UDC 616.314.17-002.3-031
DOI https://doi.org/10.35220/2078-8916-2024-54-4.14

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CLINICAL AND LABORATORY ASSESSMENT OF THE RESULTS OF EXAMINATION OF PATIENTS WITH GENERALIZED PERIODONTITIS COMPLICATED BY TRAUMATIC OCCLUSION

Studying the factors influencing the progression of the chronic course of generalized periodontitis (GP) in young individuals remains a relevant issue. Modern studies of the pathogenesis of GP focus on several conceptual approaches reflecting the principles of established patterns in the formation of infectious and dystrophic processes. The most notable research involves examining the microbiological composition of dental deposits in periodontal pockets and the vascular response accompanied by changes in the permeability of vessel walls in the microcirculatory bed and activation of local immune complexes. Clinical efforts are directed toward maintaining a stable remission of GP by reducing the number of periodontopathogens in oral eco-niches. However, the long-term use of broad-spectrum antimicrobial agents for both treatment and daily prevention creates a persistent substrate of dysbiosis in the oral cavity. This leads to atypical clinical presentations of chronic GP, even at the initial first stage of disease development. The study presents research results involving the functional activity of endothelial cells in periodontal space. A comparative analysis of functional loads on the periodontium caused by existing supra(hyper) contacts holds significant diagnostic and prognostic value. To substantiate this, it is necessary to adhere to a clinical, radiological, and functional examination protocol. This includes identifying pathological occlusion through intermaxillary impression with A-silicone, conducting orthopantomography, and 3D computed tomography of the jaws, alongside comparative assessment of software-based densitometry in areas of localized osteoporosis. This enables clinicians to detect hypercontacts and disruptions in the microstructure of cancellous bone. Additional functional analysis of occlusal relationships, differentiating contacts by time, force, and plane of occlusion using a T-scan device, holds significant practical relevance. The study found that 98.3 % of patients with initial-stage GP and a chronic course showed occlusal load imbalances due to inadequate dental restorations and carious lesions of Class I, II, and III (Black's classification). This imbalance in load leads to selective disruption of the microcirculation system in the periodontium, accompanied by cell-specific processes regulated by phagocytes, lymphocytes, and endothelial cells. Thus, trophic changes linked to hemodynamics are mediated by intercytokine response and endothelial state. A comparative analysis revealed that determining tumor necrosis factor-alpha (TNF-α) and vascular endothelial growth factor (VEGF) levels in periodontal pockets during chronic inflammation has predictive and differential diagnostic significance. A statistical increase in TNF-α concentration up to sixfold (568 %) in hypercontact areas, compared to a twofold increase (207 %) in chronically inflamed periodontal pockets, indicates a significant statistical difference ($P<0.05$) relative to the control group. VEGF-A activity showed similar trends: a 22 % increase in periodontal pockets with chronic inflammation and up to a fourfold increase (370 %) in hypercontact areas ($P<0.05$). The obtained results allow clinicians to determine the sequence and scope of therapeutic measures for periodontologists. Implementing modern diagnostic methods such as orthopantomography, 3D computed tomography, and T-scan analysis has practical importance in identifying vascular disorders and structural disorganization of periodontal tissue complexes, supported by scientific immunological research.

Key words: *periodontal pathology, occlusion disorders, traumatic occlusion, radiological changes in the periodontium, local immunity, tumor necrosis factor, vascular endothelial growth factor.*

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КЛІНІКО-ЛАБОРАТОРНА ОЦІНКА РЕЗУЛЬТАТІВ ОБСТЕЖЕННЯ ХВОРИХ НА ГЕНЕРАЛІЗОВАНИЙ ПАРОДОНТИТ, УСКЛАДНЕНИЙ ТРАВМАТИЧНОЮ ОКЛЮЗІЄЮ

Анотація. *Вивчення факторів, що впливають на прогресування хронічного перебігу генералізованого продонтиту (ГП) у молодих людей залишається*

актуальним питанням. При вивченні патогенетичних механізмів розвитку ГП на сучасному рівні, розглядається декілька концептуальних направлень, який відображають принципи загальноприйнятих закономірностей формування інфекційно-дистрофічних процесів. Найбільш визначеними дослідженнями є вивчення мікробіологічного складу зубних відкладень у пародонтальних кишенях, а також відповідь судинної реакції яка супроводжується змінами проникливості стінок судин мікроциркуляторного русла, активацією місцевих імунних комплексів. Робота клініцистів направлена на збереження стійкого періоду ремісії ГП, за рахунок зниження кількості пародонтопатогенів в еконішах порожнини рота. Але довгострокове використання широкого спектра антимікробних як лікувальних так і повсякденних профілактичних засобів породжує тривалий субстрат зв'язуючий комплекс дисбіозу в порожнині рота, що доводить до клінічно атипового хронічного перебігу ГП, навіть вже при початковому першому ступені розвитку захворювання. В роботі доведені результати дослідження, які передбачають вивчення функціональної активності ендотеліальних клітин судин в пародонтальному просторі. Порівняльний аналіз функціонального навантаження на пародонт, з боку існуючих супер(гіпер) контактів має суттєве діагностичне та прогностичне значення. Для підтвердження цього положення необхідно дотримуватися алгоритму клінічного та рентгенологічного, функціонального дослідження. Це стосується виявлення існуючої патологічної оклюзії за рахунок отримання відбитку міжщелепного стискання А-силіконом, проведення ортопантомографії та 3D-комп'ютерної томографії щелеп, з порівняльним визначенням програмної денситометрії в зонах місцевого остеопорозу. Це дає змогу лікарю-клініцисту первинно виявити гіперконтакти та порушення мікроструктур губчатої речовини кістки. Додаткове функціональне проведення аналізу оклюзійних співвідношень, з диференціацією контактів зубів по часу, силі та площині оклюзійних контактів за допомогою апарату T-scan має суттєве практичне значення. В роботі доведено, що у 98,3 % обстежених хворих на ГП початкову – I ступінь, хронічний перебіг виявлене порушення оклюзійного навантаження на пародонт, за рахунок некоректного пломбування зубів, каріозного процесу I, II, III класу за Блеком. Розбалансування навантаження передбачає вибіркове порушення системи мікроциркуляції в пародонті, що супроводжується клітинно-специфічними направленими процесами які регулюються фагоцитами, лімфоцитами, ендотеліальними клітинами. Таким чином трофічні зміни, які пов'язані з гемодинамікою опосередковані інтерцитокіновою відповіддю та станом ендотелію судин. Виявлено, при порівняльному аналізі, що визначення вмісту цитокіна фактора некрозу пухлин-альфа (ФНП-α) та судинного ендотеліального фактору росту (VEGF) у пародонтальних кишенях при хронічному запаленні має доцільний, прогностичний запитає диференційний зміст. Статистичне збільшення концентрації ФНП-α до 6 разів (568 %) в ділянках гіперконтактів, при порівнянні з вмістом де відбувається хронічне запалення у пародонтальних кишенях, що реєструється підвищенням до 2 разів (207 %) (P<0,05); вірогідність статистичної різниці по відношенню з даними показників контрольної групи обстежених. Активність вмісту VEGF-A має однонаправлене співвідношення: при хронічному запаленні вміст у пародонтальних кишенях збільшується на 22 %, а в ділянках гіперконтактів до 4 разів (370 %), (P<0,05). Отримані результати дають змогу дослідити, визначити послідовність та об'єм лікувальних заходів для лікарів пародонтологів. Доцільність впровадження існуючих сучасних методик діагностики (ортопантомографії, 3D комп'ютерної томографії, T-scan дослідження) мають практичне значення для визначення судинних розладів та структурний дезорганізації комплексу тканин пародонту, що підтверджується науковими імунологічними дослідженнями. Це обумовлює послідовність та алгоритм проведення методів та засобів лікування для отримання неоваскулізації та пролонгації фази ремісії захворювання.

Ключові слова: *патологія пародонту, порушення оклюзії, травматична оклюзія, ренгенологічні зміни пародонту, місцевий імунітет, фактор некрозу пухлин, ендотеліальний фактор росту судин.*

Generalized periodontitis involves the destruction of periodontal tissue complexes, characterized by varying degrees of interdental septa destruction and inflammatory processes in connective tissues. Currently, generalized periodontitis is a leading cause of tooth loss, and the complete understanding of its etiological factors remains unresolved. GP may not be an isolated oral disease but rather an ultimate phenotype resulting from unique pathogens and processes, primarily affecting the balance of systemic and local immunity.

The most currently accepted etiological factors suggest that GP results from the translocation of periodontopathogenic bacteria or their metabolic products through a weakened epithelial barrier. Combined with disruptions in the innate immunity of the oral mucosa, this leads to an exaggerated inflammatory response, dysbiosis, and secondary damage to the epithelial tissue at the dentoalveolar junction. This multifactorial process is accompanied by inflammatory and dystrophic damage, as evidenced by biochemical and immunobiological studies [10, 11, 13, 22].

Regarding the pathogenesis of periodontal inflammatory diseases, most research suggests that the development of inflammatory processes follows a stereotypical pattern. Tissue damage leads to the release of thrombin, fibrinogen, activated complement fractions, cytokines, and other biologically active substances. Protein-glycosaminoglycan complexes in the connective tissue of the gingiva are destroyed, free amino acids, uronic acids, amino sugars, low-molecular-weight polysaccharides, and peptides accumulate. This results in increased osmotic pressure, edema, acidosis, and hypoxia. High levels of

lipid and protein peroxidation lead to the destruction of cell membranes, accompanied by pronounced vasomotor reactions and prolonged vasodilation. The involvement of specific immune responses in the pathogenesis of gingival inflammation contributes to the generalization of this pathological process, transitioning it into a chronic phase.

At the same time, scientific findings indicate that the unstable state of the microcirculatory bed in periodontal tissues may play a critical role in the pathogenesis of chronic GP [1, 2, 4, 5, 6, 9]. Over the long term, inflammation leads to vascular and periodontal tissue damage, resulting in hemorrhagic and ischemic necrosis of connective tissue. However, the current paradigm fails to adequately explain why, at the initial stage of chronic inflammation, periodontal decompensation occurs despite subcompensated oral hygiene levels [8]. Our recent findings suggest that processes in the microcirculatory bed of the periodontal mucosa play a critical role in GP pathogenesis, indicating a link to the development of localized ischemic coagulation necrosis and subsequent periodontal destruction.

In clinical practice, dentists often limit treatment to supportive antibacterial methods and surgical interventions for advanced stages of periodontal damage. The local ecological system of the periodontal tissue complex balances between localized immune responses and antigen tolerance through apoptosis mechanisms. Bacteria promote localized immune activity while suppressing regulatory lymphocytes and immune factors, allowing pathogens to survive despite local defense mechanisms. This influences inflammation dynamics, clinical manifestations, and indirectly reflects the rate of pathophysiological processes. The imbalance of localized immune reactivity, disruption of hemato-periodontal barriers, and the stabilization of periodontal tissue equilibrium require further scientific investigation and detailed exploration of the mechanisms involved.

A comparative analysis of localized immune factor levels, tissue destruction severity, and clinical inflammation manifestations will ultimately clarify the condition of periodontal tissues and assess localized endotoxicosis manifestations.

In this context, analyzing TNF-α levels represents an intriguing diagnostic biomatrix with significant differential biomarker potential for localized tissue inflammation. TNF-α was first identified in the 1970s as a serum mediator of innate immunity capable of inducing hemorrhagic necrosis of tumors. This cytokine, recognized as a key regulator of inflammatory responses, is primarily produced by activated local monocytes and macrophages. TNF-α is a multifunctional pro-inflammatory cytokine synthesized mainly by monocytes and macrophages, playing a critical role as a low-molecular-weight mediator of intercellular interactions. Tumor necrosis factor also affects lipid metabolism, coagulation, endothelial function, stimulates the production of pro-inflammatory interleukins IL-1, IL-6, IL-8, interferon-gamma, activates leukocytes, and is one of the important factors in defense against intracellular parasites and viruses, or exerts a cytotoxic effect on cancer cells by activating apoptosis, oxidative effects on cells, and influencing nitric oxide levels. Literature data on the study of this immune marker are quite extensive. Scientific research indicates that the biological effects of TNF-α depend on its concentration. At low concentrations, the factor acts locally as a para- and autocrine regulator of autoimmune reactions in response to injury or infection. At moderate concentrations, it stimulates phagocyte formation, enhances blood clotting, and has a pyrogenic effect. Data obtained show that the production of tumor necrosis factor by bacteria (lipopolysaccharides), yeast-like fungi, and mammalian transplant cells stimulates the formation of tumor necrosis factor at the local site of donor material, making it an important diagnostic test for determining a highly effective catalyst with unique properties for measuring inflammatory cytokines in the dynamics of diagnostic observation. Investigating the molecular regulation of factors affecting the neurovascular local homeostasis of periodontal tissues, and aimed at transforming chronic inflammation among the development of various morphofunctional pathways, is a modern powerful thematic research area. [4, 20, 21, 24].

In this regard, objective evidence is discussed that the functional state of the microcirculatory system of the periodontium plays an important role in the initial disruption, forming chronic inflammation. To investigate this pathogenetic initial link in the disruption of periodontal tissues under sufficiently compensated oral hygiene conditions, as indicated by hygiene index scores, we used immunological research of the local content of vascular endothelial growth factor and tumor necrosis factor.

Vascular endothelial growth factors are highly sensitive secreted signaling proteins, best known for their role in vessel development and angiogenesis. Many non-endothelial roles of this vascular endothelial growth factor have now been established, as its receptors are expressed in numerous non-vascular cells and in cancerous tumors. The secreted VEGF

binds to its receptors in the extracellular space of the cellular membrane in a paracrine or autocrine manner, with different isoforms. The intracellularly localized vascular endothelial growth factor is poorly studied to date, but it is established as an important signaling molecule that regulates cell growth, apoptosis, metabolism, and T-cell differentiation. This signaling pertains to the direct action of the signaling molecule inside the cell without secretion and mediates events related to growth regulation and cell survival. Vascular endothelial growth factor binds to tyrosine kinase receptors on vessels, lymphatic endothelial cells, and non-specific non-endothelial cells. The involvement of vascular endothelial growth factor in the pathophysiology of chronic persistent pain is not fully studied, but the connection of molecules in this family in neuroprotection has attracted increased attention. This is of significant importance for terminating the action of vascular endothelial growth factor, weakening neovascularization, and the development of edema. Interesting data has been obtained in studying the complex role of inflammatory cytokines, tumor necrosis factor, and angiogenic factors in the development of joint inflammation [20, 21, 23, 24], activation of immune cells, and tissue damage in rheumatoid arthritis. In this regard, the bidirectional involvement in angiogenesis and T-cell differentiation provides valuable information for the development of innovative treatment methods for autoimmune processes. Numerous mechanisms are considered, including members of the endothelial factor family in inhibiting the maturation of dendritic (antigen-presenting) monocyte cells, accumulated superoxide-producing cells of myeloid origin, and the imbalance between effector T-lymphocytes and regulatory ones [14, 16, 18, 25, 26]. It should be noted that the direct angiogenic marker, VEGF, is significantly released under conditions of tissue hypoxia, causing remodeling and inflammation at the local site, promoting disease progression.

Thus, endothelial cells play a decisive role in the progression of angiogenesis, which leads to the remodulation of cells, proliferation, adhesion, migration, invasion, and survival. At the same time, angiogenic factors, such as cytokines, cell adhesion molecules, growth factors, metalloproteinases, and plasminogen activators, bind to their receptors on dendritic cells and activate signaling pathways, influencing the condition of the focus and disease development. To clarify the issue of tissue damage in the periodontium during persistent, torpid chronic inflammation, new research directed at understanding the balance between growth factor effects in the differential chronic presence of chronic trauma and chronic inflammation in the periodontium in the early stages of generalized periodontitis in young patients (18-35 years) is necessary.

The uniqueness of this scientific discussion lies in investigating the role of occlusal trauma in the pathophysiological behavior of periodontal structures when periodontal pockets have already formed, and tissue damage related to the existing dental biofilm is heterogeneous, with clinical manifestations of chronic periodontal inflammation differing in various areas of the alveolar ridges. That is, trauma resulting from pathological occlusion is associated with and works alongside existing periodontal pockets. Given that, in this clinical situation, support teeth and periodontal tissues become more prone to inflammation due to impaired angioprotective factors, there arises a need to discuss factors that influence the spread and formation of bone and subgingival pockets, which increase and are clinically determined to be deeper in the zones of occlusal trauma, on the background of the existing initial chronic inflammatory process in the periodontal tissue complex.

Thus, theoretical assessments focus on the latest achievements in the mechanisms of inflammation development, related to different mechanisms of necrosis (infectious, non-infectious, mixed types) in the periodontium, requiring further clarification and scientific support. These findings could objectively confirm the possible interrelationship between occlusal trauma of traumatic nodes and the kinetics of chronic inflammation development in patients with early-stage generalized periodontitis of chronic course. The link between functional states and the identical local immunological level of the microcirculatory system provides the possibility for evidence-based modulation of clinical cases, which is confirmed by the pathogenesis assumptions: the role of the dominant factor due to prolonged chronic occlusal disruption associated with existing chronic torpid periodontal inflammation. The designation of this role is a leading factor in enhancing further periodontal destruction, with deepening of periodontal pockets against a background of hypoxia, metabolic disturbances, and subsequent treatment already associated with biofilm activity, justifying the sequence of using the first phase of treatment for generalized periodontitis.

Objective: to investigate the improvement of diagnostic effectiveness of the local condition of the periodontium in patients with generalized periodontitis, initial stage, chronic course.

Materials and Methods. The study was conducted at the Dental Medical Center of the Bogomolets

National Medical University, Kyiv. Twenty-six patients with generalized periodontitis (initial stage, chronic course), aged 18-35 years, both male (13) and female (13), were examined, along with 13 patients in the control group. During the comprehensive local clinical examination, the following were assessed:

1. Oral hygiene status: good and satisfactory.
2. Presence of dental anomalies: progenia (first degree), deep bite (first degree).
3. Deformations and anomalies of a single dental arch: absence of secondary edentulism, displacement of the vertical incisal line, dental crowding, presence of diastemas, abnormal tooth positions, shallow oral vestibule, pathological frenulum attachment, gum recession.
4. Changes in hard tooth tissues: incorrect (without preservation of the anatomic-functional principle) placement of Class I, II, and IV fillings according to Black, increased wear of cusps and incisal edges of teeth, multiple cracks in front teeth, presence of first-degree wedge-shaped defects and cervical exposure, abrasion, and abfraction of teeth.

To substantiate the condition of the periodontal tissues, hygiene indexes were determined. All patients underwent oral hygiene procedures 15-20 days before the laboratory and scientific research. Radiographic examination included orthopantomography, 3D CT scans of the upper and lower jaws, and periapical contact radiographs. An apparatus for determining the functional state of the occlusion and traumatic points was provided by the T-scan III, and bilateral copying paper was used. Bite registration was performed with A-silicone impression material. Clinical examination included analysis of complaints, medical history (anamnesis vitae and anamnesis morbi), including the external appearance of the face and oral cavity, determination of hygiene status, and inflammation.

Statistical data processing was performed using the Statistica 7 software package with variation statistics methods, and differences were evaluated using parametric methods and Student's t-test.

During the clinical examination, attention was paid to the condition of the gums: color, swelling, comparative bleeding severity, exposure and hyperesthesia of the tooth necks, epithelial attachment along the tooth root, and condition of the anatomical tooth necks. Gingival recession and depth of periodontal pockets were determined. To obtain local immunological indicators of the inflammatory activity, the quantitative content of tumor necrosis factor (TNF-α) and the condition of the microcirculatory vessels (VEGF) in the periodontal pocket environment were assessed.

A patent application for the method of sampling hemorrhagic exudate from the periodontal pocket for laboratory studies was submitted. The research was conducted at the Department of Postgraduate Education and Internship in Dentistry at the Dental Medical Center of the Bogomolets National Medical University, Kyiv, in the Immunology and Biochemistry Department of the M.D. Strazhesko Institute of Cardiology, NAMS of Ukraine.

Inclusion criteria: presence of voluntary informed consent to participate in the study, interest in participation, absence of acute or exacerbated periodontal inflammation, no medical contraindications for the study of general somatic or mental conditions, absence of acute or exacerbated chronic somatic or infectious diseases.

Exclusion criteria: previous surgical interventions on the periodontium, correction of frenula or bands, prior orthodontic treatment, use of narcotics, alcohol, smoking.

Results. It was established that the chronic course of generalized periodontitis in young people (18-25 years old) is accompanied by symptoms of chronic inflammation and metabolic changes in the periodontal tissues. A medical documentation analysis was conducted on 182 clinically examined individuals aged 18 to 35 years, both male and female, residing in Kyiv and the Kyiv region, with no identified inflammatory-somatic diseases. Among the examined individuals, 86.4 % (157 individuals) had periodontal inflammation, with a predominance of a chronic course in 81.3 % (127 individuals). These patients were diagnosed with generalized periodontitis of the initial stage (I degree) according to the classification by M.F. Danilevsky and co-authors (1994). Among these, 99 individuals (78.2 %) underwent systemic removal of supragingival dental deposits every 6-8 months. The primary reason for seeking treatment at the O.O. Bohomolets National Medical University Dental Medical Center was the treatment of dental caries and its complications (62.9 %, 62 patients), while the rest (17 %, 36 patients) sought consultation for other dental issues.

Radiographically, orthopantomography was performed on 100 % of the patients, and 3D CT scans of the upper and lower jaws were conducted in 48% of the patients, while 52 % refused additional radiographic examination. X-ray analysis revealed uneven destruction of the cortical layer at the apex of the interdental septa in 100 % of the examined patients. In the adjacent areas of fixed osteolysis, the spongy bone tissue appeared uneven. All patients exhibited uneven changes in the architecture of

the spongy substance with varying degrees of local osteoporotic spots. When differentiating this symptom, special attention was paid to the presence of carious cavities of Classes I, II, and IV according to Black, where inadequate filling of carious cavities with improper contact surfaces was detected. Patients with such pathological changes were not included in the laboratory study group. Furthermore, attention was drawn to the relationship between the anatomical-functional features of the form and expression of the restorations' cusp.

Complaints of periodic gum bleeding and increased tooth sensitivity to chemical or thermal stimuli were reported by 61.8 % of patients, while only 38 % complained about gingival recession. Additionally, a control group of 13 patients who had received dental caries treatment and showed no periodontal pathology was included. Clinical examination and index evaluations were performed using standard methods.

Special attention was given to radiological examination: pathological wear of tooth tissues, morphological changes in teeth, the presence of hybrid zones of denticles and petrifications, reduction in volume and deformation of tooth cavities, and the alteration in X-ray echogenicity of root canal spaces. These radiological changes were considered in terms of several clinical manifestations of increased tooth wear, which can be characterized by a decrease in the thickness of hard dental tissues due to the impact of mechanical forces from the opposing jaw or lateral displacement of the lower jaw, leading to impaired microcirculation. To determine whether these manifestations were due to: a) erosion – a reduction in hard tissue thickness due to chemical agents (data from medical history), b) abfraction – loss of tooth thickness due to overloading and the formation of microcracks (additional functional study using T-scan required).

Thus, the distinction between the morphofunctional state of the teeth and the nature of changes in the spongy bone tissue of the apex of interdental septa, specifically changes in thickness, orientation, and trabecular relationships, with moderate deformation of the intertubercular spaces, is considered a differential diagnostic radiological sign for this pathology in young patients. These structural features, highlighting the relationship between the components of teeth and the pathological changes in the spongy matrix of the interdental septa, have diagnostic, prognostic, and pathognomonic significance.

Moreover, the radiological assessment of the echogenicity of the periodontal gap in diagnostic zones further specifies the inflammation process, indicating the impossibility of eliminating the leading trigger mechanism of the initial periodontal changes. A comparative analysis of changes in the structure along the entire length of the upper and lower jaws and in each interdental space is necessary. The width and saturation changes in the connective space of the periodontal gap, its thickness, tooth relief, and uniformity of the alveolar socket wall thickness should be evaluated.

The results of this study may allow a more precise connection between progressive enamel and dentin loss, changes in the tooth cavity space, and traumatic effects from endo- or exogenous factors, pointing to the likelihood of identifying the leading triggering mechanism in the development of diseases. These factors align with histological studies. Morphological research on archived material of dental blocks (Kolesova N.A. and co-authors, 2011) revealed features of bone tissue damage in the interdental septa in generalized periodontitis, Stage I, unrelated to somatic pathology or arterial hypertension. It was established that in chronic inflammatory processes in all periodontal structures (gums, periodontium, and alveolar bone), cellular infiltrates are present. Osteoplastic resorption of the cortical layer, with the spread of cellular infiltrates in the periodontal ligament and surrounding tissues, was observed, along with destruction of the fibrous component of the periodontium and infiltration of multilayered squamous epithelium.

The modern combination of highly differentiated radiological examination (orthopantomography), 3D CT, and functional studies using T-scan III allows for a thorough analysis of the morphofunctional state of the periodontium in patients. This provides practical diagnostic criteria for determining the sequence and stages of etiopathogenetic treatment tailored to each patient, considering both local and general factors and disease manifestations.

The conducted analysis of the results allows further scientific research on the diagnosis of remodeling imbalance in the periodontium in generalized periodontitis at the initial Stage I of chronic course. This primarily concerns damage to the microvascular walls, especially capillaries and venules, and the assessment of vascular permeability for blood cellular elements (leukocytes, platelets) as key immune defense factors. To objectively assess the role of the etiological damaging factor of excessive pressure on the periodontal vessels, comparative studies of tumor necrosis factor (TNF-α) and platelet-derived growth factor – vascular endothelial

growth factor (VEGF) were conducted. Changes in the cytokine profile in the chronic inflammatory zones of the periodontium and hyper (supra) occlusal zones were identified in each individual case. The comparative analysis of identical indicators in the examined patients clarified the role of traumatic loci in the spread of chronic inflammation and the development of clinical equivalents of immune deficiency in specific local interdental spaces. The pattern of changes in the cytokine profile in patients with Stage I chronic generalized periodontitis is presented as follows: compared to control values, TNF-α levels in chronic inflammatory areas of the periodontal pockets increased by 2 times (~207 %), and up to 6 times (586 %) in hyper (supra) occlusal zones, indicating significant activation of alteration and probable cell apoptosis. VEGF levels in the chronic inflammation areas of the periodontal pockets increased by 22 %, and in hyper (supra) occlusal zones by up to 4 times (~370 %) with $P < 0.05$, which is considered a determinant of functional instability in the microcirculation of periodontal pockets. Thus, the main physiological consequence of cytokine activity is the activation of the immune response, increased vascular wall permeability, and accelerated migration of effector cells to the site of inflammation. An increase in TNF-α levels nearly twice in chronic inflammation, and up to six times in areas of chronic trauma, strongly supports the dominant role of chronic occlusal overload in the mechanisms of periodontal inflammation progression. As known, the effect of cytokines depends on their concentration. Low cytokine levels regulate proper local proliferative inflammation, while high levels lead to systemic inflammatory responses, signaling an acute phase of inflammation. TNF-α regulates lymphoid cell migration, stimulates phagocytosis, enhances the expression of adhesive molecules on endothelial cells, acts as a chemoattractant for macrophages, induces apoptosis of compromised cells, and serves as an indicator of the acute inflammatory phase. Comparative analysis of TNF-α in periodontal pockets during chronic inflammation provides meaningful prognostic, differential, and local diagnostic information. Statistical increases in TNF-α concentration up to 6 times in periodontal pockets with hyper (supra) occlusion indicate an increase in acute inflammation and alteration processes, slowing blood flow, and accelerating migration of immune cells in this focal area, suggesting decreased local immunoreactivity.

Conclusions. It has been established that the formation of metabolic vascular disorders and structural disorganization of the periodontal tissue complex in patients with generalized periodontitis of initial – stage I, chronic course, occurs against the background of cytokine regulation disruption, as a nonspecific manifestation of local vascular stress, mediated by comparative expression levels of TNF-α and VEGF in periodontal pocket contents with existing traumatic occlusion. A comparative analysis of these local immunological markers during chronic inflammation in the periodontal pockets and at sites with hyper (supramaximal) contacts shows a significant statistical difference in the levels of TNF-α and VEGF-A.

The obtained results indicate the leading regulatory role of traumatic nodules in the development of inflammatory processes during the initial stage I of chronic generalized periodontitis.

Bibliography:

1. Бандрівський ЮЛ. Ефективність лікувальних заходів за даними параклінічних індексів у хворих на генералізований пародонтит початкового – I ступеня, асоційована з груповою приналежністю крові. *Клінічна стоматологія*. 2020. №2-3. С. 14-23.

2. Батіг І.В., Борисенко АВ. Вплив ортодонтичного лікування генералізованого пародонтиту на гігієнічний стан порожнини рота. Актуальні проблеми сучасної медицини. 2023;23:92-95. DOI: 10.31718/2077–1096.23.2.1.92

3. Біда ОВ, Біда ОВ. Оцінка характеру оклюзійних співвідношень на етапах ортопедичної реабілітації осіб із захворюваннями тканин пародонта, ускладнених дефектами зубних рядів. *Український стоматологічний альманах.* 2021. №1. С. 59-63.

4. Бойцанюк С.І., Островський П.Ю. Стан кісткової тканини у хворих на генералізований пародонтит за даними денситометричного обстеження. *The Scientific Heritage.* 2022. №91. С. 66-69.

5. Борисенко АВ. Порушення місцевого імунітету та цитокінового статусу у хворих на генералізований пародонтит. *Сучасна стоматологія.* 2019. №1. С. 34-37.

6. Гасюк Н.В. Особливості перебудови клітинного складу слизової оболонки порожнини рота у хворих на генералізований пародонтит. *Україна. Здоров'я нації.* 2018. №1. С. 100-105.

7. Захарова Г.Є. Нормалізація оклюзійних співвідношень у комплексі лікувальних заходів при генералізованому пародонтиті у хворих на цукровий діабет. *Сучасна пародонтологія*. 2017.№1. С. 7-12.

8. Колесова Н.А., Колесова Н.В. Структурні зміни кісткової тканин альвеолярного відростка за генералізованого пародонтиту. *Вісник проблем біології і медицини*. 2011. №2(1). С. 186-188.

9. Кузняк Н.Б, Дроник І.І. Особливості змін основних клінічних показників у хворих на хронічний генералізований пародонтит залежно від методів комплексної терапії. *Клінічна стоматологія.* 2015. №3-4. С. 109-110.

10. Мельничук А.С., Рожко М.М., Мельничук Г.М. Відновлення нормальних оклюзійних співвідношень

при комплексному лікуванні хворих на генералізований пародонтит із включеними дефектами зубних рядів. Запорізький медичний журнал. 2019. №2(113). С. 281-286.

11. Петрушанко Т.О. Оцінка дії хвороботворних факторів у пацієнтів із генералізованим пародонтитом. *Клінічна стоматологія*. 2020. №2. С. 24-32.

12. Скибчик О.В. Мікробіота пародонтальних кишень у пацієнтів з ішемічною хворобою серця та хронічним генералізованим пародонтитом. *Клінічна стоматологія*. 2021. №2. С. 47-55.

13. Червонна Н.В., Неспрядько В.П., Костюк Т.М. Порівняльна характеристика різних методів оцінки оклюзійних контактів у пацієнтів із захворюваннями тканин пародонта. *Today's problems in medicine, pharmacy and dentistry.* 2020. С. 250-252. Режим доступу: https://dspace.uzhnu.edu.ua/jspui/bitstream/lib/45290/1/9.pdf

14. Alhabdan Y.A., Albeshr A.G., Albasher A.A., Alassiri A.S., Shater M.A., Alqahtani M.A., Ageely K.T. et al. Etiology and types of necrotizing periodontal diseases. *Int J Community Med Public Health*. 2021. №8. P. 6137-6142. DOI:10.18203/2394-6040.ijcmph20214486.

15. Apte R.S., Chen D.S., Ferrara N. VEGF in signaling and disease: beyond discovery and development. *Cell*. 2019. №176(6). P. 1248-1264. DOI: 10.1016/j.cell.2019.01.021.

16. Deas D.E., Meale, B.L. Is there an association between occlusion and periodontal destruction? Only in limited circumstances does occlusal force contribute to periodontal disease progression. *Journal of the American Dental Association.* 2006. №1939. P. 137(10). DOI: 10.14219/jada.archive.2006.0050

17. Failla C.M., Carbo M., Morea V. Positive and negative regulation of angiogenesis by soluble vascular endothelial growth factor receptor-1. *International journal of molecular sciences*. 2018. №19(5). P. 1306. DOI: 10.3390/ijms19051306.

18. Fu J.H., Yap A.U. Occlusion and periodontal disease-where is the link? *Singapore dental journal*, 2007. №29(1). P. 22-33.

19. Guo X., Yi H., Li T.C., Wang Y., Wang H., Chen X. Role of Vascular Endothelial Growth Factor (VEGF) in Human Embryo Implantation: Clinical Implications. *Biomolecules*. 2021. №11(2). P. 253. DOI: 10.3390/biom11020253.

20. Harrel S.K. Occlusal forces as a risk factor for periodontal disease. Periodontol 2000. 2003;32:111-7. DOI: 10.1046/j.0906-6713.2002.03209.x.

21. Huang J.X., Lee Y.H., Leong P.Y., Wei J.C. Personalized tapering of tumor necrosis factor inhibitor in axial spondyloarthritis. *International Journal of Rheumatic Diseases.* 2024. №27(1). P. e15008. DOI: 10.1111/1756-185X.15008.

22. Jang D.I., Lee A.H., Shin H.Y., Song H.R., Park J.H., Kang T.B., Lee S.R., Yang S.H. The Role of Tumor Necrosis Factor Alpha (TNF-α) in Autoimmune Disease and Current TNF-α Inhibitors in Therapeutics. *Int J Mol Sci*. 2021. №22(5). P. 2719. DOI: 10.3390/ijms22052719.

23. Jensen A.B., Ennibi O.K., Ismaili Z., Poulsen K., Haubek D. The JP2 genotype of Aggregatibacter actinomycetemcomitans and marginal periodontitis in the mixed dentition. *Journal of Clinical Periodontology*. 2016. №43(1). C. 19-25. DOI: 10.1111/jcpe.12486. Epub 2016. DOI: 10.1016/j.biomaterials.2020.120192.

24. Lee J., Lee S., Ahmad T., Madhurakkat Perikamana S.K., Lee J., Kim E.M., Shin H. Human adipose-derived stem cell spheroids incorporating platelet-derived growth factor (PDGF) and bio-minerals for vascularized bone tissue engineering. *Biomaterials*. 2020. №255. P. 120192. DOI: 10.1016/j.biomaterials.2020.120192.

25. Lim H., Lee S.H., Lee H.T., Lee J.U., Son J.Y., Shin W., Heo Y.S. Structural Biology of the TNFα Antagonists Used in the Treatment of Rheumatoid Arthritis. *Int J Mol Sci*. 2018. №19(3). P. 768. DOI: 10.3390/ijms19030768.

26. Llorián-Salvador M., González-Rodríguez S. Painful Understanding of VEGF. *Front Pharmacol*. 2018. №9. P. 1267. DOI: 10.3389/fphar.2018.01267.

27. Long J., Hu Z., Xue H., Wang Y., Chen J. Et al. Vascular endothelial growth factor (VEGF) impairs the motility and immune function of human mature dendritic cells through the VEGF receptor 2-RhoA-cofilin1 pathway. *Cancer Sci*. 2019. №110(8). P. 2357-2367. DOI: 10.1111/cas.14091.

References:

1. Bandryvskyy, Yu.L. (2020). Efektyvnist' likuval'nyh zahodiv za danymy paraklinichnyh indeksiv u hvoryh na generalizovanyj parodontyt pochatkovogo – I stupenja, asocijovana z grupovoju prynalezhnistju krovi [The effectiveness of therapeutic measures based on paraclinical indices in patients with generalized periodontitis of the initial – stage I, associated with blood group]. *Klinichna stomatologija – Clinical Dentistry,* 2-3, 14-23. [in Ukrainian].

2. Batih, I.V., & Borysenko, A.V. (2023). Vplyv ortodontychnogo likuvannja generalizovanogo parodontytu na gigijenichnyj stan porozhnyny rota [The impact of orthodontic treatment of generalized periodontitis on oral hygiene]. *Aktual'ni problemy suchasnoi' medycyny – Current Problems in Modern Medicine,* 23, 92-95. DOI: 10.31718/2077–1096.23.2.1.92. [in Ukrainian].

3. Bida, O.V., & Bida, O.V. (2021). Ocinka harakteru okljuzijnyh spivvidnoshen' na etapah ortopedychnoi' reabilitacii' osib iz zahvorjuvannjamy tkanyn parodonta, uskladnenyh defektamy zubnyh rjadiv [Assessment of occlusal relationships at stages of orthopedic rehabilitation of individuals with periodontal tissue diseases complicated by dental arch defects]. *Ukrai'ns'kyj stomatologichnyj al'manah – Ukrainian Dental Almanac,* 1, 59-63. [in Ukrainian].

4. Boytsaniuk, S.I., & Ostrovskyi, P.Yu. (2022). Stan kistkovoi' tkanyny u hvoryh na generalizovanyj parodontyt za danymy densytometrychnogo obstezhennja [Bone tissue condition in patients with generalized periodontitis according to densitometric examination]. *The Scientific Heritage,* 91, 66-69. [in Ukrainian].

5. Borysenko, A.V. (2019). Porushennja miscevogo imunitetu ta cytokinovogo statusu u hvoryh na generalizovanyj parodontyt [Disruption of local immunity and cytokine status in patients with generalized periodontitis]. *Suchasna stomatologija – Modern Dentistry*, 1, 34-37. [in Ukrainian].

6. Hasyuk, N.V. (2018). Osoblyvosti perebudovy klitynnogo skladu slyzovoi' obolonky porozhnyny rota u hvoryh na generalizovanyj parodontyt [Features of cell composition remodeling of the oral mucosa in patients with

generalized periodontitis]. *Ukrai'na. Zdorov'ja nacii' – Ukraine. Health of the Nation*, 1, 100-105. [in Ukrainian].

7. Zakharova, H.E. (2017). Normalizacija okljuzijnyh spivvidnoshen' u kompleksi likuval'nyh zahodiv pry generalizovanomu parodontyti u hvoryh na cukrovyj diabet [Normalization of occlusal relationships in a complex of therapeutic measures for generalized periodontitis in patients with diabetes]. *Suchasna parodontologija – Modern Periodontology*, 1, 7-12. [in Ukrainian].

8. Kolessova, N.A., & Kolessoval N.V. (2011). Strukturni zminy kistkovoi' tkanyn al'veoljarnogo vidrostka za generalizovanogo parodontytu [Structural changes of bone tissue in the alveolar process during generalized periodontitis.]. *Visnyk problem biologii' i medycyny – Bulletin of Biology and Medicine Problems*, 2(1), 186-188. [in Ukrainian].

9. Kuzniak, N.B., & Dronik, I.I. (2015). Osoblyvosti zmin osnovnyh klinichnyh pokaznykiv u hvoryh na hronichnyj generalizovanyj parodontyt zalezhno vid metodiv kompleksnoi' terapii' [Features of changes in main clinical indicators in patients with chronic generalized periodontitis depending on methods of complex therapy.]. *Klinichna stomatologija – Clinical Dentistry,* 3-4, 109-110. [in Ukrainian].

10. Melnychuk, A.S., Rozhko, M.M., & Melnychuk, H.M. (2019). Vidnovlennja normal'nyh okljuzijnyh spivvidnoshen' pry kompleksnomu likuvanni hvoryh na generalizovanyj parodontyt iz vkljuchenymy defektamy zubnyh rjadiv [. Restoration of normal occlusal relationships in the complex treatment of patients with generalized periodontitis and dental arch defects]. *Zaporiz'kyj medychnyj zhurnal – Zaporizhzhya Medical Journal,* 2(113), 281-286. [in Ukrainian].

11. Petrushanko, T.O. (2020). Ocinka dii' hvorobotvornyh faktoriv u pacijentiv iz generalizovanym parodontytom [Assessment of pathogenic factors in patients with generalized period ontitis]. *Klinichna stomatologija – Clinical Dentistry*, 2, 24-32. [in Ukrainian].

12. Skibchik, O.V. (2021). Mikrobiota parodontal'nyh kyshen' u pacijentiv z ishemichnoju hvoroboju sercja ta hronichnym generalizovanym parodontytom [Microbiota of periodontal pockets in patients with ischemic heart disease and chronic generalized periodontitis]. *Klinichna stomatologija – Clinical Dentistry*, 2, 47-55. [in Ukrainian].

13. Chervonna, N.V., Nespryadko, V.P., & Kostiuk, T.M. (2020). Porivnjal'na harakterystyka riznyh metodiv ocinky okljuzijnyh kontaktiv u pacijentiv iz zahvorjuvannjamy tkanyn parodonta [Comparative characteristics of various methods of evaluating occlusal contacts in patients with periodontal tissue diseases]. *Today's problems in medicine, pharmacy and dentistry,* 250-252. Access mode: https://dspace.uzhnu.edu.ua/jspui/bitstream/lib/45290/1/9.pdf. [in Ukrainian].

14. Alhabdan, Y.A., Albeshr, A.G., Albasher, A.A., Alassiri, A.S., Shater, M.A., Alqahtani, M.A., Ageely, K.T. & et al. (2021). Etiology and types of necrotizing periodontal diseases. *Int J Community Med Public Health,* 8, 6137-6142. DOI:10.18203/2394-6040.ijcmph20214486

15. Apte, R.S., Chen, D.S., & Ferrara, N. (2019). VEGF in signaling and disease: beyond discovery and development. *Cell,* 176(6), 1248-1264. DOI: 10.1016/j.cell.2019.01.021.

16. Deas, D.E., & Meale, B.L. (2006). Is there an association between occlusion and periodontal destruction? Only in limited circumstances does occlusal force contribute to periodontal disease progression. *Journal of the American Dental Association,* 1939, 137(10). DOI: 10.14219/jada.archive.2006.0050

17. Failla, C.M., Carbo, M., & Morea,V. (2018). Positive and negative regulation of angiogenesis by soluble vascular endothelial growth factor receptor-1. *International journal of molecular sciences*, 19(5), 1306. DOI: 10.3390/ijms19051306

18. Fu, J.H., & Yap, A.U. (2007). Occlusion and periodontal disease-where is the link? *Singapore dental journal*, 29(1), 22-33.

19. Guo, X., Yi, H., Li, T.C., Wang, Y., Wang, H., & Chen, X. (2021). Role of Vascular Endothelial Growth Factor (VEGF) in Human Embryo Implantation: Clinical Implications. *Biomolecules,* 11(2), 253. DOI: 10.3390/biom11020253.

20. Harrel, S.K. (2003). Occlusal forces as a risk factor for periodontal disease. Periodontol 2000, 32, 111-7. DOI: 10.1046/j.0906-6713.2002.03209.x.

21. Huang, J.X., Lee, Y.H., Leong, P.Y., & Wei, J.C. (2024). Personalized tapering of tumor necrosis factor inhibitor in axial spondyloarthritis. *International Journal of Rheumatic Diseases,* 27(1), e15008. DOI: 10.1111/1756-185X.15008.

22. Jang, D.I., Lee, A.H., Shin, H.Y., Son,g H.R., Park, J.H., Kang, T.B., Lee, S.R., & Yang, S.H. (2021). The Role of Tumor Necrosis Factor Alpha (TNF-α) in Autoimmune Disease and Current TNF-α Inhibitors in Therapeutics. *Int J Mol Sci*, 22(5), 2719. DOI: 10.3390/ijms22052719.

23. Jensen, A.B., Ennibi, O.K., Ismaili, Z., Poulsen, K., & Haubek, D. (2016). The JP2 genotype of Aggregatibacter actinomycetemcomitans and marginal periodontitis in the mixed dentition. *Journal of Clinical Periodontology,* 43(1), 19-25. DOI: 10.1111/jcpe.12486. Epub 2016.

24. Lee, J., Lee, S., Ahmad, T., Madhurakkat Perikamana, S.K., Lee J., Kim E.M., & Shin H. (2020). Human adipose-derived stem cell spheroids incorporating platelet-derived growth factor (PDGF) and bio-minerals for vascularized bone tissue engineering. *Biomaterials,* 255, 120192. DOI: 10.1016/j.biomaterials.2020.120192. DOI: 10.1016/j.biomaterials.2020.120192.

25. Lim, H., Lee, S.H., Lee, H.T., Lee, J.U., Son, J.Y., Shin W., & Heo, Y.S. (2018). Structural Biology of the TNFα Antagonists Used in the Treatment of Rheumatoid Arthritis. *Int J Mol Sci,* 19(3), 768. DOI: 10.3390/ijms19030768.

26. Llorián-Salvador, M., & González-Rodríguez, S. (2018). Painful Understanding of VEGF. *Front Pharmacol,* 9, 1267. DOI: 10.3389/fphar.2018.01267.

27. Long, J., Hu, Z., Xue, H., Wang, Y., Chen, J. & et al. (2019). Vascular endothelial growth factor (VEGF) impairs the motility and immune function of human mature dendritic cells through the VEGF receptor 2-RhoA-cofilin1 pathway. *Cancer Sci,* 110(8), 2357-2367. DOI: 10.1111/cas.14091.