A POSSIBLE ROLE FOR EMT TRANSITION IN PARADONTITIS PATHOGENESIS

(LITERATURE REVIEW)

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Abstact:Because gingivitis and periodontitis are becoming more prevalent worldwide, inflammatory periodontal illnesses have become an important aspect of contemporary dentistry. This research examines scholarly literature to determine the connection between the development of inflammatory periodontal illnesses and the increased permeability of the gingival sulcus epithelium. Research on the features of the connection between the oral microbiota and the epithelial barrier is given special attention.

As part of the initiative, academic publications from eLIBRARY, Google Search, and PubMed were examined. Over 100 papers addressing different facets of the subject were found between 2024 and 2025. After a rigorous selection procedure, 60 papers were included in the study, including reviews and experimental research (both in vitro and in vivo). The information from these sources serves as the foundation for the following findings. An growing amount of data points to a connection between innate and adaptive immune control and disturbances in mucous membrane microbiota. Beneficial bacteria may either directly combat infections that impair the barrier's function or bolster the body's antimicrobial defences via the immune system. This process includes the epithelial-mesenchymal transition, in which epithelial cells shed their original properties and gain new ones. These alterations may cause a periodontal pocket, weaken the basement membrane, and compromise the integrity of the epithelial barrier. Dangerous bacteria may be able to infiltrate the oral cavity's tissues as a result of this disturbance. In this process, maintaining the stability of cell function and regular functioning depends on tight junctions and intercellular linkages.

Keywords: gingival crevicular fluid, tight junction protein complexes, oral microbiota, snail, epithelial barrier permeability, and epithelial-mesenchymal transitions
Annotation: Microbes are able to get deeply into the tissues due to the disturbance of the epithelial barrier, especially its permeability. Dysbacteriosis, which worsens periodontal inflammation and gingival sulcus epithelium loss, may result from this. The process of the epithelial barrier of the periodontal sulcus becoming more permeable is intricate and depends on many interrelated elements. The traits of proteins that maintain close contact between epithelial cells and the species and metabolites of pathogenic bacteria associated with the development of periodontitis are particularly important among them. Another significant factor is genetic predisposition.

Novel methods to the diagnosis, treatment, and prevention of inflammatory periodontal diseases are desperately needed, as shown by the rising incidence of gingivitis and periodontitis in both adults and children. To completely comprehend the intricate aetiology and pathophysiology of these disorders, further study is required. IBD may appear due to a variety of factors, including genetic susceptibility, immune system dysfunction, bacterial and viral infections, vitamin and trace element shortages, hormone imbalances, mechanical injuries, and stressful conditions [2, 3]. It should be emphasised that each of these elements has the potential to upset the balance and structure of the oral microbiome, which is essential for preserving health. It is now known that inflammatory periodontal illnesses are complex issues brought on by a microbiome imbalance. This changes the amount and composition of bacteria in the periodontal pocket, turning the normal periodontal microbiome into a pathogenic one. Environmental variables, immunological reaction, and microbial change initiate the inflammatory process that propels disease progression. Opportunistic and pathogenic microorganisms, especially Gram-negative bacteria, are intimately associated with the development of chronic periodontitis. These include Aggregatibacter actinomycetemcomitans, Treponema denticola, Porphyromonas gingivalis, Tannerella forsythia, and

Prevotella intermedia. Because the gingival sulcus is open and continuously exposed to the outside environment, it is especially perfect for their reproduction. The thin layer of aging-resistant epithelium eventually gives way to connective epithelium. The tooth enamel merges with the microbiological layer, which is in continuous touch with it. This ongoing exposure establishes a long-term immunological response [4-6]. One of the things that might disrupt the border epithelium is increased inflammatory activity in the gingival sulcus. Leukocytes engaged in inflammation include mononuclear leukocytes (T and B lymphocytes) and polymorphonuclear leukocytes. Additionally, different bacterial species found in the oral microflora may cause epithelial cells to produce certain cytokines. The integrity of the epithelial structure is thereafter threatened by a rise in the separation between desmosomes and modifications in the expression of proteins that guarantee strong connections between epithelial cells. T cell control of epithelial tight junctions is crucial for maintaining homeostasis or, on the other hand, for the emergence of a pathogenic state. When the intercellular connections of the epithelium are disrupted, bacterial toxins and antigens may more readily penetrate epithelial barriers and cause an inflammatory response. Periodontitis is associated with decreased expression of key epithelial markers such as E-cadherin, vimentin, and N-cadherin. Granulation tissue production, fibre growth, and increased microtrauma to the periodontal pocket epithelium are clinical indicators of this. The inflammatory process in periodontal tissues, which is driven by cells and chemicals, may cause gingival pocket cells to transdifferentiate from an epithelial to a mesenchymal phenotype. According to research, inflammatory events occur in the periodontium when the proteins that maintain tight cell-to-cell junctions break. The barrier function of the epithelium depends on these proteins. Consequently, a thorough analysis that focuses on enhancing the epithelial barrier's permeability and investigating the mechanisms behind tight junction function is crucial.

The goal of the research is to investigate how these variables impact the development of inflammatory periodontal diseases.

Materials and methods: The research analysed original works and scientific publications from databases such as eLIBRARY, Google Search, and PubMed. One hundred scientific articles were created as a consequence of the research undertaken between 2004 and 2024. The study employed search queries such as "inflammatory periodontal diseases," "epithelial barrier permeability," "oral microbiota," "tight junction protein complexes," "gingival crevicular fluid," and their Russian equivalents, "chronic periodontitis," "aggressive periodontitis," "epithelial barrier," and "increased epithelial permeability syndrome," to perform a systematic review of scientific literature. One tool for systematic analysis is the Stata checklist, which was established for systematic reviews and meta-analyses. 56 scholarly papers that satisfied tight conditions were included in the research. It comprised reviews as well as in vitro and in vivo investigations.

The goal of this systematic review was to examine and analyze the data on the function of epithelial permeability mechanisms in the development of IBD and to study the possible utility of tight junction proteins as diagnostic markers for these illnesses. The research looked at three electronic bibliographic websites: eLIBRARY, Google Search, and PubMed. The time frame covered was 2024–2025. Keywords indicating connective proteins, oral microbiota, inflammatory periodontal diseases, gingival crevicular fluid, chronic and aggressive periodontitis, and epithelial barrier permeability were used to find related papers. The search searches also contained the Uzbek counterparts of important terms. By examining the reference lists of the chosen articles, the most relevant content was found. Based on their titles, abstracts, and publication dates, 105 publications were chosen for the first stage of the systematic review. The list was then reduced to 85 items by deleting duplicates and those that didn't fulfil the standards. 60 publications, encompassing data from randomized controlled clinical trials and systematic reviews, were chosen for inclusion following the screening process. The subsequent screening resulted in the deletion of thirteen items. Exclusion criteria included the absence of a good clinical diagnosis, the non-representativeness of the study population, and the studies' ambiguous diagnostic criteria. Collaborative

discourse was utilised to address concerns over the inclusion or removal of certain research. A detailed examination of sixty scientific articles was undertaken.
The publications were selected following stringent criteria.
Patients from two age groups—young persons (18–44 years old) and middle-aged adults (45–59 years old)—were included in both laboratory (in vitro) and clinical (in vivo) research. The study's subjects had inflammatory periodontal disorders, which may show as either chronic gingivitis or chronic periodontitis. The control group, which comprised of participants without any clinical symptoms of periodontitis, was also included in the research. Periodontal tissue biopsies and oral fluid samples, including saliva and gingival crevicular fluid, were utilised to evaluate the expression and synthesis of proteins involved in the creation of tight junctions. The studies involved volunteers with clinically healthy periodontal tissues and patients with inflammatory periodontal disorders (IPD). People who had previously had periodontal surgery were excluded in order to assure reliable findings. Reviews and meta-analyses, research on children under the age of eighteen, studies on non-inflammatory periodontal disorders, studies on antimicrobial peptides in blood serum, and studies on antimicrobial peptide expression in systemic inflammatory syndromes were all removed from the assessment. Research indicates that during viral diseases, the oral microbiota changes and changes. Oral dysbiosis, which operates via several molecular pathways, is the cause of periodontitis. The importance of precise interactions between the immune system, oral microorganisms, and epithelial cells in preserving the stability and integrity of the oral mucosa has been brought to light by recent studies. According to recent studies, both innate and adaptive immune responses may be impacted by changes in the mucous membrane microbiota. Inflammation is caused by either an increase in pathobionts (symbiotic bacteria having pathogenic potential) or a reduction in symbiotic microorganisms. Microbes affect the immune system by partly controlling the activity of two important immune response cells, T helper 17 cells (Th17) and regulatory T cells (Treg) [22–24]. The body's initial line of defence, the epithelium, can

simultaneously identify and interact with the microbial makeup. An imbalance in the microbiota and related metabolic alterations may impair the barrier functions of the mucosal epithelium [25, 26].

Research findings: EMT is characterised by a shift in cell phenotype from epithelial to mesenchymal, marked by downregulation of epithelial markers like E-cadherin and overexpression of mesenchymal markers including vimentin, N-cadherin, Snail1, and Twist1 [55, 56, 57, 58]. EMT in oral epithelial cells may be brought on by periodontal infections, especially Gram-negative bacteria like Porphyromonas gingivalis and Fusobacterium nucleatum. This can lead to diminished barrier function, increased cell motility, and loss of cell-cell adhesion [58,59,60]. Important discoveries about the names of bacterial species, markers of controlled barrier transit, and the processes underpinning its function were made after the articles were examined. The study identifies many methods via which beneficial microbes influence the barrier characteristics of the gingival epithelium. Beneficial bacteria may enhance gum health in two primary ways. First, they may trigger the production of antimicrobial peptides (AMPs) by the host's immune system, which eliminates infections. Furthermore, certain beneficial microbes possess intrinsic antibacterial properties that fortify the epithelial barrier and aid in the elimination of harmful pathogens. Ultimately, the gum line is reinforced by these two processes, which are fuelled by helpful microbes. When some oral germs penetrate the gingival sulcus epithelium, the physiological barrier's integrity is jeopardised. Their presence increases the permeability of the tissue by changing the metabolic balance.

Two. Microbially damaged tissues may be rapidly regenerated since gingival sulcus cells regenerate in 6–12 days. It has been investigated how periodontopathic bacteria and their toxins affect the breakdown of the epithelial barrier in addition to the degradation brought on by neutrophils. Bacterial lipopolysaccharide (LPS) exposure has been shown in vitro to lower claudin-1 levels after JE exposure, hence reducing the degree of epithelial barrier degeneration. According to recent research, the virulence protein of P. gingivalis may break down E-cadherin, which

is essential for preserving the integrity of the gingival epithelium. In a lab context, this damage interferes with the epithelium's defence systems. The findings emphasise the significance of bacterial alteration of epithelial barrier function, which seems to be a key factor in the onset and advancement of periodontal disorders. Recent research indicates that gingival epithelial integrity may be maintained with the use of drugs, dietary supplements, and metabolites. For instance, irsogladine maleate functions as an antiulcer drug and shields the gum epithelium from periodontopathogen-induced damage by blocking the degradation of the proteins claudin-1 and E-cadherin. Vitamins C and E may help rebuild E-cadherin, which is impaired in the epithelial cells of gums infected with P. gingivalis. A research found that green tea polyphenols boost the production of proteins associated with tight cell junctions, including occludin and ZO-1, in gingival keratinocytes infected with P. gingivalis. Instead of being static, tight junctions are dynamic structures that alter over time in response to a variety of environmental stimuli. This includes external stimuli like dietary ingredients, viruses, and commensal bacteria, as well as internal stimuli like growth hormones and cytokines [54]. Studies have confirmed the presence of approximately 40 proteins in tight junctions, including claudins, occludins, and ZO-1 [50]. Another research says that catechin promotes the integrity of the oral epithelial barrier. According to the findings of the immunofluorescence technique, this impact is most likely induced by an increase in the expression or a change in the distribution of the proteins ZO-1 and occludin. A crucial component of the tight junction, ZO-1 interacts directly with the cytoplasmic actin and occludin proteins that make up the transmembrane tight junction [51]. In 1963, transmission electron microscopy allowed the discovery of tight junctions (TJs), which give a close connection between cells. Their existence in the intercellular space of epithelial cells and their relationship to paracellular transport systems have been proven by studies. Regardless of their sort (tight or leaky), TJs create an interconnected network of filaments that spans the superficial and deep layers of the epithelium, according to a more detailed investigation utilising freeze-fracture electron microscopy. Studies

have established a close link between the shape of TJ strands and the epithelium's barrier function. This relationship is demonstrated by transepithelial electrical resistance (TER), which is measured in intestinal epithelial cells. TJ strands are now believed to be protein complexes that keep the intercellular gap on the cell's apical surface together, reinforcing the epithelial barrier. The earliest component of tight junctions (TJs), the protein ZO-1, was found in 1986. Cingulin was discovered as a peripheral protein of tight junctions in 1989. As the first transmembrane protein needed for the establishment of tight junction barrier function, occludin's discovery in 1993 heralded a major advance. Other transmembrane proteins that interact with the TJ complex were discovered during further investigation. These include claudins, cell adhesion molecules (JAMs), membrane-associated domain 3 (MarvelD3), vesicle trafficking, and MAL and its analogs. It is vital to bear in mind that some tight junction proteins, including as claudin-2 and claudin-15, both help in the creation of paracellular pores that act as a natural barrier by enabling water and ions to flow through enterocytes. A detrimental cycle in which the immune response associated with barrier dysfunction exacerbates inflammatory processes in the gastrointestinal tract and promotes the development of pathological disorders may be begun by disruption of epithelial barrier function [31]. The degree of permeability, which is influenced by the structure and molecular configuration of tight junctions, is a crucial component of the permeability of the epithelial barrier. On the surface of the cell's apical membrane, certain proteins interact to create dynamic structures known as tight junctions (TJs). The positions of each of their constituent proteins may be used to differentiate them; some form a cytoplasmic scaffold, while others cross the membrane. Based on the number of transmembrane domains, transmembrane proteins that make up tight junctions (TJs) can be divided into four groups: single-span proteins, such as the adhesion molecule JAM, Crb3, and CAR; three-span proteins, such as BVES; and tetraspan proteins, such as claudins, occludin, tricellin, MarvelD3, and MARVEL proteins associated with tight junctions (TAMPs). Research on JAM, occludin, claudin, and tricellulin has shown that

these proteins regulate the intestinal epithelium's tight junction (TJ) permeability. JAMs, which belong to the immunoglobulin superfamily, are crucial for the adhesion and permeability of endothelial and epithelial cells. JAM-A, JAM-B, JAM-C, and JAM-4 are the four versions of JAM. The role of JAM-4 in the tight junction structure is still mostly unknown [44].

Tight connections are crucial for the early phases of periodontal tissues' antimicrobial defence, according to an analysis of the available data. Microbial infections may be able to get past the epithelial barrier due to inadequate permeability. This might worsen damage to the gingival sulcus epithelium and lead to periodontal inflammation by systematically upsetting the microflora balance.

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