Oral complications associated with different types of anaemia: A mini review

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ABSTRACT: In India, anaemia is a common and serious health disorder. Anaemia is said to be present when the haemoglobin level in the blood is below the lower extreme of the normal range for the age and sex of the individual. Anaemia can occur due to a variety of reasons including nutritional deficiencies, genetic disorders, parasitic infections or chronic diseases. In these patients red blood cells appear different in size and shape and contain normal or low level of haemoglobin. Red blood cells become functionally abnormal and tend to break down easily. This illness affects body health generally and makes humans more lethargic and sensitive to infections. Sever systemic complications are well known in anaemic patients. In addition, anaemia also affects oral health. Soft oral tissues as well as bony structures get significantly affected in anaemic patients. Very often, lack of colour of the gums, soreness in the tongue and caries are complaints from the anaemic patients. Oral cavity of these individuals showed more susceptibility towards inflammation and microbial attack on soft tissues. Periodontitis, atrophic glossitis and angular cheilitis are commonly observed inflammatory conditions in anaemic patients. In addition to these common oral manifestations, magenta tongue, chipmunk face, malocclusion and mental nerve neuropathy are uncommon and unique symptoms noticed in anaemic case studies. Not only haematological abnormalities but also oral hygiene play important role in development of such complications. Further, expression of these oral signs helps in the early diagnosis of anaemic conditions. This review put a light on the oral manifestations arising due to anaemia, its pathogenesis and treatment strategies which can be employed by dental practitioner.

Key Words: Anaemia, Oral complications, Inflammation, Diagnosis, Dentist's role.

INTRODUCTION:

Anaemia is a disease caused by below-normal levels of haemoglobin, a protein in red blood cells that carries oxygen to the muscles, brain and other organs. Anaemia is a functional inability of the blood to supply the tissue with adequate oxygen for proper metabolic function. It is not a disease, but rather the expression of an underlying disorder or disease. About 30% of world population is anaemic.[1] In this population, size and shape of RBCs varies which contain normal or decreased amount of haemoglobin. RBCs showed microcytic, macrocytic or hypochromic appearance and more susceptibility for haemolysis. Depending on the aetiology, anaemia is classified as i. nutritional deficiencies anaemia; ii. Anaemia due to genetic variation; iii. Anaemia following parasitic infections and iv. chronic disease-induced anaemia. Most anaemic cases are mild and easily treated. However, severe and long lasting anaemia cause significant decrease in the level of energy and damage to heart, brain, muscles and other body organs.

Oral cavity is most widely suffered part of body due to anaemia.[2] Anaemia reduces the number of red blood cells present, leading to paleness in the gums (anaemia gums).[2] This paleness can also affect the tongue and the mucous membranes inside the mouth shown as redness, swelling and pain in the tongue. Anaemia also leads to development of inflammatory conditions. Periodontitis is an inflammatory disease of the supporting tissues of the tooth caused by specific microorganisms in a susceptible host.[3] Anaemia also makes the patients more susceptible for the bacterial infections such as candidiasis.[4] Development of this condition varies according to type of anaemia.

AIM:

In the present article we attempted to review the various complications commonly noticed in the anaemic patients. Major types of anaemia were considered and details about oral as well as dental manifestations were

noted down. In addition, we also focused on underlying pathological mechanism involved in the oral symptoms following anaemia.

Iron deficiency anaemia and oral complications:

Iron deficiency is one of the most common disorders affecting humans. Iron deficiency anaemia mainly results from either blood loss or nutritional scarcity affecting mainly children and menstruating woman. It is most common type of anaemia affecting approximately 50% of world anaemic population.[5] It has many oral signs and symptoms. This includes mucosal pallor, recurrent oral ulcers, atrophic glossitis, loss of normal keratinisation, glossodynia (burning sensation in mouth) and angular cheilitis.[6, 7] Atrophic glossitis is an inflammatory disorder of the tongue mucosa leading to a smooth, glossy appearance with a red or pink background, flattening of the tongue papillae and erythematous tongues.[8] It is often accompanied by tenderness or a burning sensation. It is suggested that low levels of iron in the blood may result in decreased myoglobin concentration, a protein in red blood cells which is important for tongue's muscle tissue.[9] Angular stomatitis (cheilitis) is inflammation and painful fissures of one or both corners of the mouth and lips developing dry scaling of the lips and corners of the mouth. Furthermore, iron deficiency predisposes the patient to candidal infection. This may arise due to reduced level of lactoferrin, a protein present in saliva. Lactoferrin provides a defence function by binding with iron and withholds the iron from pathogens such as Candida. When lactoferrin levels are low, candida can proliferate on the free iron.[7,10] The deficiency of iron causes tissue hypoxia resulting in relatively severe periodontal disease expression. It is suggested that iron deficiency anaemia do not initiate periodontitis, but they may predispose, accelerate, or increase its progression.[11] Treatment strategies to treat the oral manifestations in this condition must focus on correcting the deficiency state and providing adequate energy, protein, fluids and nutrients to promote healing. An antifungal therapy is essential to treat the candidal infection in mouth.[7] Diagnosing iron deficiency anaemia by observing the atrophic tongue may play an important role in preventing future consequences such as impaired mental and motor development.[5,12]

Megaloblastic anemia and oral complications:

Megaloblastic anaemia is a macrocytic anaemia, in which distinctive morphologic abnormalities occur in red cell precursors in bone marrow, namely megaloblastic erythropoiesis. It is caused by a vitamin B12 or folic acid deficiency. This vitamin insufficiency may results from surgical resection of the ileum or small intestinal diverticula or most commonly from malnutrition.[13] Oral lesions are among the most common initial symptoms of megaloblastic anemia.[14] The oral manifestations of megaloblastic anaemia include painful atrophy of the entire oral mucous membranes and tongue (glossitis), stomatitis, oral candidiasis, diffuse erythematous mucositis mucosal ulceration (recurrent aphthous ulcers) and pale oral mucosa.[15,16] Glossitis and glossodynia are two most classic oral symptoms in patients with vitamin B12 deficiency. Characteristically, glossitis, glossodynia, glossopyrosis, gradual atrophy of the papillae of the tongue leading to bald tongue, condition known as hunter's glossitis or moeller's glossitis.[17] Magenta tongue is unique characteristic associated with B12 deficiency-induced anaemia.[16] The inflamed tongue can cause discomfort at the levels of pain, soreness, and a burning sensation to intense paresthesia.[18] Unlike other pathogenesis of anaemia, oral candidiasis is rarely found in patients with pure B12 deficiency.[19] Oral signs and symptoms may appear in anaemic patients as a result of basic changes in the metabolism of oral epithelial cells.[20] It has been observed that oral signs can be established before the development of generalized symptoms of anaemia. The dentist, who is often consulted first, has a prime opportunity and responsibility to contribute to diagnosis. Dentist may diagnose this condition based on changes in oral mucous membranes commonly reported in 50–60% of all patients with megaloblastic anaemia.[14, 21] Although, proper interpretation and correlation between megaloblastic anaemia and oral sign can be done with sound knowledge of normal blood values, patients must be referred to a hematologic centre for adequate treatment.

Sickle cell anaemia and oral complications:

Sickle-cell disease is a genetic hematological disease, in which polymerization of abnormal hemoglobin leads to morphologic alteration in erythrocytes. This disorder is caused by the production of abnormal hemoglobin S.[22] With decreased oxygen tension, the abnormal hemoglobin polymerizes, forming fluid polymers (tactoids) that cause the red cells to deform into a characteristic sickle shape which may be plugged at different areas of the microcirculation or large vessels. The hallmark features of sickle cell anaemia are chronic hemolysis

and vaso-occlusion. This is also termed as "sickle crisis" and major cause of ischemic tissue injury or devastating multisystem complications.[23] A wide spectrum of complications results from this condition. Oral and maxillofacial tissues (soft tissues as well as in bony structures) are frequently affected by sickle cells anaemic patients. When it occurs, the basic pathogenicity is similar to that in other organs. These orofacial changes include midfacial overgrowth attributable to marrow hyperplasia.[24] It is also accompanied with increased thickening of the skull and osteoporotic changes.[25] Impaired dentine mineralization, mandibular osteomyelitis, orofacial pain, craniofacial skeletal alterations such as exaggerated growth/protrusion of the midface, maxillary expansion, a predominance of vertical growth, mandibular retrusion, a convex profile, and maxillary protrusion also observed in these patients.[26] Soft oral tissues reflect paleness of the oral mucosa, delay in tooth eruption, atrophy of the tongue papillae.[26] The intrinsic opacity of enamel, malocclusion, caries and diastemata are other dental observations found in sickle cell anaemic patients.[27] Patients with sickle cell disease reported to be more susceptible to dental caries.[28] However, this correlation is not so strongly validated.[29] In adult sickle cell patients, periodontal infection may precipitate painful vaso-occlusive crises that increase the frequency of hospitalization.[30,31] Incidences of malocclusions were also observed in patients with sickle cell disease. This has been correlated to muscular imbalance, absence of labial sealing or changes in the osseous base that leading to increased orthodontic intervention.[32] Unlike other forms of anaemia, mandibular osteomyelitis is uniquely observed in sickle cell patients. This makes both its diagnosis and treatment easy.[33] The mental nerve neuropathy is one of the uncommon oral complications of sickle cell anaemia.[34,35] It is thought that hypoxia following sickling is associated with osteonecrosis of the jaw especially in the mandible may leads to development of mental nerve neuropathy.[34] The possibility of blood extravasations and hematoma secondary to sickle cell anemia-induced hemorrhage should be considered as a working diagnosis of a facial swelling in sickle cell disease.[2] Since dental complications are common in these patients, preventive dental therapy is the ideal approach. The goal of the pediatric dentist is to improve and maintain excellent oral health and to decrease the possibility of oral infections. Antibiotic therapy, irrigation and curettage can be employed for the sickle cell-induced pericoronitis and periodontal abscess.[31] Fluoride therapy and routine visits to dentist may prevent the dental complications.[36]

Thalassemia and oral complications:

Thalassemia is one of the most confusing hemoglobinopathies and is a kind of chronic inherited microcytic anemia. It is characterized by defective hemoglobin synthesis and ineffective erythropoesis.[37] While, approximately 15 million of world population are suffering from thalassemic disorders, in India nearly 12,000 infants are born every year with this anomaly.[38] Many orofacial complications in thalassaemic patients have been reported. This includes enlargement of the upper jaw (chipmunk face), varying degrees of malocclusion (overbite, open bite), higher rate of dental decay, pale gums and mucosa / lining of the mouth, teeth may be discoloured, with short crowns and roots, painful swelling of salivary glands and, reduced salivary protection and dry mouth, tooth bearing bone may have a 'chickenwire-like' radiological appearance and migration and spacing of upper anterior teeth.[38,39] Intense compensatory hyperplasia of the marrow and expansion of the marrow cavity are the vital reasons of orofacial manifestations in thalassemia.[40] Periodontitis and gingivitis are very dangerous foci of infection in these immune impaired individuals.

Chipmunk face results from maloclussion subsequent to maxillary protrusion and mandibular atrophy. This may results from the early fusion of occipital sutures concomitantly with medullary hyperplasia of the anterior maxillofacial structures.[41] High dental caries index in thalassemics may attribute not only to the negligence towards oral hygiene but also to the significantly lower level of median saliva concentrations of phosphorous and IgA. Mucosal pallor and atrophic glossitis are commonest feature particularly when haemoglobin drops below 8 mg/dl. Painful swelling of salivary glands and dry mouth may results from iron deposits.[42] It is suggested that blood transfusions since birth may reduce the chances of development of these complications to 50% or decrease the severity of symptoms.[42]

The dental treatment plan differs according to whether patient has thalassemia minor, major or intermedia. Orthodontic treatment for aligning the incisors, maxillary osteotomy for repositioning of the maxilla can be done for improved esthetic outcome in thalassemic patients with orofacial deformities and malocclusion. Splenectomy is one of the treatment modalities in a thalassemic patient.[43] However, in splenectomised

individuals, oral cavity must be prevented from being a source of bacterial spread. This requires increased radicalness in dental treatment and extreme caution in orthodontic practice.

Chronic disease induced anaemia and oral complications:

The aging of the world's population is kept on producing millions of individuals with systemic and chronic medical conditions that can affect oral health and dental treatment. Signs of systemic disease are often manifested in the oral cavity before the systemic disease itself is suspected. While some oral complications are disease specific, others may overlap with multiple chronic as well as acute state of disease and increase the clinician's level of suspicion. Anaemia of chronic disease or anaemia of chronic inflammation is a form of anaemia that results due in chronic infection, immune activation, and malignancy.[44] It is the most prevalent anaemia in hospitalized patients and is the second most prevalent anaemia after iron deficiency anaemia. These conditions produce massive elevation of interleukin-6, which stimulates hepcidin production and release from the liver, which in turn reduces the iron carrier protein ferroportin so that access of iron to the circulation is reduced. Microbial infections with herpes simplex virus -1 significantly damage the oral mucosa leading to herpes labialis or primary herpetic gingivostomatitis.[45] During infection, dormant virus residing in the sensory ganglia may get reactivated secondary to immunosuppression, stress or trauma. In diabetes, dry, cracking lips may be evident. Periodontitis and diabetes have a bidirectional relationship. Diabetes is associated with an increased prevalence and severity of periodontitis is depend on glycemic control.[46] They suggested that dental team has an important role to play in the management of people with diabetes. On the other hand, oral bacteria and periodontal disease are suspected of being contributing factors to the worsening of chronic disease states.[47] This bidirectional complication can be prevented by early diagnosis of oral manifestations.

Fanconi's anemia and oral complications

Fanconi's anaemia (FA) is an autosomal recessive disorder characterized by progressive pancytopenia. It results in decreased production of all types of blood cells. Clinical oral findings commonly described in the patient of FA include periodontal changes, such as gingivitis and aggressive periodontitis, recurrent aphthous ulcers and traumatic lesions.[48] Gingival bleeding and hyperemia are remarkable findings in patients with FA.[49] Patients also express chronic anaemia, of which the main oral clinical characteristics are pallor of the mucosa and gingival.[50] Periodontitis results from accentuated horizontal loss of alveolar bone developed due to precarious oral hygiene. This is mainly attributed to the leukocytic deficiency and the presence of microorganisms. It is suggested that gingival alterations are more associated with defective oral hygiene than hematologic conditions.[51] Agenesia and presence of supernumerary teeth are noticed in the FA patients. Alterations in calcium metabolism during odontogenesis related to vitamin D resistant rickets are suggested as plausible cause for this condition.[52] Papillary atrophy, macroglossia, melanic pigmentation and squamous cell carcinoma are the most common oral manifestations on the tongue in these patients. Reduction in salivary flow (hyposalivation) is an important oral manifestation in individuals with FA.[48, 53] Anaemia, leukopenia, and defective detoxification of oxygen radicals are not major reasons of increasing tendency toward periodontal disease in patients with FA. However, medications applied during intense immunosuppressive treatment, such as prednisolone may lead to development of such conditions.[50] Most prevalent oral manifestations in individuals with FA is extremely important so that the dentist may make a correct early diagnosis and treatment of these alterations.

Conclusion:

There is significant overlap of oral manifestations in patients with anaemia due to different causes. Thus, the top priority of a diagnostic approach to anaemic individuals relies on a detailed medical evaluation of a patient's history, understanding the patient's complaints in terms of anatomy, and a good knowledge of basic pathophysiology of the anaemia. This review explains the correlation between various oral manifestations observed in the patients with different type of anemia. Anemia induced complications targets both soft tissues as well as bone structures in oral cavity. While most of the oral symptoms are overlapping between different forms of anaemia, few are hallmarks of the specific type of anaemia. Dental management of an anaemic patient requires special concern. A dentist should have profound knowledge to manage this medically compromised state of these patients. The best way is to have a multidisciplinary approach involving a dental surgeon, a haematologist and an orthodontist to safely provide dental treatment to these patients.

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