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Review Article

# Dental Considerations of Children with Anemias - An Overview

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**Abstract**

Anaemia affects one-fourth of the world's population and iron deficiency is the predominant cause. It affects both the genders but more frequently seen in females than males. It is associated with chronic fatigue, impaired cognitive function, and diminished well-being. Anaemic disorders associated with orofacial signs and symptoms include iron deficiency anaemia, megaloblastic anaemia, sickle cell anaemia, and aplastic anaemia. The manifestations include conjunctiva and facial pallor, atrophic glossitis, angular stomatitis, dysphagia, magenta tongue, midfacial overgrowth, osteoclerosis, osteomyelitis and paraesthesia/anaesthesia of the mental nerve. Orofacial petechiae, conjunctivae haemorrhage, nose-bleeding, spontaneous and post-traumatic gingival haemorrhage and prolonged post-extraction bleeding are common orofacial manifestations. Dental management of patients of aplastic anaemia requires inter disciplinary care with the consultation of the treating dentist with haematologist. This article provides aetiology, clinical features, investigations, diagnosis and treatment of different types of anaemia.

**Keywords:** Anemia; Children; Dental management; Oral health

## Introduction

Anaemia is a term used to define a decrease in the oxygen carrying capacity of blood characterized by a decrease in the number of red blood cells, haemoglobin, and haematocrit result from blood loss (iron deficiency anaemia), decreased red cell production (Aplastic anaemia) or increased red cell destruction (Haemolytic anaemia) [1].

The World Health Organization defines anaemia as a level of Hb below 13.0 g/dL in male adults, below 12.0 g/dL in female adults who are not pregnant, and below 11.0 g/dL in pregnant women. 47 Hb levels may vary across age and race, 48 so care must be taken, particularly in the interpretation of borderline values [2].

### Classification

Anaemia can be classified morphologically, etiologically and based on Reticulocyte Production Index (RTI) (kinetic classification).

### Morphological classification

It is based on measurement of red blood cells. "There are three types of anaemias depending on RBC size (Table 1).

Etiological classification: It is based on the cause of anaemia and can be classified as per etiology as represented in (Table 2).

Based on the Reticulocyte Index (RPI) anaemias are classified as 2 types (Table 3).

### Iron deficiency anemia

Iron deficiency is the predominant cause of anaemia across countries and in both sexes, with women more commonly afflicted [1]. The prevalence of anaemia increases with age3 and in the hospital setting. Anaemia decreases the capacity for work and increases health care costs. Iron deficiency is also associated with Restless Legs Syndrome (RLS), diminished quality of life, fatigue, impaired cognitive function, and infertility, all of which may occur in the absence of anaemia and may be reversed with iron therapy.

Iron deficiency is the predominant cause of anaemia across countries and in both sexes with women more commonly afflicted [1-3]. Prevalence of anaemia increases with age3 and in the hospital setting. anaemia decreases the capacity for work and increases health care costs [4,5] iron deficiency is also associated with restless legs syndrome rls diminished quality of life fatigue impaired cognitive function and infertility all of which may occur in the absence of anaemia and may be reversed with iron therapy [1-3]. Clinical and oral manifestations 5 are shown in (Tables 4-6).

**Investigations:** Haematocrit shows microcytic and hypochromic RBC.

MCV: MCV less than 95 pm is suggestive of Iron Deficiency Anaemia (IDA).

Ferritin: Ferritin less than or equal to 45 mg/mL is suggestive of IDA. If ferritin is between 46 mg/mL and 99 mg/mL, the Serum Transferrin Receptor (TfR) is assessed. Increased TfR confirms iron deficiency anaemia.

Modified from Evstatiev R, et al, with permission [7].

**Management [6]**

1. Oral iron therapy is the first line of treatment. Hb level of lg/dL should increase every 2-3 weeks on iron therapy; however, it may take up to 4 months for iron stores to become normal.

2. Iron sulfate 300 mg provides 60 mg of element iron, whereas 325 mg of iron gluconate provides 36 mg of element iron.

3. Gastrointestinal absorption of element iron is increased




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**Table 1:** Showing morphological classification.

| | | |
|---|---|---|
| 1 | Microcytic hypochromic | Characterized by low mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH). e.g. iron deficiency anaemia, thalassemia |
| 2 | Normocytic normochromic | Characterized by normal MCV and MCH, e.g. acute blood loss, marrow infiltration, haemolysis (occasionally macrocytic) and chromic disease (occasionally microcytic hypochromic). |
| 3 | Macrocytic | Characterised by raised MCV, eg. megaloblastic anaemia |

**Table 2:** Showing etiological classification.

| |
|---|
| Due to destruction of RBC, e.g. haemolytic anaemia |
| Due to bleeding |
| Dilution of RBC by increased plasma level of hypersplenism |
| Failure of RBC production by the bone marrow |
| • Nutritional deficiency, e.g. Iron, Vitamin BIZ and Folate |
| • Ineffective red cell formation, e.g. chronic inflammation, thalassemia and renal disease |
| • Reduced bone marrow erythroid cells, e.g. aplastic anaemia, bone marrow infiltration in case of leukaemia or malignancy |

**Table 3:** Showing reticulocyte index classification.

| | | |
|---|---|---|
| 1 | Hypo proliferative (RPI < 2.5) | i.e. anaemias caused by decreased RBC production due to deficiency of nutrients or systemic disease |
| 2 | Haemolytic (RPI > 2.5) | Which can be congenital or acquired. |

**Table 4:** Showing clinical manifeastations.

| Clinical Manifestations |
|---|
| • Headaches |
| • Lack of concentration |
| • Feeling weak and tired more often |
| • Koilonychia, glossitis/dysphagia (not common in developed world). |

with acidic environment, which is achieved by giving ascorbic acid in conjunction of iron therapy.

4. Blood transfusion should be considered if patient complains of fatigue or dyspnoea on exertion and in cardiac patient with Hb less than 10 g per dL.

## Aplastic anaemia

It is a severe and frequently fatal hematologic disorder characterized by hypoplastic bone marrow and peripheral pancytopenia. Aplastic anaemia is a sporadic, noncontagious and possibly life threatening disorder formed by destruction of pluripotent stem cells in the bone marrow with an annual incidence of 2 to 6/1,000,000 [1]. Liable on affected cell lines, aplastic anaemia is linked with not only fatigue, but also bleeding due to thrombocytopenia and recurrent infections owing to neutropenia [8]. The diagnosis 'aplastic anaemia' is established by hypocellularity of the bone marrow and the remaining cells are morphologically unaffected without malignant infiltration.

It is classified as acquired or congenital. The congenital type is rare and frequently related with Fanconi's anaemia and dyskeratosis

**Table 5:** Showing oral manifestations.

| Oral manifestations |
|---|
| Angular stomatitis manifested as painful fissures at the corner of the mouth. |
| Angular cheilitis manifested as scaling of the lips and corner of the mouth, usually associated with fungal infection. |
| General pallor of lips mucosa |
| Erythematous mucositis |
| Burning mouth syndrome |
| Plummer-Vinson syndrome |
| Atrophic glossitis can be described as flattening of tongue papillae leading to smooth red tongue appearance resembling migratory glossitis |
| Tongue appears to be erythematous, atrophic, non-indurated and big in size, they do not change their position |
| Decreased healing response |

**Table 6:** Simple Scheme for the estimation of total iron need.

| Degree of Iron Deficiency | Hemoglobin Level g/dL | Dose for Body Weight <70 kg, mg | Dose for Body Weight ≥70 kg, mg |
|---|---|---|---|
| No anaemia | Normal | 500 | 1000 |
| Moderate | 10-12 (Women) | 1000 | 1500 |
| | 10-13 (Men) | | |
| Severe | 10-Jul | 1500 | 2000 |
| Critical | >7 | 2000 | 2500 |

**Table 7:** Showing causes and clinical features of Aplastic Anaemia.

| Causes | Oral manifestations |
|---|---|
| Failure In production of erythrocytes | Gingival haemorrhage |
| Acquired | Mucosal pallor |
| • Idiopathic, Autoimmune | Petechial spots |
| • Drugs: Cytotoxic | Oral ulceration and infection |
| • Idiosyncratic | Neutropenia there is a lack of resistance to infection |
| • Lnfectlous -- hepatitis | candidiasis and viral infection, |
| • Pregnancy | |
| • Paroxysmal, nocturnal | |
| • hemoglobinuria | |
| Congenital/famillal | |
| • Fanconi's anemia | |
| • Dyskeratosis congenital | |
| • Black fan-Diamond anemia | |

congenita. In more than 50% of acquired cases of aplastic anaemia, the exact cause is unidentified. Probable causes for the onset of aplastic anaemia comprise T-cell mediated auto-immune disease, iatrogenic agents, viral infection and pregnancy [1].

It is more common in Asian population than in the United States and Europe with about 6000–7000 new cases reported yearly global. It can be seen at any age but is most classically make out in children aged 2-5 years, young adults between 20 and 25 years.

A pancytopenia is identified when two of three principles are met: a neutrophil count of less than 0.5 · 109 cells/L, a platelet count less than 20 · 109 cells/L and a reticulocyte count less than 1%. When the neutrophil count is less than 0.2, the disease is then described as severe [1].

Oral manifestations are common in patients with aplastic anaemia and are directly associated with pancytopenia. These manifestations include petechial hemorrhages, gingival swelling and spontaneous bleeding, ulceration, pallor and severe periodontal disease.

Gingival bleeding is another collective manifestation concomitant with reduced platelet level seen in aplastic anaemia patients [7]. Oral traumatic and petechial haemorrhagic lesions have been related with the diminished platelet level. It was designates the risk factors linked with oral manifestations of aplastic anaemia and proposes that the level of thrombocytopenia is not essentially suggestive of the degree of petechial haemorrhage [16,17] (Table 7).

**Management [13-15]**

1. Treatment is given with parenteral vitamin B 12 cncbl a daily dose. The transfusion is only required in special cases like when Hb goes below 15% of normal or if a patient is in heart failure.

2. Dental management of patients of aplastic anaemia requires interdisciplinary care with the consultation of the treating dentist with haematologist.

3. It is advisable to perform dental treatment on the day of platelet transfusion.

**Table 8:** Showing clinical features and oral manifestations.

| Oral manifestations | Clinical features |
|---|---|
| Painful atrophic changes of entire oral mucosa | Weakness |
| Glossitis | Palpitation |
| Recurrent aphthous ulcer | Light-headedness |
| Burning mouth syndrome | Loss of appetite |
| Ulcerative gingivitis | Shortness of breath |
| Stomatitis | Diarrhoea |
| Bleeding gingivae | Peripheral numbness. |
| Denuded tongue | Smooth or tender tongue |
| Glossodynia | |
| Delayed wound healing | |
| Oral paraesthesia | |
| Loss of taste and Xerostornia | |
| Bone loss | |

4. To reduce the risk of uncontrolled bleeding during major dental treatments, the patients should take antifibrinolytics. These agents may decrease bleeding, particularly oral mucosal bleeding, in patients with thrombocytopenia by stabilization of thrombi.

5. Jones et al have reported a case of idiopathic aplastic anaemia which was treated with a combination of modalities including early platelet transfusion, oral hygiene instruction, dental prophylaxis and systemic aminocaproic acid.

6. Patients with aplastic anaemia are more susceptible to infection; therefore, dental treatment should be postponed until the patient's white blood cell count rises to a normal level.

7. Prior to the dental procedure consider prescribing antibacterial mouthwash and oral antibiotics.

8. If necessary, consultation with a haematologist.

## Megaloblastic anemia

It is the type of anaemia produced by disorders of DNA synthesis

**Table 9:** Showing clinical features and oral manifestations.

| Clinical features | Oral manifestations |
|---|---|
| Shortness of breath | Mucosa pallor |
| Headaches | Accentuated incremental line |
| Dizziness Coldness of hand and feet | Developmental defects occurring due to hypomineralization of enamel along with delayed eruption of teeth |
| Sudden pain throughout the body | Pulp stones or calcification of pulp, pulpal pain may be due to tissue infarction and thrombosis |
| Jaundice | Hypercementosis |
| | Dental caries |
| | Malocclusion, midline diastema |
| | Midfacial overgrowth due to marrow hyperplasia , Thickening of skull, Osteoporotic changes in jaw |
| | Step ladder appearance of alveolar bone |
| | Coarse trabecular pattern between the root apices and |

of erythrocyte precursors in bone marrow. Megaloblastic red blood cells are larger than the normal red blood cells and contain more cytoplasm in relation to the nucleus.

**Aetiology:** Megaloblastic anaemia can arise due to any of the following causes:

**Folate deficiency:** It can occur in case of decreased intake, poor nutrition, old age, alcoholism, haemodialysis, premature infants, spinal cord injury, small intestine disease, and tropical and no tropical sprue.

**Increased requirement:** Increased requirement corresponds with pregnancy, increased cell turnover. Chronic haemolytic anaemia and cobalamin deficiency. Impaired absorption: It can occur in cases of pernicious anaemia, gastrectomy, Zollinger-Ellison syndrome and pancreatic insufficiency.

**Drugs:** Antimetabolites, anticonvulsants, oral contraceptives, etc.

In-born errors and decreased intake [18].

Clinical features and oral manifestations are given in (Table 8).

**Management**

1. Treatment is given with parenteral Vitamin B12 (CnCBl) a daily doses.

2. Transfusion is only required in special cases like when Hb goes below 15% of normal or if patient is in heart failure.

## Sickle cell anemia

**Introduction:** Linus Pauling actually identified haemoglobin S as the abnormal haemoglobin associated with Sickle Cell Anaemia. Sickle cell anaemia is a genetic disease that primarily affects the black population. This anaemia is due to a homozygous state of the abnormal haemoglobin S. An alteration occurs on the DNA molecule involving the substitution of the amino acid valine for glutamic acid at the sixth position on the beta polypeptide chain (Rose and Kaye 1983). This biochemical variation on the DNA molecule creates a physiological change that causes sickle-shaped red blood cells to be produced. The sickle-shaped cells are the result of the haemoglobin S being deoxygenated. With a decrease in affinity of oxygen to an abnormal haemoglobin, deoxygenation will occur, again producing more sickle-shaped cells. This leads to obstruction or microvasculature

**Table 10:** Showing radiographic features of sickle cell anaemia.

| |
|---|
| Increased radiolucency of the jaw |
| Coarse trabecular pattern and decreased number of trabecular |
| 'Thin inferior border of the mandible |
| Distinct areas of osteoporosis. |
| Generalized osteoporosis |
| Step ladder effect due to horizontal rows of trabeculation and Retrusive maxilla |
| Dense lamina dura due to hyperplastic marrow. |

erythrostasis, causing vasocclusion and extensive organ damage. It is a cyclic process [19,20].

Sickle cell anaemia may be diagnosed in the sixteenth week of gestation, but manifestations normally do not appear until the sixth month after birth. Newer techniques for hemoglobin electrophoresis can be used to diagnose the abnormal hemoglobin at birth. Painful episodes or "crises" characteristic of this disease are vasocclusion, sequestration, aplastic, and to a lesser degree, hyperhemolysis.

Many factors can precipitate a sickle cell crisis, including acidosis, hypoxia, hypothermia, hypotension, stress, hypovolemia, dehydration, fever, and infection [21].

**Incidence:** Approximately one of every 500 black children in the United States has SCA. The homozygous state of this chronic hemolytic anaemia typifies the most devastating effect [22]. Persons with the sickle cell trait occasionally may show manifestations of the disease in hypoxic states caused by exposure to high altitudes or shock [23]. These patients are usually without Symptoms; however, it has been reported that systemic diseases, dehydration, infection, and hypoxia are some of the etiological factors of sickle cell Anaemia due to haemolysis, aplastic crisis, impaired growth and skeletal deformities are general features.

Clinical features and oral manifestations are given below (Table 9) [24].

Dizziness Coldness of hand and feet.

Developmental defects occurring due to hypomineralization of enamel along with delayed eruption of teeth

Sudden pain throughout the body Pulp stones or calcification of pulp, pulpal pain may be due to tissue infarction and thrombosis.

Radiographic changes are associated with sickle cell anaemia. There are a generalized radiolucency and loss of trabeculae with prominent lamina dura, caused by increased erythropoietic demands that result in the expansion of the marrow spaces. Bone growth may be decreased in the mandible, resulting in retrusion, and the teeth may be hypomineralized. Occasionally, patients with sickle cell anaemia have infarcts in the jaw, which may be mistaken for a toothache or osteomyelitis [22,25,26]. The patients experience dental pain with the absence of pathology (Table 10).

Radiographic Features are shown in (Table 10).

Many patients with sickle cell anaemia have defective spleen function or undergo a splenectomy, which leaves them more vulnerable to infection because immunoglobulin production is decreased and phagocytosis of foreign antigens is thus impaired. Most patients with sickle cell anaemia are taking low-dose daily prophylactic antibiotics, and the need for additional antibiotics for dental procedures is debatable. Some authors have recommended the use of antibiotics for all dental procedures, whereas others recommend the administration of additional antibiotics when there is an obvious dental or periodontal infection. The selection of an antibiotic is usually similar to that in cases of a heart defect [27-30].

**Dental Management** [31-35]

1. Dental appointments should be short to reduce possible stress on the patient.

2. The importance of an aggressive preventive program cannot be understated, and such a program should have the goal of maintaining excellent oral health and lessening the possibility of oral infection.

3. Dental treatment should not be initiated during a sickle cell crisis. If emergency treatment is necessary during a crisis, the only treatment that will make the patient more comfortable should be provided.

4. Patients with sickle cell anaemia may have skeletal changes that make orthodontic treatment beneficial.

5. Special care must be taken to avoid tissue irritation, which may induce bacteraemia, and the disease process may compromise the proposed treatment.

6. Careful monitoring is a necessity when proposing elective orthodontic treatment in patients with sickle cell anaemia.

7. The restoration of teeth, including pulpotomies, is preferable to extraction.

8. Polypectomy in a nonvital tooth is reasonable if the practitioner is fairly confident that the tooth can remain non infected. if the tooth is likely to persist as a focus of infection, then extraction is indicated.

9. The use of general anaesthesia for dental procedures must be approached cautiously in consultation with the haematologist and anaesthesiologist.

10. Previously, the standard protocol was to perform a direct transfusion (immediate introduction of whole blood or blood components) or an exchange transfusion (repetitive withdrawal of small amounts of blood and replacement with donor blood until a large portion of the patient blood has been exchanged) before general anaesthesia.

11. The goal of the transfusion is to increase the patient's haemoglobin level to higher than 10 g/dL and to decrease the haemoglobin 8 levels below 40%. Transfusions do not provide complete protection against venous complications, but they may temporarily improve the patient's condition and reduce the hazards of surgery.

12. The current thinking is to weigh the risks associated with transfusion prior to anaesthesia induction.

13. Suggested guidelines for performing a prophylactic transfusion before general anaesthesia have been proposed. Patients with a haemoglobin level of less than 7 g/dL and a hematocrit of less than 20% may require a transfusion.

14. Pediatric patients are usually less likely to have post-transfusion complications than are adults. A high frequency of hospitalizations is indicative of more severe anaemia, and such patients may require transfusion before surgery.

15. Minor surgeries may not require a transfusion.

16. Local anaesthetic is the preferred anaesthetic for those patients as according to Malamud and these patients belong to ASA Ill categories. The use of local anaesthetic does not affect the oxygenation of the blood molecule.

17. Oral sedation can also be used as an anxiolytic agent.

18. The use of local anaesthetic does not affect the oxygenation of the blood molecule.

19. Oral sedation can also be used as an anxiolytic agent.

For cases to be considered under general anaesthesia: [36,37]

1. Proper/adequate haemoglobin levels to be activated 15 days prior to the procedure through transfusion to prevent sickle cell anaemia crisis.

2. Optimum level to be maintained for children is 1012 g/dL. Prophylactic antibiotic to be given before the procedure in order to avoid infection.

3. Blood transfusion is used to manage acute manifestations of the disease such as aplastic crises, splenic sequestration, etc.

4. Hydroxyurea is a cytotoxic drug, which is commonly used in treatment of leukaemia and polycythaemia Vera. But it also has property to increase fetal haemoglobin and fetal haemoglobin prevents sickling of cells.

5. The only cure of sickle cell disease is hematopoietic stem cell disease [38].

## Conclusion

Hematologic diseases are a major health problem and have a greater significance to the practice of dentistry. Children with anaemias frequently exhibit oral manifestations of the condition. Prevention,

early diagnosis and proper treatment of oral complications are essential to diminish morbidity and avoid a possible outcome. Oral lesions can be the first manifestation of these anaemias; consequently, dentists should be aware of these manifestations so that an early diagnosis of the disease can be made in children. Hence, their quality of life is improved.

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