

Salivary calprotectin level in patients with oral lichen planus

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Abstract

Objectives: assessment the concentration of calprotectin in the saliva of patients with oral lichen planus compared to healthy individuals and its relation with severity of the disease . **Background:** Calprotectin, a calcium-binding protein, is a key player in the pathogenesis of numerous inflammatory diseases, such as psoriasis and acne vulgaris. However, it has not been well studied in patients with oral lichen planus. **Data Sources:** By searching and reviewing Medline databases (Pub Med and Medscape) and looking for studies that examined the possible role of calprotectin in patients with oral lichen planus available till 2022. **Study Selection:** We independently reviewed all studies to determine if they met our criteria for inclusion. We included studies that met the following criteria; 1. Written and published in English language. 2. Published in peer-reviewed journals. 3. Explain how the level of salivary calprotectin may be linked to oral lichen planus and how it may affect severity of the disease . **Data Extraction:** Studies that did not meet our criteria were excluded from our review. We assessed the quality of the studies based on whether they had ethical approval, specified eligibility criteria, used appropriate controls, and provided adequate information and well-defined evaluation measures. We used a data collection form to independently extract data from each eligible study, focusing on the outcomes that were relevant to our study. **Conclusions:** Salivary calprotectin level is increased in patients with oral lichen planus compared to healthy control subjects.

Key words : Oral lichen planus, Salivary calprotectin ,severity.

Introduction

Oral Lichen Planus (OLP) is a chronic inflammatory disease that affects the oral mucosa, including the tongue and gingival tissues. OLP affects 1.01% of the population worldwide. It is considered a potentially malignant disease and with a 1.14% probability of oral cancer development (1).

Calprotectin, belongs to the S-100 family, it is a calcium and zinc-binding protein, forming about 60% of the cytosolic proteins of neutrophils. It plays an important role in the pathogenesis of inflammation as ligand for toll-like receptor 4, mediator for the migration of polymorphonuclear leukocytes and up-regulator for neutrophils (2) .

Calprotectin can be released by different cells like; epithelial, endothelial cells, neutrophils, monocytes and macrophages. It has been regarded as a potential inflammatory biomarker. Calprotectin is connected to many inflammatory and autoimmune diseases, such as SLE, rheumatoid arthritis, Still's disease, and acute gouty arthritis (3).

This protein can be found in feces, various tissues, fluids, as well as in gingival cervical fluid and saliva (4) .

Materials and methods

Data Sources: The literature on the putative link between salivary calprotectin and OLP and its connection to severity of disease up to 2022 was sourced via a search of the Medline databases (Pub Med and Medscape) .

Study Selection: Studies were chosen after being subjected to a rigorous , objective and transparent selection process . They were included if they fulfilled the following criteria:

1. Written in English language and published .
2. Appearing in publications with a strict peer-review process.
3. Explain the relation between salivary calprotectin and OLP .

Data Extraction: Research studies were not included if they did not meet the inclusion criteria . Ethical permission , eligibility criteria , controls, information and well-defined evaluation measures were all factors in determining the study's quality . Data from each eligible qualifying study were independently abstracted using a data collection form to capture information relevant to our concerned study outcomes.

Review of literature:

Oral lichen planus

Oral lichen planus is a common mucocutaneous disease with chronic inflammatory progression that is caused by activation of immune response to skin and mucous changes (5).

The prevalence of OLP is 0.3% in non-smokers, 3.7% in people with mixed oral habits, and 13.7% in smokers. It has been reported common in females than in males by a proportion of 3:2. Oral lichen planus occurs more frequently than the cutaneous form (6).

Clinical manifestation

Clinical subtypes; OLP has six clinical variants ; reticular, erosive, papular, plaque

like, atrophic and bullous. However, few authors classified OLP into only two types: reticular (reticular, plaque-like) and erosive (atrophic, ulcerative, and bullous). The most common type is the reticular form (7).

The sites which is commonly affected are; the bilateral buccal mucosa, the tongue (the borders and the dorsum) and the gingiva, while the palate, the floor of the mouth and the lips are less commonly affected (8).

The reticular form of OLP presents as bilateral asymptomatic Wickham striae on the oral mucosa. Plaque-like OLP bears a resemblance to leukoplakia. It is characterized by a whitish appearance, typically found on the buccal mucosa (cheeks) and the dorsal surface of the tongue. Papular OLP has small white raised (papular) areas and fine striae. Papular, plaque-like, and reticular are usually asymptomatic. Erosive OLP is an ulcerative red, inflamed area. It is painful and usually ulcerate. Atrophic OLP has diffuse red lesions. Bullous OLP is characterized by a painful ulcerative surface. It presents with blisters that typically rupture and form ulcers. The erosive, bullous, and atrophic variants of OLP are collectively known as the "red form" of OLP and are associated with pain (9).

Etiopathogenesis of oral lichen planus

While the precise etiology of this disease remains unknown, certain factors may increase the risk of developing it. These factors include: genetic background, dental materials, drugs, infection, bowel diseases, food allergies, smoking, trauma, hypertension, diabetes mellitus, and autoimmune disorders (10).

Candida superinfection can make the symptoms of OLP worse, especially the erosive forms. Candida metabolism produces various cancer-causing substances, such as nitrosamines and acetaldehyde. OLP lesions that are exposed to known risk factors for oral cancer, such as smoking, alcohol consumption, or Candida superinfection, need to be monitored closely because they have a higher chance of becoming cancerous (11).

Oral lichen planus can be exacerbated by a variety of restorative materials commonly used in the oral cavity. The most frequently implicated materials include: Silver amalgam, Gold, Cobalt, Palladium, Chromium, Epoxy resins (composite) and dentures worn for a long time (12).

Smoking is linked to oral mucosa disorders that have the potential to become cancerous. According to the authors' analysis, cigarette smoke contains substances that cause chronic inflammation of the mucosal surfaces, which increases the risk of OLP malignant transformation (13).

The pathogenesis of this disease is a subject of many hypotheses. Oral lichen planus is a persistent inflammatory condition characterized by the infiltration of CD8+ T cells into the affected tissues that kill basal keratinocytes. The initiation of this process may be attributed to either the presentation of a specific antigen on the surface of keratinocytes during the early stages of the disease or the erroneous recognition of the body's own peptides as foreign antigens by the immune system. Various cell types, including keratinocytes, Langerhans cells, CD4+ and CD8+ T cells, macrophages, and mast cells, as well as the cytokines and chemokines they secrete, and proteins of the extracellular matrix all play a role in triggering the disease by activating various pathogenic pathways. (14).

Calprotectin

Calprotectin is a 36-kilodalton (kDa) protein that belongs to the S100 family of calcium-binding proteins. The name S100 comes from the fact that these proteins are soluble in 100% ammonium sulfate at neutral pH. Calprotectin makes up about 60% of the cytosolic protein in neutrophils, which are the main source of calprotectin. However, it also comes from monocytes and macrophages, but to a lesser extent (15).

Calprotectin can be found in the blood and other bodily fluids, such as urine, feces, cerebrospinal fluid, synovial fluid, and saliva. This makes it a useful marker for inflammation in many disorders (16).

Mechanism of action of calprotectin

S100A8 and S100A9 proteins are normally produced by granulocytes, monocytes, and macrophages when they are activated by pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs). However, under certain conditions, other cell types, such as endothelial cells, keratinocytes, osteoclasts, chondrocytes, and fibroblasts-like synoviocytes, can also produce and release calprotectin (17).

When calprotectin is released into the extracellular space, it builds up at sites of inflammation, interacts with proteins on the cell surface, initiating specific signaling cascades. Calprotectin binds to dedicated receptors that are implicated in diverse signal transduction pathways. These receptors include Toll-like receptor 4 (TLR4), the receptor for advanced glycation end products (RAGE), and extracellular matrix metalloprotease inducer (EMMPRIN). This interaction results in the expression of inflammatory cytokines and chemokines, as well as the generation of reactive oxygen species (ROS). All of these factors serve to amplify the inflammatory

response. Furthermore, this signaling cascade leads to increased expression of both the ligand (calprotectin) and its receptor, creating a self-perpetuating cycle of inflammation. (18).

Calprotectin Relation with different dermatological diseases :

In psoriasis, a study of 72 psoriatic patients and 70 healthy controls found that serum calprotectin levels were higher in psoriatic patients, suggesting that serum calprotectin is a marker for both the risk and severity of psoriasis. (19).

In patients with acne vulgaris, Calprotectin levels are also higher in people with acne vulgaris, and the higher the level of calprotectin, the more severe the acne. This suggests that calprotectin can be used as an accurate measure of the severity of acne vulgaris (20).

Calprotectin and oral lichen planus

In patients with Lichen planus , Calprotectin is an important inflammatory mediator in patients with lichen planus. It is secreted by myeloid cells such as neutrophils, monocytes, and macrophages, but not by lymphocytes and basophils. Calprotectin is a marker of inflammation, a part of the immune system's defense mechanisms, and a regulator of the immune system's normal functions (21) .

Calprotectin is a protein that activates TLR4 and RAGE. This allows calprotectin to mediate its functions outside of the cell. Calprotectin is therefore an important part of the inflammatory process. Lymphocytes and macrophages are both inflammatory cells that play a role in OLP. These cells release a variety of inflammatory mediators (22).

Conclusion:

From the results of present study, it is concluded that salivary calprotectin level is increased in patients with oral lichen planus.

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