ROLE OF ENDOTHELIAL DYSFUNCTION IN THE DEVELOPMENT OF HYPERTENSIVE RETINOPATHY

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Annotation. *Endothelial dysfunction (ED) plays a central role in the pathophysiology of hypertensive retinopathy, serving as an early marker and a contributing mechanism in the microvascular damage associated with chronic hypertension. This study investigates the correlation between systemic endothelial dysfunction markers—such as nitric oxide (NO), endothelin-1 (ET-1), and vascular endothelial growth factor (VEGF)—and the progression of hypertensive retinopathy in patients at different stages of arterial hypertension. A total of 120 hypertensive patients were examined using clinical, laboratory, and ophthalmologic methods including fundus photography, optical coherence tomography (OCT), and measurement of plasma biomarkers. The results demonstrated a strong association between impaired endothelial homeostasis and retinal microangiopathy, confirming that endothelial dysfunction precedes visible retinal changes. Early detection and correction of endothelial dysfunction may thus serve as an effective strategy for preventing or slowing hypertensive retinopathy progression, preserving vision, and reducing cardiovascular risk.*

Keywords: *endothelial dysfunction, hypertensive retinopathy, nitric oxide, endothelin-1, VEGF, microcirculation, vascular remodeling.*

Introduction Hypertensive retinopathy represents one of the most common microvascular complications of systemic arterial hypertension. It reflects the structural and functional changes in the retinal circulation that occur due to chronic elevation of blood pressure. Among the various mechanisms involved, endothelial dysfunction has emerged as a key pathophysiological link between systemic hypertension and retinal vascular damage.

The vascular endothelium is responsible for maintaining vascular tone, permeability, and hemostasis through the release of vasoactive substances such as nitric oxide (NO) and endothelin-1 (ET-1). In the hypertensive state, increased oxidative stress and reduced bioavailability of NO lead to endothelial dysfunction, promoting vasoconstriction, inflammation, and vascular remodeling. These alterations contribute to the narrowing of retinal arterioles, increased vascular permeability, and the development of hemorrhages, microaneurysms, and exudates typical of hypertensive retinopathy.

Moreover, elevated levels of VEGF further exacerbate vascular leakage and neovascularization in severe cases. Understanding the role of endothelial dysfunction in the onset and progression of hypertensive retinopathy is crucial for identifying early diagnostic markers and therapeutic targets. This study aims to evaluate endothelial biomarkers and correlate them with clinical and ophthalmologic findings to establish their predictive value in hypertensive retinopathy.

Materials and Methods The study included 120 patients aged 35–70 years diagnosed with essential hypertension, divided into three groups according to the Keith-Wagener-Barker classification of hypertensive retinopathy: Group I (mild, n=40), Group II (moderate, n=40), and Group III (severe, n=40). The control group consisted of 30 normotensive individuals matched by age and gender. Ophthalmologic examination involved visual acuity testing, slit-lamp biomicroscopy, and fundus evaluation using digital fundus photography. Retinal thickness and structural changes were assessed by OCT. Blood samples were collected for measuring plasma NO, ET-1, VEGF, and malondialdehyde (MDA) levels using enzyme-linked immunosorbent assay (ELISA). Endothelial function was also evaluated by flow-mediated dilation (FMD) of the brachial artery using high-resolution ultrasound. Statistical analysis was conducted using SPSS 26.0 with significance set at $p<0.05$. Correlations between endothelial markers and retinopathy grades were determined using Pearson's correlation coefficient, and multivariate regression analysis identified independent predictors of retinal changes.

Results The findings demonstrated a progressive decline in plasma NO levels and FMD percentages with increasing severity of hypertensive retinopathy ($p<0.001$). Mean NO concentration was 42.3±6.1 μmol/L in Group I, 29.8±5.4 μmol/L in Group II, and 21.4±4.9 μmol/L in Group III, compared to 61.2±7.3 μmol/L in the control group. Conversely, ET-1 and VEGF levels showed a significant elevation across groups, indicating heightened vasoconstrictive and angiogenic activity. Mean ET-1 levels increased from 3.2±0.7 pg/mL in controls to 9.1±1.2 pg/mL in Group III ($p<0.001$), while VEGF rose from 122.5±15.6 pg/mL to 268.9±22.3 pg/mL ($p<0.001$). OCT analysis revealed that central retinal thickness increased proportionally with the severity of retinopathy, correlating strongly with VEGF and MDA levels ($r=0.71$, $p<0.01$).

Multivariate analysis identified ET-1 and VEGF as independent predictors of retinal structural alteration. Patients receiving combined antihypertensive and antioxidant therapy showed partial restoration of endothelial function and stabilization of retinal findings over a 12-month follow-up period. These results confirm that systemic endothelial dysfunction not only mirrors but also contributes to the retinal vascular pathology seen in hypertensive retinopathy.

Discussion The data from this study support the hypothesis that endothelial dysfunction is both a biomarker and a pathogenic factor in hypertensive retinopathy. Reduced NO bioavailability and increased ET-1 and VEGF levels create an imbalance between vasodilation and vasoconstriction, leading to microvascular injury. The interplay of oxidative stress, inflammation, and impaired endothelial repair mechanisms accelerates vascular remodeling and disrupts the blood-retina barrier. These processes underlie the morphological features observed in fundus examinations, including arteriolar narrowing, hemorrhages, and exudates. The strong correlation between systemic endothelial markers and retinal damage suggests that endothelial assessment can serve as an early diagnostic tool before visible ocular changes occur. Therapeutic interventions aimed at restoring endothelial function—such as ACE inhibitors, angiotensin receptor blockers, statins, and lifestyle modifications—may offer protective effects on the retinal vasculature.

Additionally, the integration of non-invasive endothelial function testing into routine hypertensive care could improve risk stratification and disease monitoring. Early detection and management of endothelial dysfunction are likely to reduce not only ocular complications but also systemic cardiovascular events, given the shared microvascular pathology.

Conclusion Endothelial dysfunction plays a fundamental role in the pathogenesis of hypertensive retinopathy. The imbalance between vasodilatory and vasoconstrictive factors leads to microvascular remodeling, increased vascular permeability, and progressive retinal damage.

Monitoring biomarkers such as NO, ET-1, and VEGF provides valuable insights into disease progression and treatment response. Early correction of endothelial dysfunction through pharmacologic and lifestyle interventions can prevent or delay retinal complications and improve visual and systemic outcomes in hypertensive patients. Thus, endothelial health should be a primary focus in the prevention and management of hypertensive retinopathy.

References

1. БЕЛКА, F. S. P. C. P. (2022). В ПАТОГЕНЕЗЕ СОСУДИСТЫХ ЗАБОЛЕВАНИЙ ОРГАНА ЗРЕНИЯ У БОЛЬНЫХ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ.
2. Жалалова, Д. З., Кадирова, А. М., & Хамракулов, С. Б. (2021). Исходы герпетических кератоувеитов на фоне лечения препаратом «офтальмоферон» в зависимости от иммунного статуса пациентов. междисциплинарный подход по заболеваниям органов головы и шеи, 103.
3. ЖД, З., and А. БС. "РЕЗУЛЬТАТЫ ОЦЕНКИ УРОВНЯ ЭНДОТЕЛИНА-1 И Д-ДИМЕРОВ В СЛЕЗНОЙ ЖИДКОСТИ У ПАЦИЕНТОВ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ." SCIENTIFIC JOURNAL OF APPLIED AND MEDICAL SCIENCES 3.3 (2024): 300-307.
4. Zhalalova, D. Z. OCT angiography in the assessment of retinal and choreoretinal microcirculation in patients with uncomplicated arterial hypertension International Ophthalmological Congress IOC Tashkent 2021.
5. Zhalalova, D. Z. Evaluation of markers of endothelial dysfunction in tear fluid in patients with arterial hypertension. Journal of Biomedicine in Amaliet. Tashkent-2022, Volume No., No. WITH.
6. Жалалова, Д. З. (2021). Эндотелин-1 ва гомоцистеин даражасини артериал гипертензия фонида тур пардв узгаришларида эндотелиал дисфункциянинг маркерлари сифатида текшириш. Биомедицина ва амалиет журнали, 6(5), 203-210.
7. Jalalova, D., Axmedov, A., Kuryazov, A., & Shernazarov, F. (2022). Combined dental and eye pathology. Science and innovation, 1(8), 91-100.
8. Zhalalova, D. Z. (2022). Pulatov US MICROCIRCULATORY DISORDERS IN THE VASCULAR SYSTEM OF THE BULBAR CONJUNCTIVA WITH INITIAL MANIFESTATIONS OF INSUFFICIENT BLOOD SUPPLY TO THE BRAIN. European journal of molecular medicine, 2(5).
9. Жалалова, Д. З. (2021). ОКТ-ангиография при оценке сосудистого русла сетчатки и хориоидеи. Биология ва тиббиет муаммолари, 6(130), 211-216.
10. Жалалова, Д. З. (2022). Классификационые критерии изменений сосудов сетчатки при артериальной гипертензии. In Международная научная конференция Университетская наука: взгляд в будущее (pp. 56-64).
11. Долиев, М. Н., Тулакова, Г. Э., Кадырова, А. М., Юсупов, З. А., & Жалалова, Д. З. (2016). Эффективность комбинированного лечения пациентов с центральной

серозной хориоретинопатией. Вестник Башкирского государственного медицинского университета, (2), 64-66.
12. Жалалова, Д. З. Оценка маркеров эндотелиальной дисфункции в слезной жидкости у пациентов с артериальной гипертензиейЖурнал «Биомедицина ва амалиет». Тошкент-2022, Том №, №. С.
13. Жалалова, Д. З. (2021). ОКТ-ангиография в оценке ретинальной и хореоретинальной микроциркуляции у пациентов с неосложненой артериальной гипертензией/I Международный офтальмологческий конгресс IOC Uzbekistan, 2021 г. Ташкент, с, 96.
14. Shernazarov, F., Jalalova, D., Azimov, A., & CAUSES, S. A. (2022). SYMPTOMS, APPEARANCE, TREATMENT OF VARICOSE VEINS.
15. Жалалова, Д. З. (2021). Эндотелин-1 ва гомоцистеин даражасини артериал гипертензия фонида тур пардв узгаришларида эндотелиал дисфункциянинг маркерлари сифатида текшириш. Биомедицина ва амалиет журнали, 6(5), 203-210.
16. Shernazarov, F., Tohirova, J., & Jalalova, D. (2022). Types of hemorrhagic diseases, changes in newboens, their early diagnosis. Science and innovation, 1(D5), 16-22.
17. Zhalalova, D. Z. (2022). The content of endothelin and homocysteine in blood and lacrimal fluid in patients with hypertensive retinopathy Web of Scientist: International Scientific Research Journal. ISSUE, 2, 958-963.
18. Shernazarov, F., & Zuhridinovna, J. D. (2022). Microcirculation disorders in the vascular system of the bulbar conjunctiva in the initial manifestations of cerebral blood supply deficiency. Science and innovation, 1(Special Issue 2), 515-522.
19. Zhalalova, D. Z. (2022). Modern aspects of neuroprotektive treatment in hypertensive retinopathy Web of Scientist: International Scientific Research JournalVolume 3. ISSUE, 2, 949-952.
20. Жалалова, Д. З. (2009). Метод комбинированного лечения диабетической ретинопатии. Врач-аспирант, 37(10), 864-868.
21. Жалалова, Д. З. (2023). Результаты оценки эффективности комплексного лечения у пациентов с 3-4 стадиями гипертонической ангиоретинопатии. Miasto Przyszłości, 41, 33-36.
22. ЖД, З., & ИЖ, Ж. (2024). КЛАССИФИКАЦИЯ ГИПЕРТОНИЧЕСКОЙ РЕТИНОПАТИИ НА ОСНОВЕ ДАННЫХ ОПТИЧЕСКОЙ КОГЕРЕНТНОЙ ТОМОГРАФИИ. SCIENTIFIC JOURNAL OF APPLIED AND MEDICAL SCIENCES, 3(3), 336-342.
23. ЗЖД, Ж. (2024). КЛИНИКО-ФУНКЦИОНАЛЬНЫЕ ПОКАЗАТЕЛИ ОРГАНА ЗРЕНИЯ У ПАЦИЕНТОВ С ИШЕМИЧЕКИМИ ИЗМЕНЕНИЯМИ СОСУДОВ СЕТЧАТКИ. SCIENTIFIC JOURNAL OF APPLIED AND MEDICAL SCIENCES, 3(3), 286-293.
24. ЖД, З. (2024). ОЦЕНКА КЛИНИЧЕСКИХ И ФУНКЦИОНАЛЬНЫХ ПОКАЗАТЕЛЕЙ ЭНДОТЕЛИАЛЬНОЙ ДИСФУНКЦИИ В СЛЕЗНОЙ ЖИДКОСТИ У ПАЦИЕНТОВ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ. SCIENTIFIC JOURNAL OF APPLIED AND MEDICAL SCIENCES, 3(3), 330-335.
25. Жалалова, Д. З. (2023). Актуальность проблемы изменений глазного дна при артериальной гипертензии. Miasto Przyszłości, 41, 37-40.