

# Awareness of Oral Manifestations Related to Systemic Diseases

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**Abstract:- Any alteration in systemic functions of the body show initial signs in the oral cavity. Oral manifestations show up as ulcers or inflammations. Patients are mostly unaware of the cause of oral manifestations. As dental practitioners, we are the first to identify these signs. In order to diagnose the underlying cause for the oral signs, we must have sound knowledge about the systemic diseases, their relation to the oral cavity and its oral manifestation. This review article focuses on the various oral manifestations linked to systemic conditions and the awareness regarding these conditions.**

**Keywords:- Awareness, Oral Manifestation, Systemic diseases, Diabetes, Hematological disorders, Autoimmune diseases, Nutritional deficiencies.**

## I. INTRODUCTION

Oral cavity is the mirror of human body. Every pathology usually has its manifestations emerging first in the oral cavity. As dental practitioners have the ability to identify the oral signs, we have both positive and negative responses in relation to human systemic health and oral health. Every other specialist has only a minor reflection in the oral health when compared to systemic health. Only the periodontist has a direct reflection over the systemic diseases. In both adult and paediatric patients if the oral health is poor it is a reflection of their systemic health. A simple oral infection may also lead to a complicated systemic infection. The most common infection occurring in the oral cavity is ulcerations. This review article is a brief discussion of the impact of the systemic conditions like diabetes, hypertension, haematologic disease like leukaemia, anaemia and other vitamin deficiency or nutritional deficiencies. The awareness among the general public or the health practitioners is very less when compared to the expected.<sup>[1]</sup>

## II. ORAL MANIFESTATIONS OF SYSTEMIC DISEASES

Literature shows many conditions related to systemic diseases. This review gives a brief overview of certain oral manifestations. For a better understanding, it can be grouped under the following headings; a) Hormonal, b) Hematological, c) Gastrointestinal, d) Renal, e) Autoimmune, f) Nutritional, g) Drug Induced, h) Syndromic and i) Neoplastic disorders.

### A. Hormonal disturbances

Diabetes mellitus is a metabolic disorder caused by decreased insulin action or secretion or both, leading to hyperglycemia. Hyperglycemia for a long term becomes a risk factor for periodontal diseases. Diabetes mellitus and periodontal diseases have a complex interlink which is considered "bidirectional".<sup>[2]</sup> Periodontal diseases are considered to be the sixth complication of diabetes mellitus.<sup>[3]</sup> It is shown that periodontal diseases are more prevalent in diabetic patients and the inflammatory mechanism of periodontal diseases demonstrate adverse effects in the metabolic control of diabetes. Periodontal bacteria along with inflammatory cytokines which are produced by the inflamed periodontal tissues, enter the circulation and influence systemic inflammation. This will impair insulin mechanism leading to increased diabetes. The risk of periodontitis is determined by the level of glycaemic control.<sup>[4]</sup>

Uncontrolled diabetic patients with poor oral hygiene maintenance are prone to fungal infections like candidiasis, which is an early yet unspecific sign. They have increased candidal colony-forming units in saliva due to increased salivary glucose.<sup>[4]</sup> Halitosis is considered as the second most common oral complications in uncontrolled diabetic patients.<sup>[1]</sup> The other common oral manifestations of uncontrolled diabetes mellitus are gingivitis, periodontitis, xerostomia associated with burning mouth syndrome. Xerostomia results in increased incidence of dental caries and tooth loss. Diabetic patients also experience delayed

wound healing due to reduced cellular response like reduced blood supply.<sup>[6]</sup>

Thyroid and parathyroid hormones levels also have an effect on the oral cavity. Hypothyroidism causes fatty deposits over lips and tongue causing swelling. It also affects tooth eruption in children. Hypoparathyroidism also affects tooth eruption in children and may sometimes cause pitting type of enamel hypoplasia. Hyperparathyroidism results in loss of lamina dura resulting in ground glass appearance on radiographic examinations. In advanced cases of primary hyperparathyroidism, haemorrhage occurs within the bone especially in mandible which is referred to as brown tumour.<sup>[5]</sup>

Addison's disease is caused due to adrenal insufficiency resulting in increased release of adrenocorticotrophic hormone. ACTH contains melanocyte stimulating hormone. MSH causes bluish black hyperpigmented patches in the mouth. This hyperpigmentation is absent in secondary adrenal insufficiency.<sup>[7]</sup> Pigments can sometimes appear as melanotic macule.<sup>[1]</sup>

#### B. Hematologic disorders

Hematologic disorders exhibit non-specific and pathognomonic oral manifestations. It represents in different forms in the oral cavity based on underlying conditions. In anaemia mucosal pallor and atrophy are common. Likewise, gingival bleeding and haemorrhages are associated with coagulopathies.<sup>[8]</sup> Treatment of oral manifestations of hematologic disorders is based on the management of the underlying disease in coordination with patient's haematologist.<sup>[5]</sup>

Anemia is a condition characterised by reduction in haemoglobin and oxygen due to reduced red blood cells. Oral manifestations include pallor of oral mucosa, glossitis, reddened tongue with atrophic borders.<sup>[1]</sup>

Iron-deficiency anaemia is a condition due to insufficient dietary intake, malabsorption of iron, hemolysis, chronic blood loss and pregnancy. Oral manifestations include mucosal pallor, angular cheilitis and atrophic glossitis.<sup>[8]</sup>

Megaloblastic anaemia most commonly results from vitamin B12 or folate deficiency. Oral manifestations include atrophy of oral mucosa which is exhibited by glossitis and angular cheilitis. Tongue shows beefy red and erythematous patches on buccal mucosa which is painful and sometimes patient notice alterations in taste.<sup>[8]</sup>

Hemochromatosis is a chronic disease, characterised by the deposition of excess iron (i.e. ferritin and hemosiderin) in the body. Oral manifestations include gingival or mucosal pigmentations. Primary oral manifestation of hereditary hemochromatosis is blue-grey to brown hyperpigmentation commonly seen in palate, buccal mucosa and gingivae.<sup>[8]</sup>

Cyclic hematopoiesis is a rare disorder which is due to periodic failure of hematopoietic progenitor cells. Most commonly seen in infants and children. Oral manifestations include recurrent gingivitis and periodontitis, recurrent aphthous stomatitis. Finding of recurrent aphthous stomatitis with or without periodontal disease in child should suspect cyclic neutropenia.<sup>[8]</sup>

Sickle cell anaemia is an autosomal recessive disorder. Oral manifestations include paleness of oral mucosa which is sometimes observed as yellowish in colour due to the haemolytic nature of anaemia, papillary atrophy of tongue, delayed tooth eruption, osteomyelitis of mandible, inferior alveolar nerve damage, pulpal necrosis of healthy teeth.<sup>[9]</sup>

Thrombocytopenia is a haemorrhagic disorder which is characterised by abnormal reduction in number of circulating platelets along with extravasation of blood from capillaries. Oral manifestations include small single or multiple petechial haemorrhages, haemorrhagic blisters, ecchymosis, and spontaneous bleeding. These lesions are usually on the soft tissues such as buccal mucosa, the junction between the hard and soft palate and the gingivae.<sup>[10]</sup>

#### C. Gastrointestinal disorders

Gastrointestinal disorders consist of a vast range of disorders from inflammatory to infectious. Inflammatory bowel disorder comprises of two main forms; i) Crohn's disease and ii) Ulcerative colitis.<sup>[11]</sup>

Crohn's disease is a chronic inflammatory condition where the gastrointestinal tract especially distal ileum and colon are affected forming non-caseating granulomas. Oral lesions include gingivitis, erythematous papules and swelling of lips with cracks along the vermilion. There is presence of mucosal tags in the vestibular areas and "cobblestone" appearance of the mucosa (combination of deep ulcerations within intact portions of mucosa) causing difficulty in eating. Ulcerative lesions such as angular cheilitis and recurrent aphthous stomatitis is also seen.<sup>[11,12]</sup>

Ulcerative colitis is the chronic inflammation of the rectum and colon of the gastrointestinal tract. The important oral manifestation in this condition is Pyostomatitis vegetans, causing multiple yellowish-white pustules which may rupture and coalesce. These are mostly found on the tongue, lips, buccal mucosa, soft and hard palate.<sup>[11,12]</sup>

Gastroesophageal reflux disorder is the regurgitation of gastric contents from the stomach to the esophagus affecting the esophageal mucosa. This causes sore throat and burning sensation. When the acid reflux reaches the oral cavity, it causes erosion of teeth, which is the most important oral sign of GERD. Other oral features include ulceration, xerostomia and halitosis.<sup>[12]</sup>

#### D. Renal diseases

In Chronic Renal Failure, there are many manifestations including altered taste, gingivitis, ulcerations, candidiasis, xerostomia, etc. The important manifestation that comes under the manifestations of CRF is uremic stomatitis where the urea levels are increased causing pain and burning sensation. Decrease in platelet factor III causes bleeding tendency on the gingiva causing difficulty in brushing and causing severe pain and burning sensation. It may also be due to the anticoagulants used during the treatment of chronic renal failure that is the haemodialysis.<sup>[13]</sup>

Renal Osteodystrophy is a condition caused due to bone metabolism disorder where the patients are at high risk of fracture during dental procedures mainly extraction. Periodontal diseases such as gingival hyperplasia is also a main manifestation of CRF which leads to accumulation of plaque deposits. Gingival recession or pocket formation are also included in such cases. Mucosal lesions mainly consist of white patches and ulcerations called "UREMIC FROST" caused due to urea deposits.<sup>[13]</sup>

#### E. Autoimmune diseases

There are two types of lupus erythematosus namely discoid lupus erythematosus and systemic lupus erythematosus. It is common in United States and other related countries. The most common oral representation in this kind of auto immune disorder is angular colitis manifesting as ulcers, erythema or hyperkeratosis. In conditions particularly of DLE it is mainly ulcerated with white striae, which usually resembles lichen planus.<sup>[5]</sup>

Amyloidosis is a disorder characterised by pathologic deposition of fibrillar proteins. Amyloidosis can either be primary or secondary manifestation of neoplastic or chronic inflammatory disorders. Oral manifestations include edema, submucosal haemorrhage, macroglossia, xerostomia, glossodynia, alteration in taste. AL amyloidosis represents macroglossia. Patients with macroglossia present with enlargement or woody indurations of tongue. Scalloping of the lateral borders of tongue is seen which is due to pressure exerted by the teeth. In some cases, patients with AL amyloidosis are present with a firm yellowish nodule, composed of amyloid also occurring in palate, gingiva or buccal mucosa. Patients with localised amyloidosis represent with one or more soft yellow, red, purple or blue nodules on tongue, buccal mucosa, gingiva and palate.<sup>[5]</sup>

Pemphigus vulgaris is a mucocutaneous autoimmune disorder affecting both oral and systemic health. The skin and the mucous membrane is affected, but in most cases the oral cavity may be the only affected site where it resembles that the autoimmune system of the whole body is affected.<sup>[14]</sup>

Sarcoidosis is a condition where the accumulation of epithelioid granuloma is the oral manifestation of severe chronic systemic disease. In this condition the salivary glands, mainly the parotid glands are enlarged leading to xerostomia and increasing risk of dental caries.<sup>[14]</sup>

Orofacial Granulomatosis is another immune mediated disorder where the soft tissues and other peri oral tissues like lips are enlarged with the signs of linear ulceration.<sup>[14]</sup>

#### F. Nutritional deficiency

Vitamin -A deficiency is often due to the lack of intake of Vit-A rich foods. Oral manifestations include decreased oral epithelial tissue development, enamel hypoplasia, periodontitis, and impaired tooth formation.<sup>[15]</sup>

Vitamin -D deficiency is responsible for calcium homeostasis, bone remodelling and cell proliferation and differentiation. It is due to lack of adequate sunlight exposure and intake of Vit-D rich foods. Oral manifestations include amelogenesis and dentinogenesis imperfecta. Enamel hypoplasia and maturation defects in permanent teeth. Children from familial X-linked recessive hypophosphatemia rickets only represents with dentin dysplasia, dentinogenesis imperfecta and dental abscesses without any infection or trauma.<sup>[15]</sup>

Vitamin -K (Phylloquinone) Oral signs include gingival bleeding and sub mucosal haemorrhage.<sup>[8]</sup>

Vitamin - C deficiency leads to scurvy which is characterised by connective tissue defects. Oral manifestations include hyperkeratosis, petechia, inflamed and bleeding gums. Xerostomia, due to alterations in oral-periodontal-ecosystem there is increase in oxidative stress and it is susceptible to infections.<sup>[15]</sup>

Vitamin B has many subclassifications of oral manifestations; Vitamin-B2 (Riboflavin, Lactofavin) deficiency leads to erythema of oral mucosa, glossodynia, cheilosis, atrophic glossitis representing a magenta colour, and angular cheilitis. Vitamin - B3 (Niacin, Nicotinic acid) deficiency results in mucosal edema, angular cheilitis, chelosis, bright red glossitis, gingival erythema, burning mouth and dental caries. Vitamin - B6 (Pyridoxine, Pyridoxal, pyridoxamine) deficiency causes cheilosis, angular stomatitis, atrophic glossitis and gingival erythema. Vitamin - B12 deficiency causes glossitis, aphthous stomatitis, atrophy of papillae, reddened tongue, burning sensation of tongue, dysphagia, angular stomatitis and pallor of oral tissues.<sup>[8]</sup>

#### G. Drug Induced

Certain drugs used for systemic diseases tend to cause side effects which become visible in the oral cavity. Antihypertensive drugs such as ACE inhibitor and diuretics cause xerostomia leading to an increased risk of caries, dysgeusia, difficulty in mastication associated with burning sensation. Other drugs causing xerostomia are omeprazole, indinavir, tramadol, loratadine, and cetirizine. Gingival hyperplasia is caused due to calcium channel blockers or phenytoin taken by the hypertensive patients which causes lichenoid reactions. It starts with interdental papilla inflammation followed by generalised inflammation of gingiva along with accumulation of plaque.<sup>[17]</sup>

Sometimes, anticoagulants cause spontaneous bleeding of gums or while eating. Other groups of drugs like antidepressants and antihistamines cause bleeding on trauma to periodontal tissues. Oral ulcerations occur more commonly in elderly patients who take self-prescribed medications of aspirin and potassium tablets. Prescribed medications like NSAID, sulfonamides, barbiturates, beta-blockers, dapsone, salicylates and tetracycline are also shown to cause ulcers in oral cavity.<sup>[17]</sup>

#### H. Syndromic disorders

In Sjogren Syndrome, the most common oral manifestation is Xerostomia. If the patient is affected with any other autoimmune disorder such as SLE or any other syndrome, then the parotid gland is affected leading to increased risk of dental caries. The absence of saliva may pave way to many other complications such as, mucous membrane appearing red dry wrinkled and tongue may also appear ulcerated. It is always triggered with Non-Hodgkin's lymphoma.<sup>[5]</sup>

Ulcers such as recurrent aphthous stomatitis is one of the major manifestations in autoimmune disorder like Behcet syndrome. RAS is the most common manifestation where only non-keratinized mucosa of the oral cavity is affected. It usually appears as browned tender surface with fibrin as slough.<sup>[5]</sup>

Gardner Syndrome, an autosomal dominant disorder, is characterised by intestinal polyposis which may transform into colonic adenocarcinoma. There may be supernumerary teeth (peg lateral). Impacted teeth with compound odontoma, osteoma and epidermoid cyst of jaw are noticed during radiographic examinations. Presence of more than four osteomas must raise a doubt of Gardner syndrome.<sup>[18]</sup>

Peutz-Jeghers Syndrome is also an autosomal dominant condition forming hamartomatous polyposis in the intestine. Oral signs include freckles around the lips and vermilion border with brown painless patches over the buccal mucosa, labial mucosa and tongue.<sup>[18]</sup>

#### I. Neoplastic disorders

Leukaemia is a malignant condition of hematopoietic cells, which is characterised by bone marrow destruction and proliferation of malignant leukocytes.<sup>[8]</sup> It is one of the most life-threatening cancers and needs early treatment.<sup>[1]</sup> Most common oral symptom is pallidness of mucosa and extreme bleeding in gingiva. Gingival enlargement, ecchymosis, petechia, mucosal ulcers, haemorrhages are also common findings of leukaemia within the oral cavity.<sup>[5]</sup>

Lymphomas are malignancies of lymphocyte cells. These tumors most commonly develop in the lymph nodes. There are two types of lymphomas. Hodgkin lymphomas (HL) and Non-Hodgkin lymphomas – (NHL). Both are more common in men than women. Oral manifestations are more likely to occur in NHL particularly in AIDS associated B-cell lymphoma and Burkitt's Lymphoma. Lymphoid tissues of Waldeyer's ring as well as the gingiva and vestibule are preferentially affected by NHL. Painless, with or without

traumatic ulceration, soft masses also involve the palate, buccal mucosa and gingiva.<sup>[8]</sup>

Multiple myelomas due to over production of immunoglobulin light chains. It is a plasma cell dyscrasia. When seen radiographically multiple 'punched out' lesions are seen. Up to 30% of patients with multiple myeloma have tooth loss, involvement of mandible associated with pain, paresthesia and swelling. Marrow infiltration by malignant plasma cells causes thrombocytopenia leading to gingival bleeding and oral petechia. Plasmacytomas are found on gingiva or hard palate which appear as dome shaped nodules.<sup>[8]</sup>

Squamous cell carcinoma is the one of the most common malignant neoplasm associated with the oral cavity. It affects the gingival mucosa, tongue, buccal mucosa and lingual mucosa, leaving an ulcerative lesion. They may be proliferative or necrotic in nature.<sup>[14]</sup>

### III. CONCLUSION

Oral manifestations are mostly because of underlying systemic disease complications. Patients are unaware of these signs and are often neglected. There are many diseases with similar oral presentations. Many a times dentists are the people who direct the patients to the general physicians for treatment of systemic diseases. Currently a lot of research is going on to check the relationship between periodontal and systemic diseases. They have even identified malignancy, cognitive disorders and even erectile dysfunction to be associated with periodontal diseases. There is a need for more CDE programmes to increase the awareness about these facts among dentists. As dentists, we must be able to make appropriate diagnosis and increase awareness among patients and general public.

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