ISSN Print: 2394-7489
ISSN Online: 2394-7497
IJADS 2023; 9(4): 283-289

www.oraljournal.com
Received: 01-08-2023
Accepted: 03-09-2023

María Concepción Treviño-Tijerina
Consultant Prosthodontist, Dent-O-Care Multi-Speciality Clinic & Implant Centre, Jammu, Jammu and Kashmir, India

Julia Garza-Villarreal
Consultant Prosthodontist, Dent-O-Care Multi-Speciality Clinic & Implant Centre, Jammu, Jammu and Kashmir, India

Sara Sáenz-Rangel
Consultant Prosthodontist, Dent-O-Care Multi-Speciality Clinic & Implant Centre, Jammu, Jammu and Kashmir, India

Norma Cruz-Fierro
Consultant Prosthodontist, Dent-O-Care Multi-Speciality Clinic & Implant Centre, Jammu, Jammu and Kashmir, India

Corresponding Author:
María Concepción Treviño-Tijerina
Consultant Prosthodontist, Dent-O-Care Multi-Speciality Clinic & Implant Centre, Jammu, Jammu and Kashmir, India

Dental dilemmas in blood disorders: Navigating oral health in hematological diseases

María Concepción Treviño-Tijerina, Julia Garza-Villarreal, Sara Sáenz-Rangel and Norma Cruz-Fierro

DOI: https://doi.org/10.22271/oral.2023.v9.i4e.1881

Abstract
Introduction: The circulatory system is highly complex, and any dysfunction within the blood circulatory system can lead to blood diseases. Hemoglobinopathies are among the most common recessive diseases affecting humans worldwide.
Objective: To analyze literature and describe the oral manifestations and dental management of patients with leukemia, anemia, hemophilia, and thalassemia.
Methodology: A thorough search was conducted on PubMed using the keywords: hematological diseases, anemia, thalassemia, hemophilia, leukemia.
Results: Leukemia manifests with oral symptoms, gum bleeding, and petechiae within the oral mucosa, and its management can be divided into three phases. Patients with anemia present paleness of the mucosa, dental mineralization disorders, higher incidence of caries and periodontitis, and require prophylactic antibiotics before surgical procedures. In hemophilia, bleeding from different parts of the oral cavity and prolonged gingival bleeding are common. Factor replacement therapy is indicated for all patients with moderate to severe hemophilia A and B. Patients with thalassemia often present with a convex profile and class II skeletal pattern, and any dental surgical procedure should be performed under antibiotic cover and immediately after transfusion.
Conclusions: Hematological diseases pose a significant challenge to dentists. It is crucial to understand the oral manifestations of each to provide timely and appropriate treatment, and to take the right measures for each patient depending on their condition.

Keywords: Haematological deseases, anemia, thalassemia, hemophilia, leukemia

Introduction

Overview of Pediatric Blood Disorders

Blood disorders in children encompass a spectrum of conditions ranging from benign to severe malignancies, profoundly influencing their life quality, developmental progress, and, often, life expectancy. These disorders, impacting the blood system crucial for oxygen transport, immune defense, and coagulation, can arise from genetic and environmental factors or their combination [1]. Each year, around 300,000 children are diagnosed with significant hemoglobinopathies [2], with 5.2% of the global population carrying a hemoglobinopathy. Of these, 17% suffer from thalassemia, and 83% from sickle cell anemia [3]. While most anemias are acquired, hereditary causes account for about 7% [4].

Thalassemia, a group of inherited hemoglobin disorders, is characterized by inadequate globin chain production, leading to unbalanced hemoglobin synthesis and eventually, anemia [5]. Leukemia, particularly Acute Lymphoblastic Leukemia (ALL), a common pediatric cancer originating in the bone marrow, accounts for 20% of all childhood cancers. Despite treatment advancements, ALL remains a therapeutic challenge but boasts a promising prognosis, with a current 5-year overall survival rate of 90% [6]. It involves an excessive production of immature and abnormally differentiated leukocytes [7]. Hemophilia, stemming from genetic mutations affecting blood clotting, primarily impacts males and requires vigilant management to prevent life-threatening hemorrhages, especially in traumatic or surgical contexts [8].

These hematological diseases, affecting blood and hematopoietic organs, often manifest first in the oral cavity [9], ranging from minor mucosal changes to severe symptoms, crucially

affecting children's quality of life. Unfortunately, these signs are frequently overlooked, leading to delayed diagnosis and treatment. With advancements in medical technology and hematology research, the prognosis for these patients has significantly improved [1]. This report focuses on the oral manifestations of pediatric hematological disorders, aiming to enhance understanding and guide care based on an extensive literature review, thereby underscoring the significance of these manifestations in clinical practice.

Results

Acute Lymphoblastic Leukemia in Pediatrics

Acute Lymphoblastic Leukemia (ALL) stands out as the most commonly diagnosed cancer in children, characterized by an aggressive growth of immature lymphocytes [10]. This disease accounts for 80% of all pediatric leukemias and 25% of all childhood cancers, making it the leading type of pediatric cancer [11]. In ALL, there is a marked increase in the production of blastocysts, immature cells in the bone marrow and blood.

ALL is categorized based on the affected lymphocyte type into B-cell or T-cell variants, each with unique genetic characteristics. B-cell leukemia is more prevalent in pediatric cases, constituting about 85% of instances, whereas T-cell leukemia accounts for the remaining 15% [12]. The treatment for ALL is divided into three stages: remission induction, intensification, and maintenance, often involving the use of antimetabolites like 6-mercaptopurine (6-MP) over a period of two to three years after diagnosis [13]. While a majority of patients reach complete remission, the prognosis for children with high-risk ALL is less favorable, often compounded by the increased toxicity and side effects of intensified treatments [14]. Relapse in post-remission stages is typically linked to resistance of leukemic cells to treatment [15]. Notably, survival rates have seen a significant increase, particularly in B-cell ALL, exceeding 90%, in contrast to more modest improvements in Acute Myeloid Leukemia (AML) survival rates [16]. ALL incidence is observed to be higher in Caucasian and Hispanic populations, with a significant rise in Latin American countries [17].

Oral Indicators in Leukemia Cases

Leukemia's oral manifestations are often early indicators of the condition. Common signs include gingival bleeding, petechiae on the oral mucosa, along with inflammatory infiltrates, mucosal erosions, tongue discomfort, ulcers, and gingival hyperplasia [9]. Patients might also present with systemic symptoms like hemorrhages, fatigue, anorexia, and fever, which are indicative of bone marrow involvement [18]. Treatments like chemotherapy and radiotherapy contribute to a range of acute and chronic oral complications. The immunosuppression resulting from these treatments heightens the risk of oral infections and soft tissue trauma, exacerbating patient outcomes in terms of morbidity, mortality, and healthcare costs [19]. Post-chemotherapy, patients often develop oral lesions and suffer from impaired oral health, increased caries risk, and dysbiosis of the oral microbiota [20]. This necessitates a specialized periodontal and dental approach for leukemia patients, involving meticulous planning and coordination with hematology experts [21, 22].

Dental Care Protocol for Leukemia Patients

Dental care for leukemia patients involves a three-phase approach: pre-treatment, during treatment, and post-treatment [23-24]. Prior to chemotherapy, it's essential to extract teeth with uncertain prognosis, complete dental scaling, and apply preventive therapy. Temporary fillings are recommended for carious teeth, deferring permanent treatments until remission. For pain relief during brushing, 0.12% chlorhexidine mouthwash can be effective against oral mucositis. Treating fungal infections like candidiasis with oral nystatin (100,000 units/ml) and managing herpes simplex lesions with Acyclovir are also part of the regimen [25]. Non-essential dental procedures should be avoided during active leukemia treatment. Long-term follow-up, varying from yearly to lifelong, with regular assessments, is crucial for managing the dental health of these patients [23, 24].

The Impact and Management of Anemia

Anemia, defined by reduced hemoglobin levels, presents a significant global health concern. The World Health Organization's 2019 report highlights that anemia affects 500 million women and 269 million children, making it a leading cause of disability, particularly among women and young children [26]. Iron deficiency anemia (IDA) is notably one of the primary causes of disability worldwide. Iron deficiency manifests in two forms: absolute, indicating complete depletion of iron reserves, and functional, where reserves are sufficient but not effectively utilized due to conditions like inflammation [27, 28]. This deficiency is alarmingly common in children, especially in preschoolers, with a prevalence of 47.4% [29].

Hemolytic anemia is characterized by reduced lifespan of red blood cells due to their destruction. In response, the bone marrow increases erythrocyte production, a process driven by erythropoietin, leading to a higher percentage of reticulocytes in the blood (>2%) [30]. Acquired aplastic anemia (AA), a life-threatening condition resulting from bone marrow failure, is often caused by an autoimmune response targeting hematopoietic stem cells [31]. Sickle cell anemia (SCA) is a genetic disorder causing recurrent damage to various organs [32], while pernicious anemia (PA) arises from vitamin B12 deficiency due to poor absorption, linked to a lack of intrinsic factor [33].

Oral Symptoms in Anemic Patients

In sickle cell anemia, patients often display distinctive maxillofacial features, including mandibular retrusion, maxillary protrusion, and pale oral mucosa. They tend to experience higher rates of dental caries and severe periodontitis than typical [34]. Common oral symptoms include gingivitis, periodontitis, tooth rotation, and agenesis. These conditions are frequently associated with immune system deficiencies, anemia, and leukopenia, compounded by poor oral hygiene [35]. Anemia can also weaken children's innate immunity, reducing salivary HβD3 levels and increasing vulnerability to dental caries [36].

Dental Care for Anemic Patients

Anemic individuals face a heightened risk of infections due to compromised neutrophil response and decreased spleen function. Prophylactic antibiotics, such as penicillin V, amoxicillin, or clindamycin, are recommended prior to dental procedures to mitigate infection risks [34]. Intravenous options, like clindamycin or ampicillin, are alternatives for pre-treatment administration. Dental surgeries are considered safe under controlled anemia conditions, provided there are no recent vaso-occlusive incidents. A multidisciplinary approach involving constant communication with healthcare professionals is essential in managing these patients [36].

Hemophilia and Its Implications

Hemophilia encompasses two rare genetic disorders, Hemophilia A (HA) and Hemophilia B (HB), arising from deficiencies in critical coagulation factors, linked to genes on the X chromosome. HA is characterized by reduced factor VIII (FVIII) levels, while HB results from insufficient factor IX (FIX). Hemophilia severity is categorized as severe (less than 1 IU/dL or less than 1% of normal), moderate (1 to 5 IU/dL or 1 to 5% of normal), or mild (5 to 40 IU/dL or 5 to 40% of normal) [37]. The primary symptom, bleeding, typically occurs post-trauma or surgery, with the severity corresponding to the clotting factor deficiency. This bleeding can manifest in various body parts, including muscles, joints, soft tissues, and, in severe cases, critical areas like the neck, throat, chest, gastrointestinal system, or brain [8]. The primary treatment involves regular exogenous infusions of FVIII [38]. Hemophilia is uniformly distributed across all ethnic groups worldwide, affecting approximately 1 in 10,000 live births. HA is more prevalent, constituting 80-85% of cases [39].

Oral Health in Hemophilia

People with hemophilia often experience prolonged bleeding in the oral cavity and extended gingival bleeding, sometimes during natural processes like tooth eruption. A significant complication is the development of hemophilic pseudotumors in the jaw due to recurrent subperiosteal bleeding episodes [40]. Research indicates that individuals with hemophilia have similar oral hygiene, caries prevalence, and dental care needs as those without the condition, except for increased spontaneous bleeding [41]. However, it's observed that children with hemophilia generally have poor oral hygiene and a high demand for dental care, with a reported dental caries prevalence of 73.3% and a treatment need of 93.90% [42].

Dental Protocols for Hemophilia Patients

Effective dental care for hemophilia patients involves a set of comprehensive guidelines, including the use of replacement therapy, antifibrinolytic agents, and local hemostatic measures before surgical interventions, along with nerve block techniques, particularly the inferior alveolar nerve block [43]. For dental extractions, a combination of systemic and local therapies is necessary, as local measures alone are inadequate. Factor replacement therapy is mandatory in moderate to severe cases of Hemophilia A and B, and in types 2 and 3 von Willebrand disorders, while systemic hemostatic treatments are considered for milder cases, with dosages tailored to disease type and severity [44].

Surgical dental procedures should be planned in hospital settings with prior consultations with hematologists to assess hemophilia severity, factor VIII inhibitor presence, and to determine appropriate replacement therapy and dosage. For severe hemophilia patients without factor VIII inhibitors, most oral procedures are feasible post-replacement therapy. NSAIDs are contraindicated due to their impact on platelet activity and increased bleeding risk; alternatives like paracetamol and codeine are recommended. Intramucosal local anesthesia is preferred for mild to moderate hemophilia, avoiding intramuscular injections [45].

In managing systemic conditions requiring special dental care, hemophilia is particularly significant. Ongoing antiplatelet or anticoagulant therapy may increase postoperative bleeding risks, compared to those who adjust their medication regimen. To control bleeding, applying tannic acid with compression post-extraction and using local hemostasis agents like ferric sulfate are effective strategies [46].

Thalassemia: A Comprehensive Overview

Thalassemia, a widespread hereditary blood disorder, impacts about 5% of the world's population, with higher prevalence in the Mediterranean, Middle East, Africa, and Southeast Asia [47]. Each year, approximately 300,000 children are diagnosed with thalassemia, underscoring its public health significance [48]. Beta-thalassemia, characterized by reduced or absent beta-globin chain synthesis, leads to beta-thalassemia major in severe cases, increasing the risk of blood transfusion-related viral infections [49]. This condition is divided into minor, intermediate, and major variants, based on the genetic mutation severity [50].

Beta-thalassemia major can be life-threatening without proper treatment, which typically includes regular blood transfusions and iron chelation therapy, with bone marrow transplantation as a potential cure [51]. Affected patients often encounter complications like growth delays, malnutrition, and organ damage due to iron overload [52]. Facial deformities, known as 'rodent facies,' are a distinctive feature of thalassemia major [53]. Common symptoms include paleness, lethargy, and delayed physical development [54]. Managing transfusion-dependent thalassemia requires iron chelation to minimize organ damage caused by iron overload [2].

Oral Implications in Thalassemia Patients

Beta-thalassemia (βT) leads to notable craniofacial and dentoalveolar changes due to expanded bone marrow and increased blood cell turnover [55]. Patients often exhibit a convex facial profile and a class II skeletal pattern, significantly differing from healthy individuals [56]. Beta-thalassemia major patients are prone to dental caries, periodontal diseases, and oral infections, often having smaller dental crowns, constricted dental arches, and tooth discoloration [57]. They show elevated RANKL/OPG ratios in saliva and serum and increased IL-6 and IL-8 levels in gingival fluid [58]. Higher DMFT indexes, tooth retention, gingival pigmentation, and plaque prevalence are observed compared to control groups [59]. Regular periodontal screenings are vital for these patients to maintain oral health and manage periodontal diseases effectively [60]. Despite the high incidence of dental issues, children with β-thalassemia major often maintain a good oral health-related quality of life [61].

Dental Care Strategies for Thalassemia

Dental care for thalassemia patients requires advanced knowledge of the specific thalassemia type, current hemoglobin levels, and body iron overload due to the complication risks associated with frequent transfusions [62]. Tetracycline, metronidazole, and erythromycin estolate should be avoided, with paracetamol preferred over NSAIDs and aspirin. Sedation or anesthesia may be used to ensure patient comfort and cooperation during dental treatments. Factors like potential immunodeficiency, liver conditions, splenectomy history, and cardiovascular issues are crucial considerations. Prophylactic antibiotics are recommended, and dental surgeries should ideally be scheduled immediately after transfusions to minimize risks [62]. Careful patient selection, thorough evaluation, and meticulous planning and execution are key to preventing complications and achieving optimal outcomes in dental care for thalassemia patients [63].

Conclusions

This article has delved into various pediatric hematological disorders, emphasizing the importance of specialized dental

approaches in their management. Disorders such as leukemia, anemia, hemophilia, and thalassemia not only pose significant challenges to children's general health but also have a substantial impact on their oral health. Hematological.

Diseases in Dental Practice: Challenges and Approaches: Hematological diseases pose unique challenges in dental practice, where in-depth knowledge of their oral manifestations is critical. Recognizing these signs allows dentists to prevent and tailor treatments to the specific needs of each patient, thereby avoiding serious complications.

Leukemia and Dentistry: Coordination and Prevention: In leukemia patients, collaboration with the medical team is crucial for scheduling dental treatments. Prior to starting chemotherapy, essential preventive dental procedures are needed to minimize the risk of infections and complications. Preventive dentistry plays a key role in maintaining the patient's oral and overall health.

Dental Management in Anemic Patients: Anemic patients require careful dental management due to their susceptibility to infections. The use of antibiotic prophylaxis and thorough assessment of their nutritional and immunological status are imperative, demanding a comprehensive dental approach that extends beyond local treatment in the mouth.

Hemophilia: Multidisciplinary Management and Hospital Treatments: For patients with hemophilia, collaboration with the hematologist and factor replacement therapy are essential, especially for invasive procedures that should be carried out in hospital settings for appropriate monitoring and management of potential adverse events, such as bleeding.

Dental Approach in Thalassemia Patients: Dental management of thalassemia patients requires meticulous planning, emphasizing antibiotic prophylaxis and the timing of blood transfusions. It is vital to consider the peculiarities of thalassemia, including oral manifestations and systemic complications, to ensure safe and effective dental care.

Dentistry and Hematology: Comprehensive Collaboration. In all these cases, joint follow-up with the hematologist is vital for a comprehensive understanding of the patient's condition and collaborative decision-making. This ensures that dental procedures are performed under the safest conditions and with the least possible risk, underscoring the significant contribution of dentistry to the overall well-being of patients with hematological diseases and the importance of evidence-based practice and interdisciplinary collaboration.

Conflict of Interest
Not available

Financial Support
Not available

References
1. Bain BJ. Bone Marrow Pathology. Wiley-Blackwell; c2022.
2. Di Maio S, Marzuillo P, Mariannis D, Christou S, Ellinides A, Christodoulides C, *et al*. A Retrospective Long-Term Study on Age at Menarche and Menstrual Characteristics in 85 Young Women with Transfusion-Dependent β-Thalassemia (TDT). Mediterr J Hematol Infect Dis. 2021;13(1):e2021040. Available from: https://pubmed.ncbi.nlm.nih.gov/34276909/
3. Mekelenkamp H, van Zanten H, de Vries M, Lankester A, Smiers F. How to Facilitate Decision-Making for Hematopoietic Stem Cell Transplantation in Patients With Hemoglobinopathies. The Perspectives of Healthcare Professionals. Front Pediatr. 2021;9:690309. Available from: https://pubmed.ncbi.nlm.nih.gov/34485192/
4. Lolascon A, Rivella S, Anagnou NP, Camaschella C, Swinkels D, Muckenthaler MU, *et al*. The EHA Research Roadmap: Anemias. Hemasphere. 2021;5(7):e607. Available from: https://europepmc.org/article/med/34522846
5. Shafique F, Ali S, Almansouri T, Van Eeden F, Shafi N, Khalid M, *et al*. Thalassemia, a human blood disorder. Braz J Biol. 2021;83:e246062. Available from: https://www.scielo.br/j/bjb/a/73sD7WKNCqMVfBgh6zsTkSQ/
6. Hun M, Xie M, She Z, Abdirahman AS, Li C, Wu F, *et al*. Management and Clinical Outcome of Posterior Reversible Encephalopathy Syndrome in Pediatric Oncologic/Hematologic Diseases: A PRES Subgroup Analysis With a Large Sample Size. Front Pediatr. 2021;9:678890. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8280768
7. Zhang L, Bu Z, Shen J, Shang L, Chen Y, Zhang P, *et al*. MicroRNA-221 regulates cell activity and apoptosis in acute lymphoblastic leukemia via regulating PTEN. Exp Ther Med. 2021;22(4):1133. Available from: https://pubmed.ncbi.nlm.nih.gov/34504582/
8. Johnston K, Stoffman JM, Mickle AT, Klaassen RJ, Diles D, Olatunde S, *et al*. Preferences and Health-Related Quality-of-Life Related to Disease and Treatment Features for Patients with Hemophilia A in a Canadian General Population Sample. Patient Prefer Adherence. 2021;15:1407-17. Available from: https://www.dovepress.com/preferences-and-health-related-quality-of-life-related-to-disease-and--peer-reviewed-fulltext-article-PPA
9. Ptasiewicz M, Maksymiuk P, Chałas R. Changes of Dentition State in Leukemic Patients during Chemotherapy. Int J Environ Res Public Health. 2021;18(15):8193. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8346006
10. Guo H, Li N, Sun Y, Wu C, Deng H, Xu L, *et al*. MYBL2 Gene Polymorphism Is Associated With Acute Lymphoblastic Leukemia Susceptibility in Children. Front Oncol. 2021;11:734588. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8456030
11. Von Beek C, Alriksson L, Palle J, Gustafson AM, Grujic M, Melo FR, *et al*. Dynamin inhibition causes context-dependent cell death of leukemia and lymphoma cells. PLoS One. 2021;16(9):e0256708. Available from: https://pubmed.ncbi.nlm.nih.gov/34492077/
12. Lejman M, Kuśmierczuk K, Bednarz K, Ostapińska K, Zawitkowska J. Targeted Therapy in the Treatment of Pediatric Acute Lymphoblastic Leukemia-Therapy and Toxicity Mechanisms. Int. J Mol. Sci. 2021;22(18):9827. Available from: https://pubmed.ncbi.nlm.nih
13. Jantararoungtong T, Wiwattanakul S, Tiyasirichokchai R, *et al*. TPMT*3C as a Predictor of 6-Mercaptopurine-Induced Myelotoxicity in Thai Children with Acute Lymphoblastic Leukemia. J Pers. Med. 2021;11(8):783. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8400562
14. Schraw JM, Woodhouse JP, Bernhardt MB, *et al*. Comparison of the blood, bone marrow, and cerebrospinal fluid metabolomes in children with b-cell acute lymphoblastic leukemia. Sci. Rep. 2021;11(1):19613. Available from:

https://pubmed.ncbi.nlm.nih.gov/34608220/
15. Chen D, Camponeschi A, Nordlund J, *et al*. RAG1 co-expression signature identifies ETV6-RUNX1-like B-cell precursor acute lymphoblastic leukemia in children. Cancer Med. 2021;10(12):3997-4003. Available from: https://pubmed.ncbi.nlm.nih.gov/33987955/
16. Stokke JL, Bhojwani D. Antibody-Drug Conjugates for the Treatment of Acute Pediatric Leukemia. J Clin Med. 2021;10(16):3556. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8396964
17. Mejia-Arangure JM, McNally RJQ, Pombo-de-Oliveira MS. Editorial: Prevention in Acute Leukemias in Children. Front Public Health. 2021;9:700739. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8381149/
18. Shahriari M, Shakibazad N, Haghpanah S, Ghasemi K. Extramedullary manifestations in acute lymphoblastic leukemia in children: a systematic review and guideline-based approach of treatment. Am. J Blood. Res. 2020;10(6):360-374. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7811904
19. Kowlessar A, Naidu R, Ramroop V, *et al*. Oral health among children attending an oncology clinic in Trinidad. Clin Exp Dent Res. 2019;5(6):665-669. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6934352
20. Morais EF, Lira JA, Macedo RA, *et al*. Oral manifestations resulting from chemotherapy in children with acute lymphoblastic leukemia. Braz J Otorhinolaryngol. 2014;80(1):78-85. Available from: https://pubmed.ncbi.nlm.nih.gov/24626896/
21. Wang Y, Zeng X, Yang X. Oral Health, Caries Risk Profiles, and Oral Microbiome of Pediatric Patients with Leukemia Submitted to Chemotherapy. Biomed Res Int. 2021;2021:6637503. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7834790
22. Cammarata-Scalisi F, Girardi K, Strocchio L. Oral Manifestations and Complications in Childhood Acute Myeloid Leukemia. Cancers (Basel). 2020;12(6):1634. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7352340
23. Santiago MC, Espinoza HSC. Manejo odontopediátrico de paciente con leucemia linfoblástica aguda. Arch Inv Mat Inf. 2013;5(2):74-79. Available from: https://www.medigraphic.com/pdfs/imi/imi-2013/imi132d.pdf
24. Lopez M, Santiago A. Oral ulcers in pediatric patients with leukemia: Clinical management and outcomes. Int. J Pediatr. Dent Care. 2021;7(1):43-49.
25. Lowal KA, Alaizari NA, Tarakji B, Petro W, Hussain KA, Altamimi MA, *et al*. Dental considerations for leukemic pediatric patients: an updated review for general dental practitioner. Mater. Sociomed. 2015 Oct;27(5):359-62. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4639337
26. Organización Mundial de la Salud. Anemia Datos y cifras [Internet]. Ginebra: OMS; c2023. [cited 2023 Nov 8]. Available from: https://www.who.int/es/news-room/fact-sheets/detail/anaemia
27. Sun J, Wu H, Zhao M, Magnussen CG, Xi B. Prevalence and changes of anemia among young children and women in 47 low- and middle-income countries, 2000-2018. E Clinical Medicine. 2021 Sep 17;41:101136. Available from: https://pubmed.ncbi.nlm.nih.gov/34585127/
28. Giordano G, Napolitano M, Di Battista V, Lucchesi A. Oral high-dose sucrosomial iron vs intravenous iron in sideropenic anemia patients intolerant/refractory to iron sulfate: A multicentric randomized study. Ann Hematol. 2021 Sep;100(9):2173-2179. Available from: https://pubmed.ncbi.nlm.nih.gov/33263170/
29. Neef V, Schmitt E, Bader P, Zierfuß F, Hintereder G, Steinbicker AU, *et al*. The Reticulocyte Hemoglobin Equivalent as a Screening Marker for Iron Deficiency and Iron Deficiency Anemia in Children. J Clin Med. 2021 Aug 9;10(16):3506. Available from: https://pubmed.ncbi.nlm.nih.gov/34441801/
30. Reyes Mera MK, Montes Mendoza GA, Mero Barcia VM, Romero Burgos MM. Diagnóstico y síntomas de una anemia hemolítica. RECIMUNDO. 2021;5(1):322-329. Available from: https://www.recimundo.com/index.php/es/article/view/1016
31. Shah YB, Priore SF, Li Y, Tang CN, Nicholas P, Kurre P, *et al*. The predictive value of PNH clones, 6p CN-LOH, and clonal TCR gene rearrangement for aplastic anemia diagnosis. Blood Adv. 2021 Aug 24;5(16):3216-3226. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8405198/
32. Taksande A, Jameel PZ, Pujari D, Taksande B, Meshram R. Variation in pulmonary function tests among children with sickle cell anemia: A systematic review and meta-analysis. Pan Afr Med J. 2021 Jun 18;39:140. Available from: https://pubmed.ncbi.nlm.nih.gov/34527156/
33. Li X, Thomsen H, Sundquist K, Sundquist J, Försti A, Hemminki K. Familial Risks between Pernicious Anemia and Other Autoimmune Diseases in the Population of Sweden. Autoimmune Dis. 2021 Jan 12;2021:8815297. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7815416/
34. Aulestia-Viera PV, Dourado Cardoso Alves I, Moura Chicrala G, da Silva Santos PS, Valente Soares Junior LA. Manejo odontológico del paciente con anemia falciforme: revisión integrativa. Revista Odontología. 2020;22(2):92-107. Available from: https://revistadigital.uce.edu.ec/index.php/odontologia/article/view/2203
35. Peisker A, Raschke GF, Guentsch A, Roshanghias K, Schultze-Mosgau S. Management of dental extraction in a female patient with fanconi anemia. J Dent (Tehran). 2014 Sep;11(5):613-9. Available from: https://www.hindawi.com/journals/crid/2020/3161053/
36. Faheem S, Maqsood S, Hasan A, Imtiaz F, Shaikh F, Farooqui WA, *et al*. Associations of early childhood caries with salivary beta defensin-3 and childhood anemia: a case-control study. BMC Oral Health. 2021 Sep 14;21(1):445. Available from: https://bmcoralhealth.biomedcentral.com/articles/10.1186/s12903-021-01810-x
37. Hotea I, Brinza M, Blag C, Zimta AA, Dirzu N, Burzo C, *et al*. Current therapeutic approaches in the management of hemophilia-a consensus view by the Romanian Society of Hematology. Ann Transl Med. 2021 Jul;9(13):1091. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8339806
38. Kun H, Xu W, Zhou M, Li X, Xu Z, Fang Y, *et al*. Pharmacokinetics and complementary evaluation system-based guidance on prophylaxis of paediatric patients with

haemophilia A in China with Kovaltry: protocol of the LEAP study. BMJ Open. 2021 Jul 5;11(7):e048432. Available from: https://europepmc.org/article/pmc/pmc8258559
39. Mehta P, Reddivari AKR. Hemophilia; c2021. In: StatPearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; c2021. PMID: 31869071. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551607/
40. Parvaie P, Shaygan Majd H, Ziaee M, *et al*. Evaluation of gum health status in hemophilia patients in Birjand (a case-control study). Am. J Blood. Res. 2020 Jun 15;10(3):54-59. Available from: https://pubmed.ncbi.nlm.nih.gov/32685260/
41. Kanjani V, Annigeri RG, Hanagavadi S, *et al*. Comparative analysis of oral health and treatment necessities in hemophilia individuals of Davangere population: A case control study. J Family Med Prim Care. 2020 Sep 30;9(9):4774-4777. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7652167
42. Reddy KS, Reddy NV, Niharika P, *et al*. Oral Health Status and Treatment Needs among Hemophilic Children in Hyderabad, Telangana, India. Int J Clin Pediatr Dent. 2019 Jan-Feb;12(1):30-32. Available from: https://pubmed.ncbi.nlm.nih.gov/31496568/
43. Avendaño Córdova KB, Rueda Ventura MA, Isidro Olán LB. Manejo estomatológico del paciente pediátrico con hemofilia: Reporte de casos. Multidisciplinary Health Research. 2020, 5(1). Available from: https://revistas.ujat.mx/index.php/MHR/article/view/4385
44. Grigorita O, Omer L, Juodzbalys G. Complications and Management of Patients with Inherited Bleeding Disorders During Dental Extractions: A Systematic Literature Review. J Oral Maxillofac Res. 2021 Jun 30;12(2):e1. Available from: https://pubmed.ncbi.nlm.nih.gov/34377378/
45. Laino L, Cicciù M, Fiorillo L, *et al*. Surgical Risk on Patients with Coagulopathies: Guidelines on Hemophiliac Patients for Oro-Maxillofacial Surgery. Int J Environ Res Public Health. 2019 Apr 17;16(8):1386. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6518229
46. Báez Desangles J, Thomas-Knipping T. Hemorragia postquirúrgica, posible complicación de la cirugía bucal, causas y tratamiento. Santo Domingo: Uni Ibero. 2021. Available from: https://repositorio.unibe.edu.do/jspui/handle/123456789/430
47. He S, Li D, Yi S. Molecular Characterization of α- and β-Thalassaemia Among Children From 1 to 10 Years of Age in Guangxi, A Multi-Ethnic Region in Southern China. Front Pediatr. 2021 Aug 23;9:724196. Available from: https://www.frontiersin.org/articles/10.3389/fped.2021.724196/full
48. Asawasudsakorn N, Lauhasurayotin S, Poparn H, *et al*. Prenatal Diagnosis Leads to Early Diagnosis of Transfusion-Dependent Thalassemia and Better Growth Outcomes. Glob Pediatr. Health. 2021 Sep 9;8:2333794X211046104. Available from: https://pubmed.ncbi.nlm.nih.gov/34527771/
49. Mirzaei G, Shamsasenjan K, Jafari B, *et al*. Prevalence of HBV and HCV infection in beta-thalassemia major patients of Tabriz city, Iran. New Microbes New Infect. 2021 Jul 6;43:100912. Available from: https://pubmed.ncbi.nlm.nih.gov/34401191/
50. Wang H, Chen M, Xu S, *et al*. Abnormal regulation of microRNAs and related genes in pediatric β-thalassemia. J Clin Lab Anal. 2021 Sep;35(9):e23945. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8418487
51. Albagshi MH, Saad M, Aljassem AM, Bushehab AA, Ahmed NH, Alabbad MM, *et al*. Blood Demand and Challenges for Patients With Beta-Thalassemia Major in Eastern Saudi Arabia. Cureus. 2021 Aug 26;13(8):e17470. Available from: https://pubmed.ncbi.nlm.nih.gov/34603865/
52. Mahmoud RA, Khodeary A, Farhan MS. Detection of endocrine disorders in young children with multi-transfused thalassemia major. Ital J Pediatr. 2021 Jul 31;47(1):165. Available from: https://ijponline.biomedcentral.com/articles/10.1186/s13052-021-01116-2
53. Bouguila J, Besbes G, Khochtali H. Skeletal facial deformity in patients with β thalassemia major: Report of one Tunisian case and a review of the literature. Int J Pediatr Otorhinolaryngol. 2015 Nov;79(11):1955-8. Available from: https://pubmed.ncbi.nlm.nih.gov/26363895/
54. Abu Shosha GM, Al-Kalaldeh M, Shoqirat N. Nurses' experiences of psychosocial care needs of children with thalassaemia and their families in Jordan: A phenomenological study. Nurs. Open. 2021 Jul 20. Available from: https://pubmed.ncbi.nlm.nih.gov/34288571/
55. Einy S, Ben-Barak A, Kridin K, Aizenbud D. Craniofacial Deformities in Patients With Beta-Thalassemia: Orthodontic Versus Surgical Correction-A Systematic Review. J Pediatr. Hematol. Oncol. 2020 Apr;42(3):198-203. Available from: https://pubmed.ncbi.nlm.nih.gov/31851070/
56. Kularatne WN, Jayasinghe RM, Diyunugala MC, Bandara D, Abeysundara S, Perera I. Sociodemographic profile and oral health status of thalassemic patients attending the National Thalassaemia Centre, Kurunegala, Sri Lanka. J Investig Clin Dent. 2018 May;9(2):e12293. Available from: https://pubmed.ncbi.nlm.nih.gov/28862373/
57. Oren D, Dror AA, Bramnik T, Sela E, Granot I, Srouji S. The power of three-dimensional printing technology in functional restoration of rare maxillomandibular deformity due to genetic disorder: a case report. J Med Case Rep. 2021 Apr 12;15(1):197. Available from: https://pubmed.ncbi.nlm.nih.gov/33845912/
58. Lotinun S, Atjanasuppat K, Limsuvech J, Leelahavanichkul A, Svasti S, Krishnamra N. Nephrectomy Does not Exacerbate Cancellous Bone loss in Thalassemic Mice. Sci Rep. 2020 May 8;10(1):7786. Available from: https://www.nature.com/articles/s41598-020-64681-2
59. Al-Raeesi S, Kowash M, Hassan A, Al-Halabi M. Oral manifestations and dentofacial anomalies in β-thalassemia major children in Dubai (UAE). Spec Care Dentist. 2018 Jan;38(1):25-30. Available from: https://pubmed.ncbi.nlm.nih.gov/29278272/
60. Akcalı A, Yıldız MS, Akcalı Z, Huck O, Friedmann A. Periodontal condition of patients with Thalassemia Major: A systematic review and meta-analysis. Arch Oral Biol. 2019 Jun;102:113-121. Available from: https://pubmed.ncbi.nlm.nih.gov/30999065/
61. Fadel HT, Zolaly MA, Alharbi MO, Qarah LA, Alrehili MS, Alamri AD, *et al*. Oral Health Profiles and Related Quality of Life in Thalassemia Children in Relation to

Iron Overload: A Cross-Sectional Study. Int J Environ Res Public Health. 2020 Dec 16;17(24):9444. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7766577
62. Helmi N, Bashir M, Shireen A, Ahmed IM. Thalassemia review: features, dental considerations and management. Electron Physician. 2017 Mar 25;9(3):4003-4008. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5407235
63. Al Hasani KM, Bakathir AA, Al-Hashmi AK, Al Rawahi B, Albakri A. Modified Le Fort I Osteotomy and Genioplasty for Management of Severe Dentofacial Deformity in β-Thalassemia Major: Case report and review of the literature. Sultan Qaboos Univ Med J. 2020 Aug;20(3):e362-e367. Available from: https://pubmed.ncbi.nlm.nih.gov/33110654/

How to Cite This Article
Treviño-Tijerina MC, Garza-Villarreal J, Sáenz-Rangel S, Cruz-Fierro N. Dental dilemmas in blood disorders: Navigating oral health in hematological diseases. International Journal of Applied Dental Sciences. 2023;9(4):283-289.