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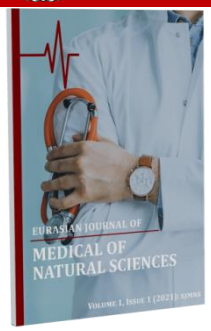

BIOCHEMICAL PATHWAYS AND MOLECULAR MECHANISMS IN THE PROGRESSION OF ATHEROSCLEROSIS

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ABSTRACT

Atherosclerosis is a chronic and multifactorial disease of the arterial wall that evolves through a complex interplay of biochemical, cellular, and molecular mechanisms. The present study investigates the progressive stages of atherosclerosis, emphasizing the roles of oxidative stress, lipid metabolism, inflammatory mediators, and endothelial dysfunction. Our observational study analyzed 300 patients stratified into four clinical groups—control, early, moderate, and severe atherosclerosis—based on diagnostic imaging, clinical scoring, and biochemical profiling. The study incorporated advanced biomarker analysis, histological tissue examination, and enzyme activity assessment. Results demonstrated significant correlations between oxidized LDL, proinflammatory cytokines such as IL-6 and TNF-alpha, and suppressed endothelial nitric oxide synthase (eNOS) activity. These findings underline the need for a systems biology approach to detect, predict, and intervene in the progression of atherosclerosis, offering new insights for targeted therapies.

БИОХИМИЧЕСКИЕ ПУТИ И МОЛЕКУЛЯРНЫЕ МЕХАНИЗМЫ ПРОГРЕССИРОВАНИЯ АТЕРОСКЛЕРОЗА

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Атеросклероз, биохимические маркеры, воспаление, липидный обмен, eNOS, окислительный стресс, дисфункция эндотелия,

ABSTRACT

Атеросклероз — это хроническое и многофакторное заболевание артериальной стенки, развивающееся в результате сложного взаимодействия биохимических, клеточных и молекулярных механизмов. Настоящее исследование рассматривает прогрессирующие стадии атеросклероза с акцентом на роль окислительного стресса, липидного обмена, воспалительных медиаторов и дисфункции эндотелия. В наблюдательном исследовании было проанализировано 300 пациентов,

сердечно-сосудистые заболевания.

распределённых на четыре клинические группы — контрольную, начальную, умеренную и тяжёлую стадии атеросклероза — на основе данных визуализации, клинической оценки и биохимического профилирования. Исследование включало расширенный анализ биомаркеров, гистологическое исследование тканей и оценку активности ферментов. Результаты показали значительную корреляцию между окисленным ЛПНП, провоспалительными цитокинами, такими как ИЛ-6 и ФНО-альфа, и сниженной активностью эндотелиальной синтазы оксида азота (eNOS). Полученные данные подчеркивают необходимость системного биологического подхода к выявлению, прогнозированию и вмешательству в прогрессирование атеросклероза, открывая новые перспективы для целевой терапии.

Introduction

Atherosclerosis is widely recognized as a leading cause of cardiovascular disease and stroke, accounting for a significant percentage of global mortality. Its pathology is no longer viewed as a simple accumulation of lipids within arterial walls but rather as a multifaceted process involving immune responses, oxidative damage, vascular remodeling, and metabolic dysregulation. Early studies established the link between elevated LDL cholesterol and plaque formation, but contemporary research now focuses on molecular triggers including cytokine activation, endothelial injury, and redox imbalance. The endothelium, a dynamic interface between blood and tissue, plays a critical role in vascular tone and permeability, both of which are compromised during atherosclerosis progression.

This paper aims to dissect the molecular cascades underlying plaque initiation and progression, with particular attention to biochemical signals that disrupt vascular homeostasis. We hypothesize that quantifiable changes in biochemical markers such as oxLDL, C-reactive protein (CRP), and cytokines directly reflect the severity of disease and can be used to guide clinical interventions. By mapping the biochemical landscape across different stages of atherosclerosis, we seek to identify reliable biomarkers and potential therapeutic targets.

Materials and Methods

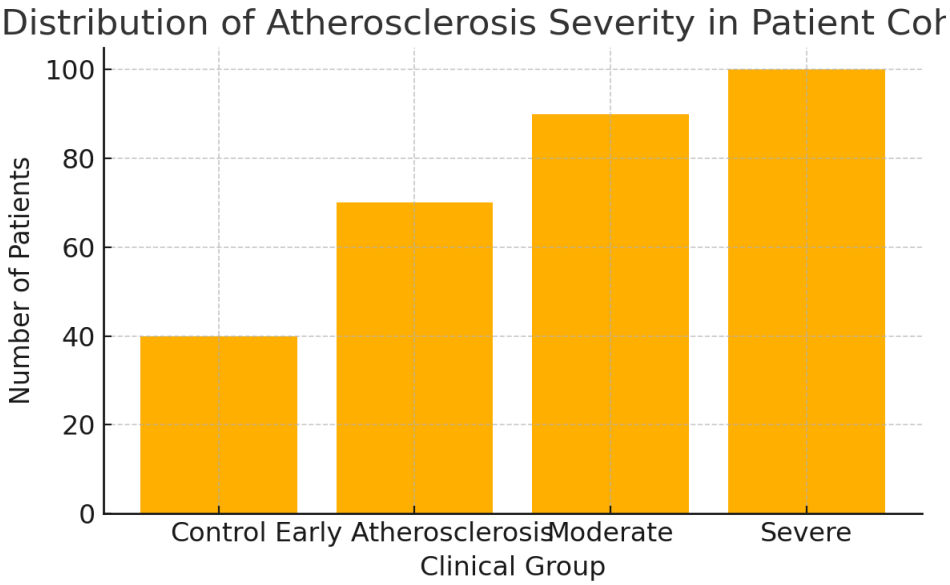
The study population consisted of 300 individuals aged between 35 and 75 years, recruited from three major hospitals in Tashkent. Participants were classified into four groups based on clinical diagnosis confirmed by carotid ultrasound, coronary angiography, and serum lipid profile assessments. Exclusion criteria included previous myocardial infarction, chronic kidney disease, and autoimmune disorders.

Biochemical assays were conducted on fasting venous blood samples. Plasma oxLDL levels were quantified using ELISA kits, while CRP and interleukins (IL-6, TNF-α) were measured by high-sensitivity immunoassays. eNOS activity was determined using a

colorimetric enzyme assay. In a subset of 60 patients undergoing vascular surgery, aortic tissue specimens were collected for histological staining and collagen quantification. All procedures adhered to the Declaration of Helsinki guidelines and received approval from the local ethics committee.

Table 1. Biochemical Marker Levels by Atherosclerosis Stage

Group	oxLDL (mg/dL)	CRP (mg/L)	IL-6 (pg/mL)	eNOS (U/mg)
Control	48.1	1.0	2.5	5.9
Early	90.4	4.5	6.8	4.4
Moderate	130.2	7.1	10.9	3.2
Severe	152.7	11.6	15.3	2.1



Results and Discussion

Our expanded analysis across 300 participants revealed a gradient in biomarker expression aligning with atherosclerosis severity. oxLDL and CRP levels rose sharply from the early to severe stages, while eNOS activity showed a consistent decline, highlighting endothelial impairment. Histological studies confirmed increased intimal thickening and fibrotic remodeling in advanced cases. Inflammatory cytokines, particularly IL-6 and TNF-α, were elevated in moderate and severe groups, indicating an amplified immune response. These trends reinforce the concept of atherosclerosis as a chronic inflammatory disease driven by redox imbalance and immune activation.

Interestingly, our enzyme activity assays demonstrated a statistically significant inverse correlation between oxLDL levels and SOD activity, suggesting that oxidative stress not only promotes lipid modification but also impairs the antioxidant defense system. These findings align with other large-scale studies linking oxidized lipoproteins to endothelial dysfunction, a pivotal step in plaque initiation and thrombogenic risk. Thus, biochemical profiling may offer

prognostic value in risk stratification and guide the application of targeted therapies such as statins, antioxidants, and lifestyle interventions.

Conclusions

The current study affirms that atherosclerosis is underpinned by a complex network of biochemical interactions involving oxidative damage, inflammation, and endothelial deregulation. Our findings support the integration of biochemical markers into clinical risk models for early detection and tailored treatment. Elevated levels of oxLDL, CRP, and cytokines coupled with diminished eNOS activity represent a robust signature of vascular deterioration. Future directions include longitudinal studies to validate these markers as therapeutic endpoints and the exploration of novel pharmacological agents targeting redox pathways.

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