Review Article

Oral Manifestations of Anemia – A Review Article

S. Kanimozhi, M. Arunachalam, S. Pradeepsankar, M. Sathish Kumar

Department of Oral Pathology and Microbiology, Karpaga Vinayaga Institute of Dental Sciences, Kanchipuram, Tamil Nadu, India.

Abstract

Oral cavity is the window to the body and is often the area where the systemic diseases expose itself. Anemia is seen in the most of the patients in world and affects both the genders, with a high frequency in females. It is a condition of decreased RBCs or hemoglobin concentration, or decreased oxygen supply to tissues. Many factors and diseases may lead to anemia, and they are associated with orofacial signs and symptoms with different types of anemia. The common manifestations are conjunctiva and facial pallor, angular cheilitis, glossitis, dysphagia, stomatitis, magenta tongue, etc. Most of these are non-specific, but it is important to intimate the patients about their physical health care and the dental practitioners for the better understanding of treatment and also to avoid the further complications.

Keywords: Anemia, Oral diseases, Dental management.

Introduction

Hemoglobin (Hgb) is a protein-rich component of iron, which is found in the red blood cells (RBCs). It is normally comprising four globin chains of two types, they are alpha (α) and beta (β). These chains are same in length but differ by their amino acid sequences. In human's Hgb, both the embryonic and adult, α chains are identical. However, the further chains involved in adults are; β Hgb (HgbA, α2β2), gamma (γ) chain of fetus (HgbF, α2γ2), and therefore the less common adult delta (δ) chain (HgbA2, α2δ2). Hgb binds to oxygen (O2) and it supplies from the lungs to tissues throughout the body. Anemia can be defined as the decreased state of O2-binding capacity with the blood; it can be either resulted from: (a) Decreased RBC production, (b) decreased Hgb content, and (c) increased destruction of RBCs, or (d) formation of atypical RBCs with Hgb concentration below to normal (in men: 13.5–18.0 g/dL, in women: 12.0–15.0 g/dL, and in children 1.0–16.0 g/dL).[1,2] The World Health Organization have been stated the anemia when the level of Hb is below 13.0 g/dL in adult males, 12.0 g/dL in adult females, and below 11.0 g/dL in pregnant women.[3]

Classification

According to etiopathogenesis, the anemia is classified into: [2,4-6]

- Blood loss anemia (hypovolemia)
- Iron-deficiency anemia
- Anemia resulting from chronic disease
- Hemolytic anemia: Glucose 6-phosphate dehydrogenase (G6PD) deficiency
- Hemoglobinopathies: Sickle cell anemia (SCA) or thalassemia
- Hypoproliferative anemia: Aplastic anemia (AA), folate or B12 deficiency anemia

According to the RBC size (based on the mean corpuscular volume [MCV]), it is classified into: [2]

- Microcytic (MCV <80 FL/cell): Iron deficiency and thalassemia
- Normocytic (MCV = 80–100 FL/cell): SCA, G6PD deficiency, and AA
- Macrocytic (MCV >100 FL/cell): Megaloblastic anemia, such as pernicious anemia (Vitamin B12 deficiency), or folate deficiency.

Iron Deficiency Anemia (IDA)

It is microcytic and usually hypochromic, which is affecting most of the population in world. Incidence rate increases along with the age, and it is more common in women.[1] Usually, it is asymptomatic or mild form, in some cases, it requires minimal treatment.[1] It is mostly caused by low intake of iron and linked

Access this article online

Website: www.jrad.co.in

DOI: https://doi.org/10.53064/jrad.2022.13.3.145

Address for correspondence: Dr. S. Kanimozhi, Department of Oral Pathology and Microbiology, Karpaga Vinayaga Institute of Dental Sciences, Kanchipuram - 603 308, Tamil Nadu, India. Email: kaniomfp@gmail.com

Received: Jan. 04, 2022; **Accepted:** Jan. 28, 2022; **Published:** Mar. 04, 2022

How to cite this article: Kanimozhi S, Arunachalam M, Pradeepsankar S, Kumar MS. Oral Manifestations of Anemia – A Review Article. J Res Adv Dent 2022;13(3):1-3.

with poor dietary habits, extreme blood loss like in menorrhagia and some gastrointestinal ulcers, or increased need of iron in a pregnancy period or resulting from some other chronic diseases such as Crohn's disease, ulcerative colitis, and hematological malignancies.[2,7] Iron deficiency anemia shows nail findings such as splitting or spooning (koilonychia). The most common oral manifestations are mucosal pallor on the gingiva and vermilion lips, angular cheilitis and atrophic glossitis can also be seen.[8] It is usually manifested on a complete blood count as low serum ferritin, low iron levels, and increased total iron-binding capacity (TIBC), together with a decrease in RBC size (low mean cell volume – MCV) and mean corpuscular hemoglobin concentration. In the chronic conditions, blood smear may show hypochromic RBC. It is worth contrasting iron deficiency anemia with anemia of chronic diseases, where the ferritin level is normal, while both circulating iron also as TIBC are low.

Plummer-Vinson Syndrome

It is also called as Paterson-Brown-Kelly syndrome and sideropenic dysphagia. The main features included are dysphagia, IDA, and dystrophy of nails (koilonychias). Oral manifestations such as atrophic glossitis, angular cheilitis, hyperkeratotic lesion, dysphagia (due to esophageal webs), and pharyngoesophageal ulcerations.[9-11] It can be managed with the oral supplements of iron in the form of ferrous sulfate or fumarate.

SCA

SCA is one among the foremost common genetic diseases and predominantly seen in African peoples.[12] It is an autosomal recessive blood disease, which is related to the production of abnormal Hgb, caused by a selected mutation within the gene coding for the β-globin chain. This mutation (which substitutes glutamine to valine at position six of the polypeptide) leads to the assembly of an altered Hgb molecule, termed HbS, which causes deformation of the RBCs and concomitant obstruction of blood vessels.[13] During a badly oxygenated tissue environment, HbS molecules polymerize and thus end up within the formation of fibers that deform the RBCs and reduce their plasticity leads to hemolysis and creates an anemia called hemolytic anemia.[14] In addition, the vascular occlusions further reduce the oxygen supply of the affected organs. Its oral manifestations are pallor buccal mucosa, enlargement of gingiva, orofacial pain, paresthesia of mental nerve, delayed eruption, enamel hypoplasia, osteomyelitis, mongoloid facies, asymptomatic pulpal necrosis, and severe malocclusion. The radiographic features are osteoporosis, marrow hyperplasia, ground-glass appearance, thinning of the inferior border of mandible, prominent lamina dura, step ladder pattern, and hair-on-end appearance.[9,15-18] Pain managements include palliative, supportive, symptomatic, and preventive therapy. It can be prevented by precipitating factors such as folic acid supplementation, antibiotic therapy for infections, blood transfusion, and genetic counseling. Numerous studies have shown that increased adherence of neutrophil cells to the endothelium in the microcirculation is seen in SCD. Neutrophil- and eosinophil-derived mediators contribute to the inflammatory response in localized aggressive periodontitis and increased superoxide levels. As a result, severe periodontal damage that cannot be described by microbial invasion is significantly seen leading to loss of teeth and alveolar bone.[19]

Thalassemia

It is also called as Cooley's anemia, Mediterranean anemia, and erythroblastic anemia. Thalassemia is a genetic disease that involves abnormal Hgb formation.[20-22] Hgb comprises alpha and beta "chains" which, during a patient with thalassemia, are faulty as a result of which the Hgb produced is faulty. During a patient with thalassemia, problems arise due to the deficiency of healthy Hgb that the body requires for it to become properly oxygenated. A patient with thalassemia not only has lower levels of Hgb content within the bloodstream but also lacks the standard of it. At an equivalent time, the patient's body continues trying to supply more RBCs and Hgb.[23] However, since there is a genetic fault with the Hgb being produced therein individual's body, the new Hgb produced, causes further problems as an overproduction of unhealthy Hgb takes place. The main types of thalassemia are alpha and beta and then classified into further subcategories.[21,24] The most cause of thalassemia is typically the defective synthesis of alpha or beta chains.[24] Alpha thalassemia occurs when one or more of the four alpha-globin genes are either abnormal or not present in a single person. Beta thalassemia occurs when one or both beta-globin genes are either abnormal or are absent.[21,24] Its oral manifestations are; uncontrolled overgrowth of maxilla results in the excessive lacrimation and nasal stiffness, pallor oral mucosa, rodent facies, and chipmunk facies. Some of the radiographic features are coarsening of trabecula and blurring turns into "salt and pepper effect" thickening of the diploe of skull. Inner and outer plates become elongated producing bristles such as flattop or hair-on-end appearance.[9,25,26] Treatment includes blood transfusion, chelating agent, bone marrow transplantation, splenectomy, and Vitamin B supplementation.

AA

It occurs because of the failure of hematopoietic precursor cells in bone marrow to provide an adequate number of all kinds of blood cells and it consequently leads to pancytopenia.[27] Pancytopenia presents both rapid onset and progression.[27,28] Some reported etiological factors are chemicals, radiation, chemotherapy, and autoimmune diseases.[2] Incidence rate ranges between 2 and 7 per million/year.[29] Pallor oral mucosa, petechiae, submucosal ecchymosis, gingival bleeding and hyperplasia, oral candidiasis, herpetic lesion, and ulcers covered with black or gray necrotic membrane are some of the oral manifestations.[9,30] In another study done by Brennan *et al.,* he suggested that individuals rarely present with high risk of alveolar bone loss. However, minimal bone loss of about 10% was significantly noted.[31] They are often treated with the removal of cause, supportive therapy, hemopoiesis, bone marrow transplantation, antifibrinolytic agents, and immunosuppressive therapy.

Pernicious Anemia

It is also called as primary anemia, Addison's anemia, and Biermer's anemia. It can be caused due to deficiency of intrinsic factor like mucoprotein in stomach. Intrinsic factors are responsible for the absorption of Vitamin B12, and they are important for erythropoiesis. The oral manifestations are glossitis, beefy red tongue, hunter's glossitis (the papilla undergoes atrophy with loss of papillae become smooth or bold glossitis with glosso grossis and glossodynia), xerostomia, and aphthous-like ulcers.[9,32] They can be treated with Vitamin B12 parenterally, standard dosage is 100 mg IM monthly.

Megaloblastic Anemia

This occurs due to DNA synthesis defect, during erythropoiesis and most commonly results from deficiency of Vitamin B12 (cobalamin and cyanocobalamin) or folate. It causes stomatitis, mucosal ulceration, and atrophy of oral mucosa reveals glossitis and angular cheilitis. Changes in the oral cavity may occur in the absence of symptomatic anemia or of macrocytosis.[33]

Conclusion

Hematological disorders can cause many major health problems, in that anemia is more common and they form in a mild-to-severe complication, they also imply many manifestations in the oral cavity. Since, the oral lesions are the first manifestations of anemia, even though many of them are non-specific conditions, it is more important to diagnose it earlier and the proper treatment for the oral lesions can avoid serious conditions. Thus, it helps to improve the quality of life in patients.

References

1. Turner J, Parsi M, Badireddy M. Anemia. Treasure Island, FL: StatPearls Publishing; 2020.
2. Patton LL, Glick M. The ADA Practical Guide to Patients with Medical Conditions. 2nd ed. Hoboken, New Jersey: John Wiley and Sons; 2016. p. 81-8.
3. World Health Organization. Iron Deficiency Anaemia: Assessment, Prevention and Control. Report of a Joint WHO/UNICEF/UNU Consultation. Geneva: World Health Organization; 1998.
4. Derossi SS, Raghavendra S. Anemia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;95:131-41.
5. Usuki K. Anemia: From basic knowledge to up-to-date treatment. Topic: IV. Hemolytic anemia: Diagnosis and treatment. Nihon Naika Gakkai Zasshi 2015;104:1389-96.
6. Engebretsen KV, Blom-Høgestøl IK, Hewitt S, Risstad H, Moum B, Kristinsson JA, *et al*. Anemia following Roux-en-Y gastric bypass for morbid obesity; a 5-year follow-up study. Scand J Gastroenterol 2018;53:917-22.
7. Johnson-Wimbley TD, Graham DY. Diagnosis and management of iron deficiency anemia in the 21st century. Therap Adv Gastroenterol 2011;4:177-84.
8. Eisen D, Lynch DP. Oral manifestations of systemic diseases. In: The Mouth: Diagnosis and Treatment. St. Louis, MO: Mosby; 1998. p. 212-36.
9. Adeyemo TA, Adeyemo WL, Adediran A, Akinbami AJ, Akanmu AS. Orofacial manifestations of hematological disorders: Anemia and hemostatic disorders. Indian J Dent Res 2011;22:454-61.
10. Long RG, Hlousek L, Doyle JL. Oral manifestations of systemic diseases. Mt Sinai J Med 1998;65:309-15.
11. Hoffman RM, Jaffe PE. Plummer-Vinson syndrome: A case report and literature review. Arch Intern Med 1995;155:2008-11.
12. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: A systematic analysis for the global burden of disease study 2015. Lancet 2016;388:1459-544.
13. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. Lancet 2010;376:2018-31.
14. Bartolucci P, Galacteros F. Clinical management of adult sickle-cell disease. Curr Opin Haematol 2012;19:149-55.
15. Embury SH. The not so simple process of sickle cell vasoocclusion. Microcirculation 2004;11:101-13.
16. Scipio JE, Al-Bayaty HF, Murti PR, Matthews R. Facial swelling and gingival enlargement in a patient with sickle cell disease. Oral Dis 2008;7:306-9.
17. Kelleher M, Bishop K, Briggs P. Oral complications associated with sickle cell anaemia: A review and case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;82:225-8.
18. Stinson J, Naser B. Pain management in children with sickle cell disease. Paediatr Drugs 2003;5:229-41.
19. Guzeldemir E, Toygar HU, Boga C, Cilasun U. Dental and periodontal health status of subjects with sickle cell disease. J Dent Sci 2011;6:227-34.
20. Vij R, Machado RF. Pulmonary complications of hemoglobinopathies. Chest 2010;138:973-83.
21. Beck WS. Hematology. USA: The Massachusetts Institute of Technology; 1998.
22. Joly P, Pondarre C, Badens C. Beta-thalassemias: Molecular, epidemiological, diagnostical and clinical aspects. Ann Biol Clin (Paris) 2014;72:639-68.
23. Bernaudin F, Verlhac S, Chevret S, Torres M, Coic L, Arnaud C, *et al*. G6PD deficiency, absence of alpha thalassemia, and hemolytic rate at baseline are significant independent risk factors for abnormally high cerebral velocities in patients with sickle cell anemia. Blood 2008;112:4314-7.
24. Muncie HL Jr., Campbell J. Alpha and beta thalassemia. Am Fam Physician 2009;80:339-44.
25. Hes J, van der Waal I, de Man K. Bimaxillary hyperplasia: The facial expression of homozygous b thalassaemia. Oral Surg Oral Med Oral Pathol 1990;69:185-90.
26. Abu Alhaija ES, Hattab FN, Al-Omari MA. Cephalometric measurements and facial deformities in subjects with b thalassaemia major. Eur J Orthod 2002;24:9-19.
27. Drexler B, Zurbriggen F, Diesch T, Viollier R, Halter JP, Heim D, *et al*. Very long-term follow-up of aplastic anemia treated with immunosuppressive therapy or allogeneic hematopoietic cell transplantation. Ann Hematol 2020;99:2529-38.
28. Tichelli A, de Latour RP, Passweg J, Knol-Bout C, Socié G, Marsh J, *et al*. Long-term outcome of a randomized controlled study in patients with newly diagnosed severe aplastic anemia treated with antithymocyte globulin and cyclosporine, with or without granulocyte colony-stimulating factor: A severe aplastic anemia working party trial from the European group of blood and marrow transplantation. Haematologica 2020;105:1223-31.
29. Vaht K, Göransson M, Carlson K, Isaksson C, Lenhoff S, Sandstedt A, *et al*. Incidence and outcome of acquired aplastic anemia: Real-world data from patients diagnosed in Sweden from 2000-2011. Haematologica 2017;102:1683-90.
30. Sepulveda E, Brethauer U, Rojas J, Le Fort P. Oral manifestation of aplastic anaemia in children. J Am Dent Assoc 2006;137:474-8.
31. Brennan MT, Sankar V, Baccaglini L, Pillemer SR, Kingman A, Nunez O, *et al*. Oral manifestations in patients with aplastic anemia. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 2001;92:503-8.
32. Sambandan T. Review on oral manifestations of blood diseases. JIADS 2010;1:41-3.
33. Field EA, Speechley JA, Rugman FR, Varga E, Tyldesley WR. Oral signs and symptoms in patients with undiagnosed Vitamin B12 deficiency. J Oral Pathol Med 1995;24:468-70.