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Review article

An Overview on the Relation Between Blood Disorders, Periodontitis and Dental Caries

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Abstract
The relationship between blood disorders, periodontitis, and dental caries reveals a complex interaction between oral health and systemic conditions. Dental caries, caused by bacterial biofilms and environmental factors, and periodontitis, a chronic inflammatory disease, are both associated with significant systemic implications. This review highlights the bidirectional link between these oral conditions and hematological disorders such as anemia, leukemia, and thalassemia. Periodontitis-induced inflammation can disseminate systemically, impacting hematopoietic functions and contributing to blood disorders. Conversely, hematological diseases can exacerbate periodontal issues by impairing immune responses and altering blood parameters, as observed in conditions like cyclic neutropenia and sickle cell anemia. The systemic effects of periodontitis are characterized by elevated markers, including C-reactive protein (CRP) and IL-6, amplifying chronic inflammation. This interrelationship underscores the necessity of integrative healthcare strategies. Regular monitoring of systemic markers, proactive management of periodontal inflammation, and addressing underlying hematological conditions are essential for improving patient outcomes. This review advocates for a holistic diagnostic and therapeutic approach to manage the coexisting challenges of oral and systemic health conditions effectively.
Keywords: Oral Health, Blood Disorders, Periodontitis, Dental Caries.

Introduction

Currently, it is often known that poor dental health is intimately linked to chronic disorders. There are many similarities between severe systemic disorders and oral disease situations. Accordingly, prevalent risk factors because the body's first line of defense is the mouth. According to the World Health Organization (WHO), an individual's oral cavity health is vital to preserving their health and well-being and is a major factor in determining their general health [1].

In the majority of developed nations, dental caries continues to be a serious oral health issue, impacting 60–90% of students and the great majority of adults. While it seems to be less widespread and less severe in the majority of African countries, it is also the most common oral illness in a number of Asian and Latin American nations [2,3]. Additionally, according to research conducted in developed nations, smoking is a significant risk factor for adult periodontal disease and accounts for over half of instances of periodontitis in this age range. Quitting smoking lowers risk, and in nations where tobacco use is declining, the frequency of periodontal disease has dropped [4]. Moreover, risk factors or symptoms related to oral health could indicate the beginning of a disease or a condition that is getting worse.

As a definition, the main cause of dental caries, also referred to as tooth decay, is acid generated by bacteria that breaks down the tooth's hard tissues, including the cementum, dentin, and enamel. Dental caries, on the other hand, has a complex etiology that involves interactions between environmental factors (such as food, salivary flow and composition, fluoride exposure), bacterial biofilms (dental plaque), and the tooth structure itself. Destructive factors that aid in tooth demineralization and protective factors that encourage tooth remineralization are dynamically balanced as a result of this interplay [5,6].

Because of the occurrence of various inflammations in the body and their aftereffects, including proinflammatory cytokines and other inflammatory mediators released into the bloodstream in excess, this review article focuses on various mechanisms that may lead to the association between dental caries and blood disorders. The effect of this inflammation on blood cell production may lead to hematological issues.

Association between some of blood disorders and periodontitis

Chronic inflammation of the periodontium is the hallmark of periodontitis, a clinical condition that can lead to alveolar bone destruction and the loss of periodontal ligaments. Periodontitis in its advanced stages might cause tooth loss [7,8]. One of the most prevalent oral inflammatory diseases, periodontitis is caused by a dysbiosis, or imbalance, between the human immune system and the oral microbiota. Poor dental hygiene, smoking, genetic predisposition, and other systemic diseases like diabetes or hematological disorders are risk factors, and it is linked to bacterial plaque [8,9].

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The occurrence of periodontitis is linked to several hematological illnesses through a number of currently understood causes and mechanisms. The hematopoietic system may be impacted by inflammation brought on by periodontal disease. An immune system reaction and oxidative stress may result from the increased release of pro-inflammatory cytokines and inflammatory mediators into the circulation caused by gingivitis and periodontitis. Therefore, some of blood disorders may result from this inflammation's impact on the generation of blood cells, such as leukocytes and platelets. Additionally, certain blood disorders such anemia, leukemia, and multiple myeloma are linked to certain periodontal illnesses [10-12].

It is important to note that over the years, numerous studies have shown that periodontal inflammation, in addition to causing a local inflammatory reaction, can also reveal extensive systemic effects. Dependently, the presence of any systemic conditions, such as diabetes mellitus, hypertension, hematological diseases, cardiovascular disease, respiratory disorders, endocrine disorders, etc., can either individually or collectively contribute to a local inflammatory reaction that results in the complete loss of teeth and their associated structures [13,14].

Bacteria in the mouth can cause inflammation and infections that can transfer to the bloodstream and impact the hematopoietic system's health. As a result, blood infections (bacteremia) and hematological problems may result from bacteria that infect the gingiva entering the bloodstream through routine dental flossing or brushing. Because of this, there is a clear correlation between hematologic disorders and periodontal disease, which doctors and dentists need to take into consideration while diagnosing and treating patients [14]. More excitingly, periodontitis exhibits unique hematologic patterns, including leukocytosis and/or anemic values, according to the hematogenic point of view [15].

Furthermore, once the bacteria enter the bloodstream, the blood-borne periodontal bacteria raise serum levels of C-reactive protein (CRP) and IL-6, which intensifies the chronic inflammatory state [16,17]. Surprisingly, the primary systemic route of dissemination for periodontal hazardous compounds is the circulatory system. With potentially disastrous results, these attackers increase the inflammatory machinery and increase the systemic inflammatory state [18]. Remarkably, patients with generalized aggressive periodontitis who receive long-term therapy see a significant decrease in blood inflammatory markers. According to these results, periodontitis should be continuously managed to preserve systemic health [19]. Therefore, helpful and specific information on systemic and periodontal infection may be obtained by examining systemic circulatory markers, including neutrophils [20, 21], the neutrophil to lymphocyte ratio (NLR) [22], platelets [23], the platelet to leukocyte ratio (PLR) [24], and erythrocyte counts [25].

On the other side, blood disorders may have the opposite impact, as they can exacerbate periodontitis. Actually, hematologic diseases may impact gingival and periodontal health through a number of methods. Therefore, numerous noteworthy alterations in blood count parameters in patients with periodontal disease have been the focus of numerous investigations in recent years. One of the most important observations in this context, that higher leukocyte counts are linked to severe chronic periodontitis, primarily in relation to neutrophils and lymphocytes. The results of people with severe disease as opposed to those with mild disease make this especially clear [26]. Neutrophils are essential for maintaining tissue integrity, carrying out antimicrobial immune defense tasks, and promoting wound healing at mucosal barriers. By efficiently managing infections and maintaining mucosal integrity through mechanisms like phagocytosis, degranulation, and the release of neutrophil extracellular traps (NETs), these prodigious white blood cells act as the first line of defense against microbial threats [27]. Neutrophils mainly exit blood vessels and pass through the gingival junctional epithelium until they reach the periodontal pocket (Figure 1), [28].

Periodontitis and anemia

Hypochromic microcytic anemia, which is characterized by a decrease in the mean corpuscular volume (MCV), hemoglobin (HGB), hematocrit (HCT), and red blood cell count, develops during periodontitis. Furthermore, there was an increase in erythrocyte sedimentation rate (ESR) and red blood cell width (RDW) values [29]. Similarly, patients with sickle cell anemia frequently exhibit characteristic maxillofacial characteristics, such as pale oral mucosa, maxillary protrusion, and mandibular retrusion. They typically have higher than average rates of severe periodontitis and dental cavities [30].

Equally, about 5% of people worldwide suffer from thalassemia, a common hereditary blood disorder that is more common in the Mediterranean, Middle East, Africa, and Southeast Asia [31], patients with this condition frequently have a convex facial profile and a class II skeletal pattern, which sets them apart from healthy people [32]. Beta thalassemia major patients frequently have smaller dental crowns, constricted dental arches, and discolored teeth, and they are more likely to experience dental caries, periodontal disorders, and oral infections [33]. Al-Wahadni et al. examined the potential correlation between β-thalassemia major and deteriorating dental caries and periodontal disease in a 2002 study. Using several periodontal indices and the decayed, missing, and filled teeth (DMFT) index, respectively, plaque deposits, gingivitis, periodontitis, and dental caries were evaluated in 61 afflicted patients and 63 healthy persons aged 6 to 18. Dental caries was observed to be more common in the thalassemia patient group than in

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healthy individuals [34, 35]. As a result of a forementioned evidences, people with thalassemia and those with poor health are more likely to have active dental disease (Figure 2).

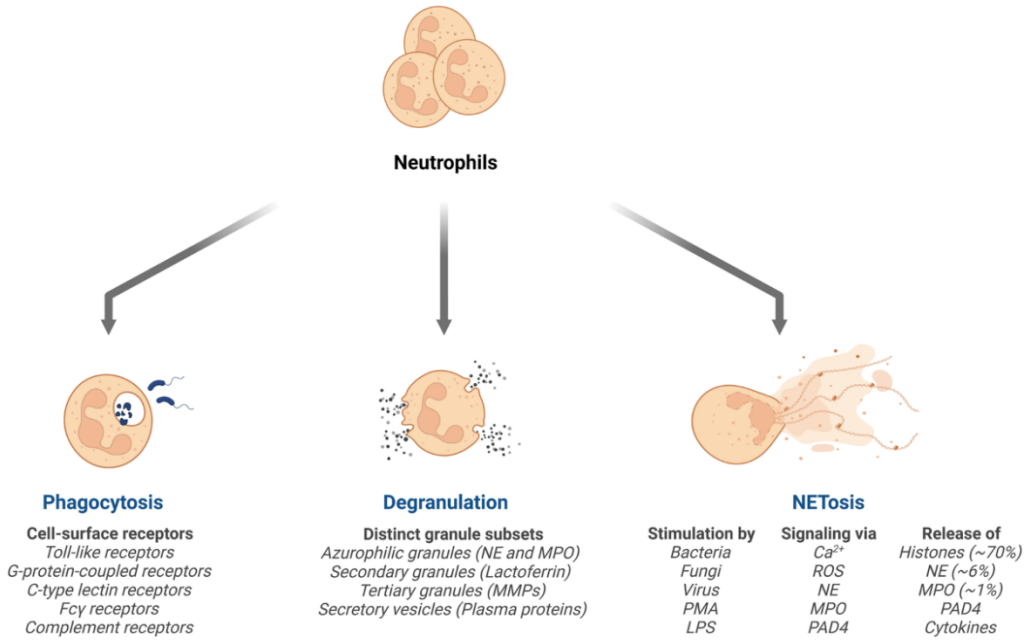

Figure 1. Neutrophils' intrinsic antimicrobial defense systems. Three main processes—phagocytosis, degranulation, and neutrophil extracellular trap formation (NETs)—are how neutrophils mediate antimicrobial defense. There are several cell surface receptors that initiate phagocytosis (the main receptors are listed). A range of enzymes and antibacterial substances, including those present in their granules (the main types of neutrophil granules and their contents are listed), are also secreted by neutrophils. Lastly, intracellular pathways that mediate the creation and release of NETs can be activated by a variety of stimuli, as illustrated [28].

Figure 2. Oral and dental manifestations of β-thalassemia [36].

Leukocyte disorders and oral health

Infections like gingivitis are frequently reported in cyclic neutropenia (CN) [37,38]. A fast pattern of periodontal deterioration resembling severe periodontitis was observed in a number of pediatric CN cases [39,40]. Moreover, periodontal disease is a typical feature of leukemias, which are defined by a disorderly proliferation of WBCs in BM [41], especially in the acute forms of this blood illness [42,43].

Blood disorders' effects on dental caries

Numerous biological, microbiological, behavioral, psychological, and environmental factors can contribute to dental caries, a complex, noncommunicable illness [51]. Dental caries still affects 29.4% of the world's population, making it one of the most common diseases. Dental caries is becoming more common despite a

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lot of work to identify, forecast, and stop it [52]. Symptomatically, loss of teeth is a sign of poor oral health and the final stage of conditions such periodontal disease and dental caries [53]. It is known currently that Dental caries can cause pulpitis and periapical infections when the infection extends from the dentin and carious enamel into the pulp. In order to prevent the spread of bacteria, pulp must be removed. An infected, rotting tooth may get so bad that extraction is required if treatment is not received. One of the most common blood disorders prevalent in Africa and middle east region is sickle cell anemia. Lower salivary flow, mental nerve neuropathy, increased plaque and calculus deposition, radiographic abnormalities, hypo-mineralization of the enamel, delayed tooth eruption, dental caries, malocclusion, and hyper-cementosis are common oral manifestations reported in sickle cell anemic patients. Because sickle cell disease patients are more likely to experience dental complications due to changes in their dental structure, medications that contain sucrose, and an increased susceptibility to infections, which always rises with poor oral hygiene, the dentist's role is crucial (Table 1) [54].

Table 1. A summary table based on current research showing how different blood diseases affect the prevalence of periodontitis and tooth caries

Blood Disorder		**Effect on Dental Caries and Periodontitis**	**Key Findings**	**References**
Anemia	Iron-Deficiency	Increased susceptibility to periodontitis due to reduced oxygenation and impaired healing.	Periodontal inflammation worsens in anemic patients; iron deficiency may impair oral mucosal health and immune response.	[44, 45]
	Sickle Cell Anemia	Higher risk of periodontal and dental issues due to vascular complications and tissue hypoxia.	Sickle-shaped red cells impair blood flow to oral tissues, reducing their ability to resist infection and heal after periodontal damage.	[45, 46, 47]
Leukemia		Elevated risk of periodontitis and dental caries due to immune suppression and gingival hyperplasia.	Leukemia patients exhibit significant periodontal destruction; compromised immunity exacerbates microbial infection.	[44, 45, 48]
Multiple Myeloma		Increased periodontitis risk associated with systemic bone loss and altered immune function.	Bone resorption linked to myeloma contributes to alveolar bone loss; immune dysregulation heightens susceptibility to periodontal pathogens.	[44, 46]
Cyclic Neutropenia		Severe periodontal damage due to periodic immune suppression affecting neutrophil counts.	Fluctuating neutrophil levels lead to recurrent oral infections, significantly affecting periodontal and dental health.	[44, 45]
Clonal Hematopoiesis		Linked to chronic inflammation and potential periodontal damage due to heightened inflammatory mediators.	Patients with clonal hematopoiesis show increased markers of systemic inflammation, which may exacerbate periodontal tissue destruction.	[44]
Hemophilia		Hemophiliacs were reported to have significantly higher gingival indices and more alveolar bone loss than controls.	Congenital coagulation disorders are risk factors for dental caries, gingivitis, peri odontitis. Moderate to severe periodontitis was more prevalent among hemophilia patients and subsequent alveolar bone loss	[49]
ABO blood groups		Individuals with specific blood types may be more prone to oral diseases.	The AB blood group had the significantly highest mean DMFS score, while the O blood group had the lowest mean DMFS score	[50]

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On the other hand, regarding thalassemia, Galanello et al. demonstrate that thalassemia patients may have a greater incidence of dental caries because their salivary immunoglobulin A (IgA) levels are lower, which increases the microbial population and hence contributes considerably to the higher caries incidence. Caries is more common in people with lower IgA levels, but carelessness also plays a significant part in these cases. They seek dental care when the patient is in pain and are more interested in complex bodily health conditions. Increased levels of thalassemia are linked to a higher incidence of dental caries [55]. Furthermore, patients with Von Willebrand Disease (VWD), one of the blood illnesses, typically experience greater mucosal bleeding; the severity of the bleeding is significantly influenced by VW factor levels. The most prevalent dental condition in such case is dental caries. A major contributing factor to the development of caries is dental plaque on the tooth surface. The likelihood that a carious lesion will spread deeply into the dentin and enamel and necessitate a thorough repair or tooth extraction rises if the disease is not adequately treated in a timely manner [56].

Conclusion

The complex relationship between oral health and systemic illnesses is highlighted by the interaction of blood disorders, periodontitis, and tooth caries. While periodontitis is a chronic inflammatory disease with systemic effects, dental caries, a common oral health problem, results from a complex interplay between bacterial biofilms, environmental variables, and tooth structure. There is a reciprocal association between both diseases and hematological illnesses. Oral diseases can cause inflammation that spreads throughout the body, impacting hematological processes and causing blood disorders such thalassemia, leukemia, and anemia. By affecting immunological responses and changing blood parameters, blood disorders such as sickle cell anemia and cyclic neutropenia can worsen periodontal diseases. Elevated levels of CRP and IL-6 indicate the systemic inflammatory response brought on by periodontitis, underscoring the necessity of integrative care techniques. To improve patient care, healthcare providers need to take these relationships into account. The risk of systemic problems can be reduced by aggressive management of periodontal inflammation and routine monitoring of systemic indicators. In a similar vein, treating underlying hematological problems is essential to enhancing oral health results. When diagnosing and treating patients with coexisting oral and systemic illnesses, the data highlights the value of a comprehensive approach. In summary, this review aimed to highlight the key conclusions drawn from some recent research regarding the close connection, to a significant degree, between common blood disorders and oral diseases like gingivitis and tooth decay, as well as the key symptoms that may manifest in either an acute or chronic form. Numerous studies on this crucial subject are desperately needed in the future, particularly with regard to the preventative and therapeutic elements.

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Conflicts of Interest

The authors declare no conflicts of interest.

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المستخلص

تكشف العلاقة بين اضطرابات الدم والتهاب دواعم السن وتسوس الأسنان عن تفاعل معقد بين صحة الفم والحالات الجهازية. يرتبط تسوس الأسنان الناجم عن الأغشية الحيوية البكتيرية والعوامل البيئية والتهاب دواعم السن، وهو مرض التهابي مزمن، بعواقب جهازية كبيرة. تسلط هذه المراجعة الضوء على الارتباط الثنائي الاتجاه بين هذه الحالات الفموية والاضطرابات الدموية مثل فقر الدم وسرطان الدم والثلاسيميا. يمكن أن ينتشر الالتهاب الناجم عن التهاب دواعم السن على نطاق واسع، مما يؤثر على وظائف الدم ويساهم في اضطرابات الدم. وعلى العكس من ذلك، يمكن أن تؤدي الأمراض الدموية إلى تفاقم مشاكل اللثة عن طريق إضعاف الاستجابات المناعية وتغيير معايير الدم، كما هو الحال في حالات مثل نقص العدلات الدورية وفقر الدم المنجلي. تتميز التأثيرات الجهازية لالتهاب دواعم السن بعلامات مرتفعة، بما في ذلك البروتين التفاعلي سي وIL-6، مما يؤدي إلى تضخيم الالتهاب المزمن. تؤكد هذه العلاقة المتبادلة على ضرورة استراتيجيات الرعاية الصحية المتكاملة. إن المراقبة المنتظمة للعلامات الجهازية، والإدارة الاستباقية لالتهاب اللثة، ومعالجة الحالات الدموية الكامنة، كلها أمور ضرورية لتحسين نتائج المرضى. وتدعو هذه المراجعة إلى اتباع نهج تشخيصي وعلاجي شامل لإدارة التحديات المتزامنة للحالات الصحية الفموية والجهازية بشكل فعال.

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