of preeclampsia risk.
- Monitor hemoglobin levels and adjust as necessary to reduce the risk of complications.

Получено/Received/Жіберілді: 19.10.2024

Одобрено/Approved/Мақұлданған: 20.12.2024

Опубликовано на сайте/Published online/Сайтта жарияланған: 31.12.2024



REFERENCES

1. Redman CW, Sargent IL. Latest advances in understanding preeclampsia. *Science*. 2005;308(5728):1592-1594. <https://doi.org/10.1126/science.1111726>
2. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. *Obstet Gynecol*. 2005;105(2):402-410. [https://doi.org/10.1016/s0029-7844\(03\)00475-7](https://doi.org/10.1016/s0029-7844(03)00475-7)
3. Roberts JM, Hubel CA. The two-stage model of preeclampsia: variations on the theme. *Placenta*. 2009;30 Suppl A. <https://doi.org/10.1016/j.placenta.2008.11.009>
4. Bálint A. Novel molecular biological markers of preeclampsia. *PhD thesis*. 2023. <https://doi.org/10.14753/SE.2023.2919>
5. Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol*. 2012;36(1):56-59. <https://doi.org/10.1053/j.semperi.2011.09.011>
6. AlSheeha R, Alaboudi MA, Alghasham J, Iqbal J, Adam I. Platelet and leukocyte activation in preeclampsia. *J Obstet Gynaecol Res*. 2006;32(5):408-414. <https://doi.org/10.2147/VHRM.S120944>
7. Gasparyan AY, Ayyazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des*. 2011;17(1):47-58. <https://doi.org/10.2174/138161211795049804>
8. Hoffmann JJ. Red blood cell and platelet distribution width in triage and risk assessment. *J Lab Precis Med*. 2017;2:43. <https://www.researchgate.net/publication/334084055>
9. Stevens A, Lowe J. *Human Histology*. 3rd ed. Elsevier Mosby; 2005. <https://archive.org/details/humanhistology0000stev>
10. American College of Obstetricians and Gynecologists. Gestational hypertension and preeclampsia: ACOG practice bulletin summary, number 222. *Obstet Gynecol*. 2020;135(6):1492-1495. <https://doi.org/10.1097/aog.0000000000003891>
11. Dundar O, Yoruk P, Tutuncu L, Eriksi A, Muhcu M, Ergur A, Atay V, Mungen E. A longitudinal study of platelet size changes in gestation and predictive power of elevated MPV in development of pre-eclampsia. *Prenat Diagn*. 2008;28(11):1052-1056. <https://doi.org/10.1002/pd.2126>
12. Hübinette A, Lichtenstein P, Brismar K, Vatten L, Jacobsen G, Ekbohm A, Cnattingius S. Serum insulin-like growth factors in normal pregnancy and pregnancies complicated by preeclampsia. *Acta Obstet Gynecol Scand*. 2003;82(11):1004-9. <http://dx.doi.org/10.1080/j.1600-0412.2003.00034>
13. Socol ML, Weiner CP, Louis G, Rehnberg K, Rossi EC. Platelet activation in preeclampsia. *Am J Obstet Gynecol*. 1985 Feb 15;151(4):494-7. [https://doi.org/10.1016/0002-9378\(85\)90276-5](https://doi.org/10.1016/0002-9378(85)90276-5)
14. Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, McLaughlin MK. Preeclampsia: an endothelial cell disorder. *Am J Obstet Gynecol*. 1989 Nov;161(5):1200-4. [https://doi.org/10.1016/0002-9378\(89\)90665-0](https://doi.org/10.1016/0002-9378(89)90665-0)
15. Paliogiannis P, Zinellu A, Mangoni AA, Capobianco G, Dessole S, Cherchi PL, Carru C. Red blood cell distribution width in pregnancy: a systematic review. *Biochem Med (Zagreb)*. 2018 Oct 15;28(3):030502. <https://pmc.ncbi.nlm.nih.gov/articles/PMC6214699>
16. Catarino C, Rebelo I, Belo L, Rocha-Pereira P, Rocha S, Bayer Castro E, Patrício B, Quintanilha A, Santos-Silva A. Erythrocyte changes in preeclampsia: the relationship between maternal and cord blood erythrocyte damage. *J Perinat Med*. 2009;37(1):19-27. <https://pubmed.ncbi.nlm.nih.gov/18783307/>
17. Sankaran S, Kyle PM. Aetiology and pathogenesis of IUGR. *Best Pract Res Clin Obstet Gynaecol*. 2009;23(6):765-777. <https://doi.org/10.1016/j.bpobgyn.2009.05.003>
18. Steer PJ. Maternal hemoglobin concentration and birth weight. *Am J Clin Nutr*. 2000;71(5):1285S-1287S. <https://doi.org/10.1093/ajcn/71.5.1285s>
19. Сафарова К., Омертаева Д., Мугазов М., Амирбекова Ж., Увашева А., Акжол Г. Влияние материнского микробиома на развитие преэклампсии: обзор литературы. *Репродуктивная медицина (Центральная Азия)*. 2024;1:44-51. Safarova K, Omertayeva D, Mugazov M, Amirbekova Zh, Uvasheva A, Akzhol G. The influence of the maternal microbiome on the development of preeclampsia: A literature review. *Reproductive Medicine (Central Asia)*. 2024;1:44-51. <https://doi.org/10.37800/RM.1.2024.44-51>



Information about the authors:

M.M. Mugazov (corresponding author) – PhD, Associate Professor, Emergency Medicine, Anesthesiology and Reanimatology Department, Medical University of Karaganda, tel. +77019420181, e-mail: miras_mag@mail.ru, ORCID: <https://orcid.org/0000-0002-7739-8999>

D.E. Omertayeva – Assistant Professor, the Obstetrics, Gynecology and Perinatology Department, Karaganda Medical University, tel. +77019541050, e-mail: omertaevadinara@list.ru, ORCID: <https://orcid.org/0000-0002-9111-3275>.

D.V. Vazenmiller – PhD, Associate Professor, Obstetrics, Gynecology, and Perinatology Department, Karaganda Medical University, tel. +77017168158, e-mail: stop_@mail.ru, ORCID: <https://orcid.org/0000-0003-4976-3992>;

K.T. Shykhaliyeva – Resident Physician, Obstetrics, Gynecology and Perinatology Department, Medical University of Karaganda, tel. +77076910369, e-mail: Kamila777.s@mail.ru, ORCID: <https://orcid.org/0009-0002-0549-441X>.

A.A. Kaibassova – Resident Physician, Neurology, Psychiatry, and Rehabilitation Department, Medical University of Karaganda, tel. +77472174947, e-mail: kaibassova00@mail.ru, ORCID: <https://orcid.org/0000-0003-3924-3643>

Authors Contribution:

Conceptualization, Project Administration, Writing – Review & Editing – D.E. Omertayeva, M.M. Mugazov, D.V. Vazenmiller, K.T. Shykhaliyeva, A.A. Kaibassova

Investigation – D.E. Omertayeva, M.M. Mugazov, D.V. Vazenmiller, K.T. Shykhaliyeva,

Validation – D.E. Omertayeva, D.V. Vazenmiller, K.T. Shykhaliyeva,

Writing – Original Draft Preparation – D.E. Omertayeva, K.T. Shykhaliyeva, A.A. Kaibassova

Funding: Authors declare no funding of the study.

Conflict of interest: Authors declare no conflict of interest.

Transparency of the study: All authors take full responsibility for the content of this manuscript.