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ARQUIVOS EM ODONTOLOGIA

The importance of the dentist in the early diagnosis of leukemia: a scoping review

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Aim: Our study aims to estimate how dentists can contribute to the early diagnosis of leukemia through recognizing oral manifestations and initiating timely referrals.

Methods: We conducted a scoping review search of the literature that analyzed the dentist's role in the early diagnosis of leukemia, as well as its manifestations in the oral cavity. We followed the PRISMA-ScR guidelines. The electronic searches were carried out in PubMed, Embase, Web of Science, Scopus, and Google Scholar as a source of gray literature.

Results: From a total of 3.578 potentially eligible articles, 34 were selected for full-text methodology assessment, and 20 were included in the scoping review. The most common oral manifestations suggestive of leukemia are: ulcers, severe bleeding, gingival hyperplasia, necrosis in the gingival papillae, petechiae, and color change in the mucosa.

Conclusion: The dentist plays a crucial role in the early diagnosis of leukemia. When encountering the oral manifestations, systemic signs and symptoms presented in this scoping review, it is essential to promptly request complementary tests to aid in accurate diagnosis and a timely intervention.

Uniterms: leukemia; oral manifestations; dentists.

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INTRODUCTION

Leukemia is a hematological neoplasia that originates in the bone marrow, characterized by the abnormal and uncontrolled production of immature leukocytes, which can compromise normal hematopoietic function.[1] In 2022, Brazil registered 7.105 individuals who had succumbed to this disease.[2]

Although the diagnosis still relies on several clinicopathologic criteria, in its 5th edition (2022), the World Health Organization (WHO) updated the classification of Haematolymphoid Tumours. This update aimed to improve diagnostic accuracy.[3] Table 1 summarizes the different types of leukemia and their features.

Table 1. Leukemia divided into types and characteristics.

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Leukemia	Type	Characteristics
Chronic Myeloid Leukaemia	Myeloproliferative Neoplasms (MPN)	BCR::ABL1 fusion resulting from t(9;22)(q34;q11). There is a significant proliferation of cells from the myeloid lineage, followed by a progressive loss of cellular differentiation, culminating in a picture of acute leukemia. With target tyrosine kinase and disease preservation, the incidence of progression has decreased.

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(conclusion)

Chronic Neutrophilic Leukaemia	MPN	BCR::ABL 1-negative MPN with blood neutrophilia, bone marrow hypercellularity due to neutrophilic granulocyte proliferation and hepatosplenomegaly.
Chronic Eosinophilic Leukaemia	MPN	Proliferation of morphologically abnormal eosinophils and eosinophil precursors leading to persistent hypereosinophilia in blood and bone marrow.
Juvenile Myelomonocytic Leukaemia	MPN	It is a neoplasm of early childhood. Aggressive cases usually have somatic mutations involving PTPN11 and germline pathogenic variants with neurofibromatosis type 1.
Chronic Myelomonocytic Leukaemia	Myelodysplastic/ Myeloproliferative Neoplasms	Characterized by sustained peripheral blood monocytosis and combinations of mutations. This condition occurs when monocytes, still maturing in the bone marrow, begin to grow uncontrollably. This excessive growth fills the bone marrow, inhibiting the development of other blood cells.
Acute Myeloid Leukaemia (AML)	-	Clonal proliferation of myeloid precursors with a reduced capacity to differentiate into more mature cellular elements.
Acute Lymphocytic Leukaemia	-	Originates from B- or – lymphocyte progenitor. There is an accumulation of blast lymphocytes and suppression of normal cells.

Sources: Khoury et al. [3]; Mohebbi et al. [4] ; Zhang et al. [5]

The interval between the onset of the first signs and symptoms of leukemia and its definitive diagnosis remains a cause for concern, despite advancements in healthcare access. A retrospective study conducted by Aboelkhir et al.[6] compared the challenges faced by different hematology centers worldwide in establishing the diagnosis. The study reported an average diagnostic delay of 28 days in Qatar, 32 days in both India and Rwanda, and 30 days in Brazil. The shortest interval was observed in China, with a mean time of 21 days to diagnosis.

Part of this delay may be related to the lack of clinical recognition of early manifestations, particularly those affecting the oral cavity. Some studies have investigated the extramedullary manifestations of leukemia, including oral findings. [7] Although not all of them are directly associated with disease progression or prognosis, certain recurrent oral changes show clinical relevance and may serve as important diagnostic clues, warranting greater attention and further investigation in future research.

Primary studies and systematic reviews have emphasized these oral manifestations as potential indicators for early diagnosis. [8-11] In this context, the strategic role of the dentist in the early suspicion of the disease is highlighted. Busjan et al. [10] report that in approximately 25% of cases, the dentist was the professional responsible for raising the diagnostic hypothesis.

Despite the recognized importance of early detection, there remains a gap in the literature regarding the role of dental professionals in this process, especially concerning how and when they contribute to early diagnosis. Therefore, conducting this scoping review is justified by the need to understand how the dentist's approach is necessary and essential in formulating the diagnostic hypothesis and referring patients for medical care. Accordingly, this study may provide valuable insights into these issues and assist clinicians in making more informed decisions when referring these patients.

Thus, the aim of the present literature review is to investigate and synthesize the available evidence on how dentists can contribute to the early diagnosis of leukemia through recognizing oral manifestations and initiating timely referrals.

METHODS

This scoping review involved multiple steps: definition of the theme and guiding question; elaboration of the inclusion and exclusion criteria; searching for publications in the selected databases; categorizing, analyzing the studies and critically evaluating the selected studies; presenting the results with critical analysis and synthesis of the review. To conducting this, the guiding question was: "what is the role of the dentist in the early diagnosis of leukemia?".

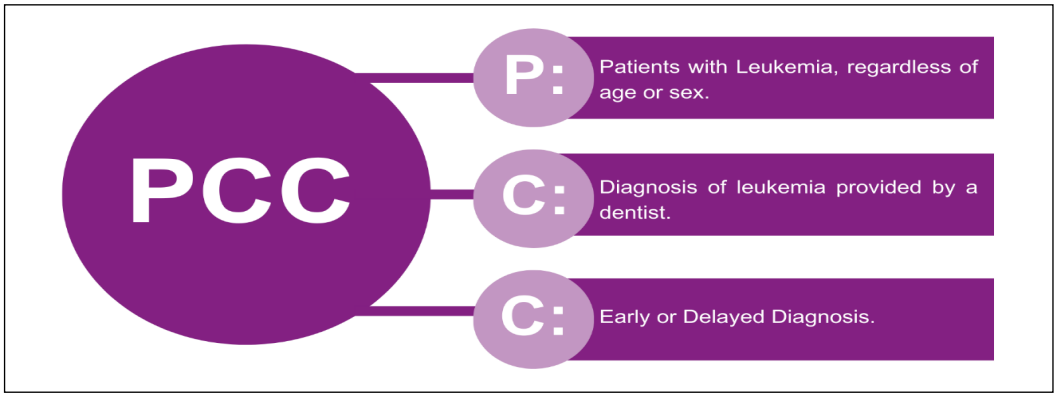
Protocol and registration

The methodology of the present article followed the guidelines of the PRISMA-ScR[12], which presents the recommended items for systematic reviews and extension of meta-analyses and scoping reviews. Subsequently, after all authors had reviewed and approved this protocol, it was registered on September 25th, 2024 and last updated on August 1st, 2025 in the Open Science Framework (OSF; Center for Open Science, Charlottesville, United States)[13], available online with the registration number DOI: 10.17605/OSF.IO/ZPR7K.

Eligibility criteria

The research question was formulated based on the PCC (Population, Context and Concept) acronym (Figure 1).

Figure 1. PPC illustration.



Source: Own authors. Figure generated with Canva.com.

Therefore, this review included both primary and secondary research studies, case reports, case series and observational studies (cross-sectional), as well as evidence synthesis studies such as integrative reviews. To be included, the following criteria were used: (1) Patients with leukemia; (2) Clinical oral, radiological evaluation or supplementary tests; (3) Having enough data regarding the dentist approach; (4) Initial clinical suspicion raised by a dentist, regardless of whether the final diagnosis was confirmed by a multidisciplinary team.

However, the exclusion criteria were as follows: (1) Studies in which the dentist did not play a role in raising the initial clinical suspicion or identifying suggestive oral signs of leukemia; (2) Not enough data for a proper data extraction; (3) Articles published before 2013; (4) Narrative reviews, letters, book chapters, conference abstracts, clinical guides, panels, articles describing techniques, and opinion articles.

Databases and search strategy

Searches were carried out in PubMed, Embase, Scopus, Web of Science, and Google Scholar as a source of grey literature. The search strategy employed in PubMed (Table 2) included indexed terms (MeSH) and their synonyms. Some adjustments were made to align the strategy with the specific requirements of each database. For further information, refer to Appendix 1. On Google Scholar database, only the first hundred hits were considered.

Table 2. Database and search strategy.

Database	Search strategy
PubMed	(“leukaemia”[All Fields] OR “leukemia”[MeSH Terms] OR “leukemia”[All Fields] OR “leukaemias”[All Fields] OR “leukemias”[All Fields] OR ((“acute”[All Fields] OR “acutely”[All Fields] OR “acutes”[All Fields]) AND (“leukaemia”[All Fields] OR “leukemia”[MeSH Terms] OR “leukemia”[All Fields] OR “leukaemias”[All Fields] OR “leukemias”[All Fields] OR “leukemia s”[All Fields])) OR (“leukemia”[MeSH Terms] OR “leukemia”[All Fields] OR “leucocythemia”[All Fields])) AND (“early diagnosis”[MeSH Terms] OR (“early”[All Fields] AND “diagnosis”[All Fields]) OR “early diagnosis”[All Fields] OR (“early diagnosis”[MeSH Terms] OR (“early”[All Fields] AND “diagnosis”[All Fields]) OR “early diagnosis”[All Fields] OR (“early”[All Fields] AND “detection”[All Fields]) OR “early detection”[All Fields]) OR ((“initial”[All Fields] OR “initially”[All Fields] OR “initials”[All Fields] OR “initiate”[All Fields] OR “initiated”[All Fields] OR “initiates”[All Fields] OR “initiating”[All Fields] OR “initiation”[All Fields] OR “initiations”[All Fields] OR “initiator”[All Fields] OR “initiators”[All Fields]) AND (“diagnosable”[All Fields] OR “diagnosi”[All Fields] OR “diagnosis”[MeSH Terms] OR “diagnosis”[All Fields] OR “diagnose”[All Fields] OR “diagnosed”[All Fields] OR “diagnoses”[All Fields] OR “diagnosing”[All Fields] OR “diagnosis”[MeSH Subheading]))) AND (“oral manifestations”[MeSH Terms] OR (“oral”[All Fields] AND “manifestations”[All Fields]) OR “oral manifestations”[All Fields] OR (“oral manifestations”[MeSH Terms] OR (“oral”[All Fields] AND “manifestations”[All Fields]) OR “oral manifestations”[All Fields] OR (“oral”[All Fields] AND “manifestation”[All Fields]) OR “oral manifestation”[All Fields]) OR ((“mouth”[MeSH Terms] OR “mouth”[All Fields] OR “oral”[All Fields]) AND (“complicances”[All Fields] OR “complicate”[All Fields] OR “complicated”[All Fields] OR “complicates”[All Fields] OR “complicating”[All Fields] OR “complication”[All Fields] OR “complication s”[All Fields] OR “complications”[MeSH Subheading] OR “complications”[All Fields])) OR (“mouth diseases”[MeSH Terms] OR (“mouth”[All Fields] AND “diseases”[All Fields]) OR “mouth diseases”[All Fields] OR (“mouth”[All Fields] AND “disease”[All Fields]) OR “mouth disease”[All Fields]) OR ((“mouth”[MeSH Terms] OR “mouth”[All Fields] OR “oral”[All Fields]) AND (“diagnosis”[MeSH Subheading] OR “diagnosis”[All Fields] OR “findings”[All Fields] OR “diagnosis”[MeSH Terms] OR “finds”[All Fields] OR “signs and symptoms”[MeSH Terms] OR (“signs”[All Fields] AND “symptoms”[All Fields]) OR “signs and symptoms”[All Fields] OR “finding”[All Fields]))

We also searched the reference lists of included studies and relevant systematic reviews for additional studies. In addition, all included studies were reviewed for potential retractions, either due to error or fraud, ensuring the reliability and accuracy of the research base.

All the references obtained from the search were imported into the web software Rayyan (Qatar Computing Research Institute, Doha, Qatar)[14] for duplicate removal, and the selection phases were then carried out in the same software.

Selection of studies

Three reviewers were involved in this process to minimize a potential selection bias. In the first phase, two review authors (V.F.S.F and L.R.D.M) independently and blindly screened the titles and abstracts. We coded the potential studies as "included" for studies that fit in the inclusion criteria, "maybe" for potentially eligible or unclear records, and "excluded" for those not meeting the criteria. To ensure consistency across all reviewers, Cohen's kappa inter-rater reliability score was calculated on a random sample of one hundred studies retrieved from the study pool; this yielded a score of 0.899, indicating excellent agreement. We resolved any conflicts by discussion. Moreover, studies categorized as "maybe" were subjected to further discussion. If it was not possible, we consulted a third review author (B.S.B.L) and reached a consensus. In the second phase, the same two review authors applied the eligibility criteria while reading the full text of the studies that had been previously included. We attempted to resolve any conflicts through discussion. If consensus could not be reached, a third reviewer (B.S.B.L) was consulted, and the impasse was resolved in a meeting.

We planned to document the selection process in sufficient detail to complete the PRISMA flow diagram, following the PRISMA 2021 reporting standards.

Data extraction

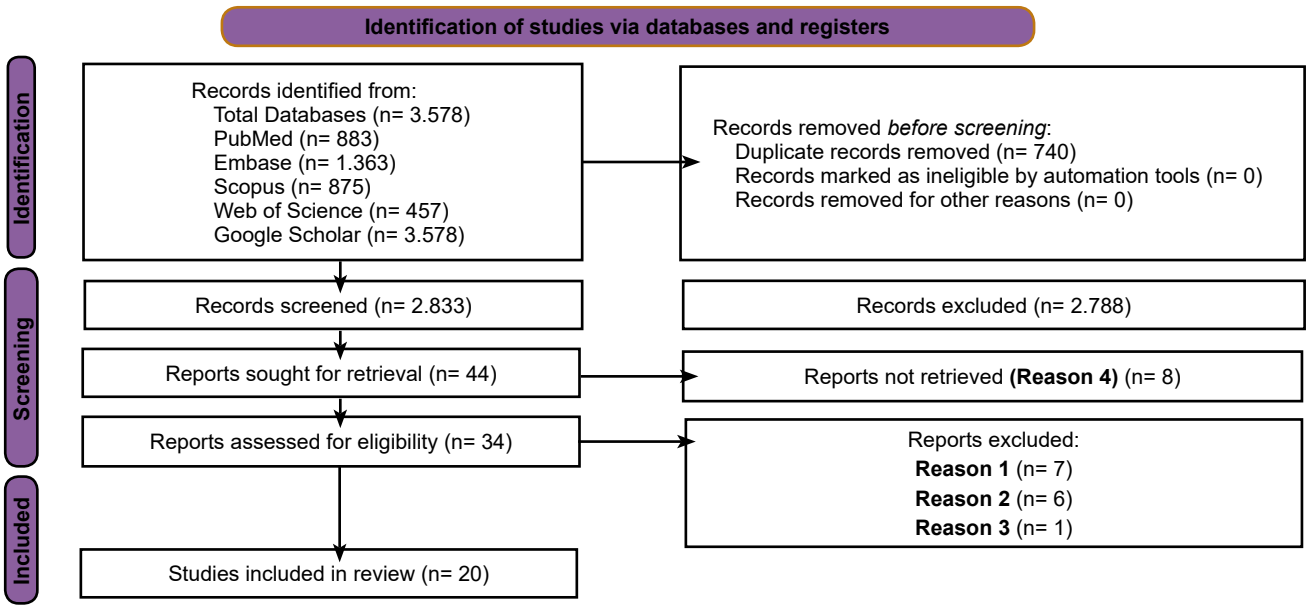
For included studies, an author (L.R.D.M) collected the data and two other reviewers (V.F.S.F and E.G.M) cross-checked the data. We independently extracted relevant information and data from the full-text articles onto a customized data extraction sheet. We extracted the following data from each included study: study identification, study design, date and country of study, sample size, sex, age, diagnostic methods, oral findings, and dentist's approach. Two independent reviewers conducted the selection, and in case of any bias, discussions were held to reach an agreement. If any important data was unclear or missing, we would contact the corresponding authors by e-mail to request it, enabling the retrieval of unpublished data. If no response was received, data that could not be retrieved were marked in the table as missing or not provided.

RESULTS

Selection of sources of evidence

The first search strategy resulted in 3.578 studies (Figure 2). After duplicate removal and considering the inclusion and exclusion criteria, 20 articles were selected.

Figure 2. Flowchart depicting the process of search and selection of included studies.

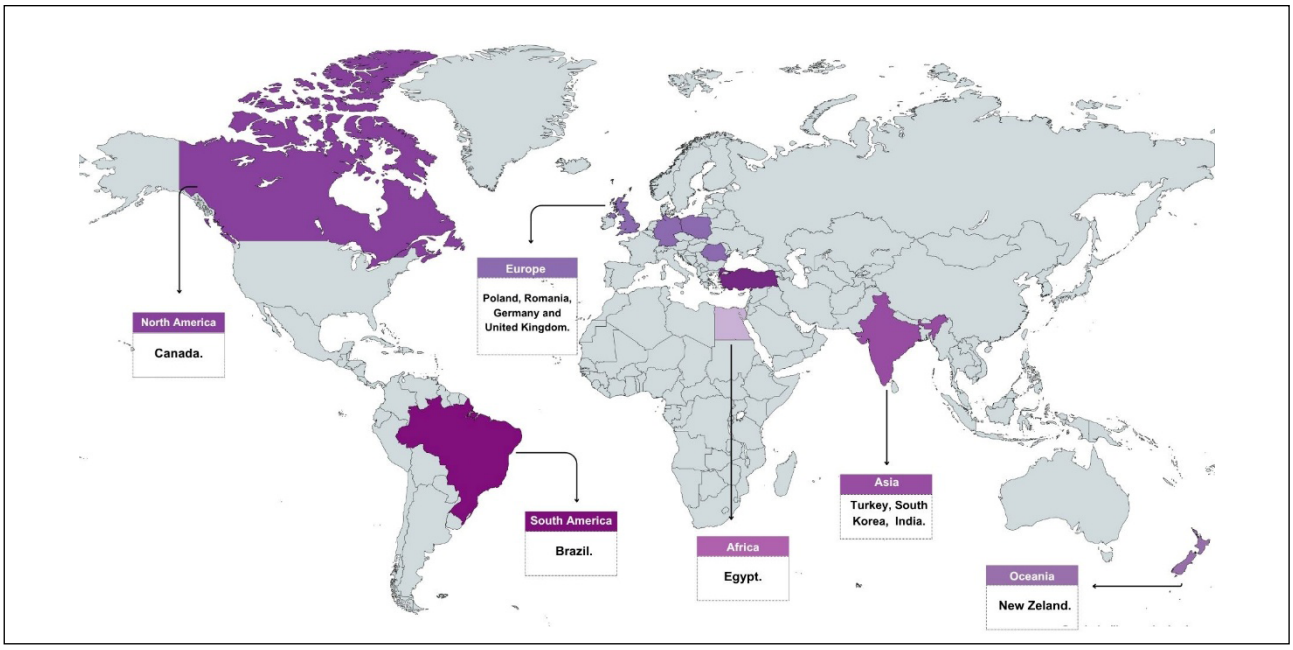


Source: Page et al. [15]
Notes: Reasons for exclusion: Reason 1- Dentist did not play a role in raising the initial clinical suspicion or identifying suggestive oral signs of leukemia; Reason 2 - Not enough data about the dentist approach; Reason 3 - Wrong study design; Reason 4 - Full text not found for full reading.

Bibliometric analysis and characteristics of sources of evidence

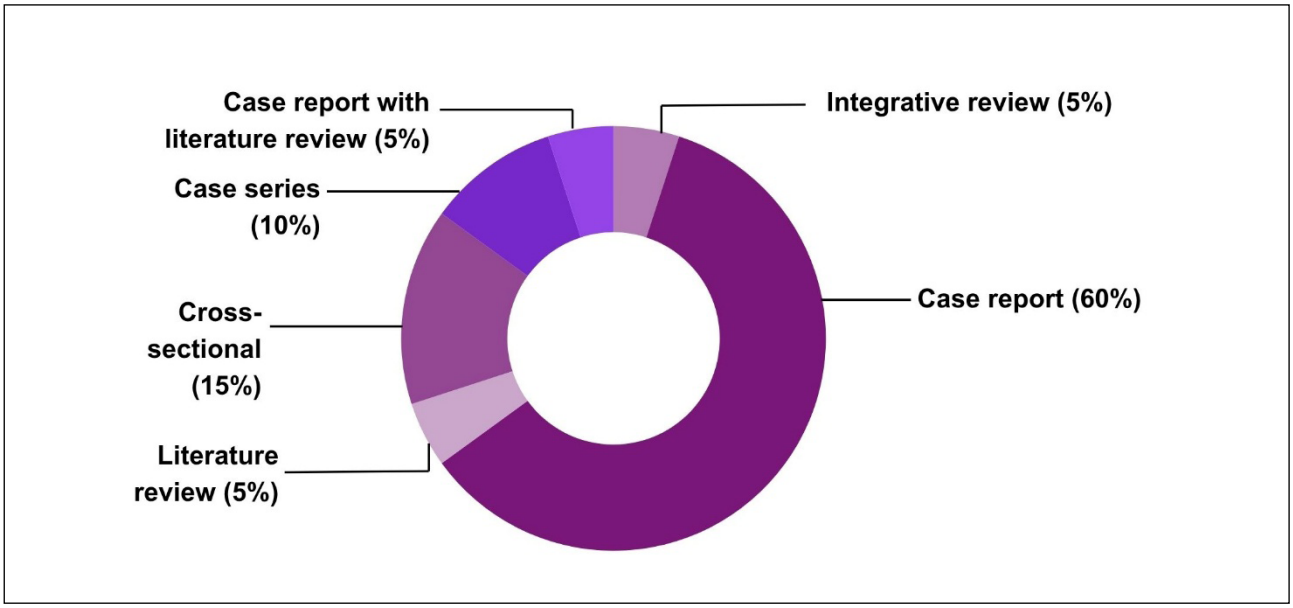
The articles were conducted in 10 countries across 6 continents (Figure 3). Most of the articles were conducted in Asia, being eight articles in India [16- 23], one in Turkey [24] and one in South Korea [25]. Europe accounted for four articles; one in Germany [26], Romania [27], United Kingdom [28] and Poland [29]. South America was represented by three articles in Brazil [30-32]. North America had one contribution, conducted in Canada [33]. Oceania also contributed with one article in New Zealand [34]. Similarly, one article was conducted in Egypt[35], representing, then, Africa. The publication years were 2013 (n=1), 2014 (n=3), 2015 (n=2), 2017 (n=1), 2018 (n=5), 2020 (n=1), 2021 (n=2), 2022 (n=3), 2023 (n=1), and 2025 (n=1). The sample size ranged from 1 to 263 individuals, aged from 6 to 74 years old.

Figure 3A - Bibliometric analysis on studies characteristics. Worldwide distribution of selected studies on the role of the dentist in the early diagnosis of leukemia on the continents of South America, North America, Europe, Oceania, Asia, and Africa (n=20).



Source: Own authors. Figures generated using MapChart.net and canva.com, respectively.

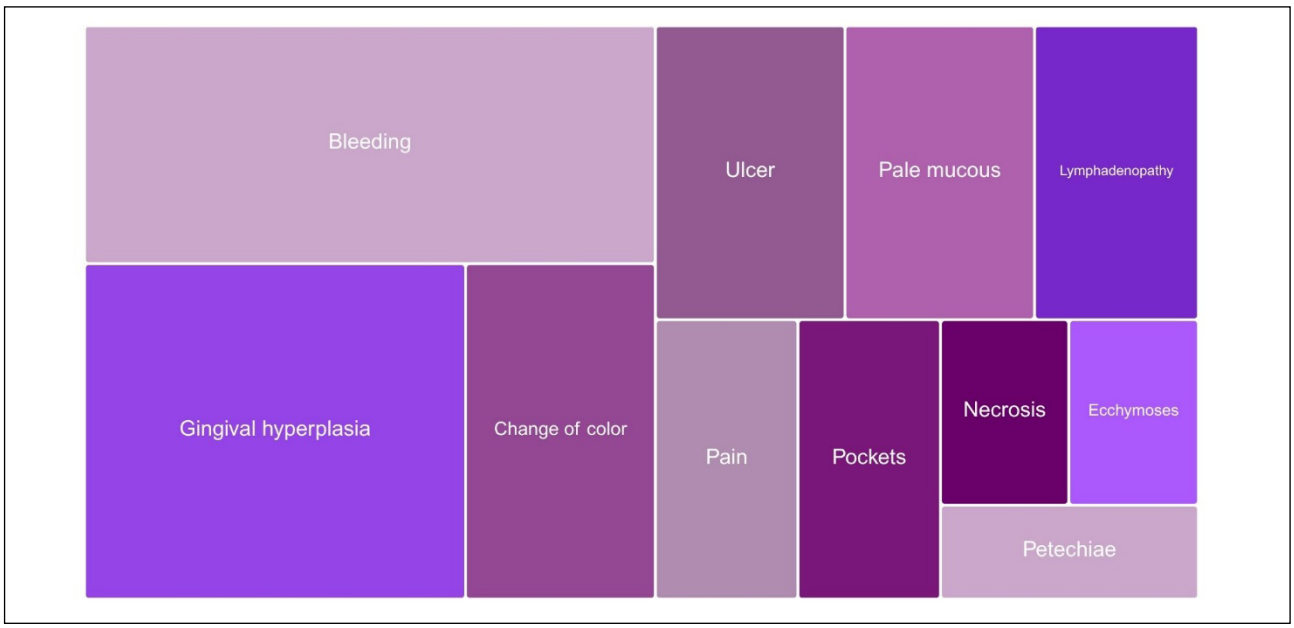
Figure 3B. Bibliometric analysis on studies characteristics. Prevalence of included publications distributed according to the study design (n=20).



Source: Own authors. Figures generated using MapChart.net and canva.com, respectively.

The included studies revealed a range of oral manifestations, with bleeding being the most frequently reported (17 mentions), followed closely by gingival hyperplasia (16 mentions). Changes in gingival color were described in 8 cases, while both pale mucosa and ulcerations were each reported in 7 instances. Lymphadenopathy appeared in 6 reports, and pain and periodontal pockets were noted 5 times each. Less frequent findings included necrosis (3 mentions), ecchymoses (3 mentions), and petechiae (3 mentions), as shown in Figure 4.

Figure 4. Treemap chart showing the citations of the oral signs and symptoms in the included studies.



Source: Own authors. Figure generated with Canva.com.

Results of individuals sources of evidences

A comprehensive description of an individual study characteristics is provided within Table 3. In the Table 4 are consolidated all blood test results along with the laboratory standard.

Table 3. Description of the individual characteristics of the studies.

(continues)

Study Identification	Study design	Date of study/ Country	Sample size (F:M)	Age	Diagnosis methods	Oral findings	Dentist's approach
Quispe *et al.* Hematology, Transfusion and Cell Therapy.	Integrative review.	2022, Brazil.	33 individuals 12 F: 19 M	6-74	Clinical, Oral and radiographic evaluation, and blood count as a complementary test.	In soft issue: ulcer, erosion, spontaneous bleeding, ecchymosis, color change of the bluish or pale mucous and necrosis. In hard tissues: cortical expansion, osteolytic areas teeth mobility and severe vertical bone loss.	The early diagnosis is essential as it allows the patient to seek timely treatment. When oral findings are present, it is easier for the patient to consult a dentist due to the visibility of the mouth. This enables the professional to perform an early diagnosis and provide appropriate referral to an oncologist. If necessary, the dentist can perform an incisional biopsy.

(continues)

Michalak *et al.* Via Médica.	Case report.	2022, Poland.	1 F	52	Oral examination, blood count and orthopantomographic.	Gingival hyperplasia, necrotic lesions of the gingival papillae, severe bleeding and gingival pockets. The radiograph showed horizontal bone loss and a periapical lesion on the tooth 37.	The dentist must evaluate the condition of the oral cavity considering both at the clinical and radiographic implications. Ideally, before starting the oncologic treatment, the oral cavity should be sanitized, which includes endodontic treatment, periodontal care, extract teeth with possible infection focus, assessment of current restorations. Effective collaboration between dentists and hematology specialists plays a crucial role in preparing patients for treatment of the underlying disease.
Mester *et al.* Medical Hypothesis	Literature review	2018, Romania.	-	-	Oral examination.	Gingival bleeding, oral ulcer, gingival hyperplasia, laryngeal pain.	Early recognition by the dentist of oral manifestations of the signs of leukemia essential to ensure immediate referral to a hematologist and appropriate treatment. Before chemotherapy, extraction of non-restorable teeth, gingival debridement, caries treatment, and the use of antibiotics, should be done.
Busjan *et al.* Clin Oral Invest	Cross-sectional.	2017, Germany.	39 individuals 19 M : 20 F	>18	Anamnesis, oral examination, microbiologic analysis.	Gingival hyperplasia, petechiae, mucosal pallor, caries, bacterial, fungal, viral infection.	High caries prevalence and increased periodontal inflammation.
Rosa *et al.* Acta stomatol Croat.	Case report.	2018, Brazil.	1 M	47	Oral and physical examination and blood count	Mucosa pallor due to anemia, gingival hyperplasia, spontaneous gingival bleeding and epistaxis, hematoma in the gingiva, patient was weak, pale, febrile and presenting ecchymoses in the left ventral surface of his tongue.	According to the findings, the diagnosis was inconclusive. Because of that, the blood count was indicated, revealed anemia, severe thrombocytopenia and leukocytosis with blasts pre-dominance (75%). The patient died 3 days after admission to the hospital.
Lim; Kim. Journal of Periodontal & Implant Science	Case series.	2014, South Korea.	2 F	49 and 59	Oral examination, radiographic evaluation, and blood count.	The patient presents with generalized gingival hyperplasia. In the posterior maxillary area, there was diffuse enlargement extending to the alveolar mucosa. Radiographic examination revealed generalized horizontal bone loss, generalized periodontal abscess. There are probing depths ranging from 6 to 9 mm, along with bleeding on probing.	Patients with hematological malignancies, including leukemia, should undergo clinical and radiographic examination to assess the presence of oral manifestations of the malignancy, periodontal disease, and osteolytic lesions. Furthermore, strict oral hygiene instructions and the elimination of potential sources of oral infection should precede any cancer treatment.

(continues)

Aurora; Arasaretnam; Hobkirk. Bulletin of the National research Centre.	Case report.	2022, United Kingdom.	1F	34.	Clinical oral examination, imaging examination, blood count.	Bilateral posterior pain in the mandible and gingival hyperplasia with continuous bleeding.	The pre-admission oral biopsy, obtained from the operculum, revealed mucosal infiltration by immature myeloid cells.
Watson *et al.* JADA.	Cross-sectional.	2018, Canada.	263.	Not reported.	Clinical oral examination, dental radiographs and blood counts when suspected.	Oral petechiae, oral bleeding, acute oral infection, non-odontogenic infections, gingival hyperplasia.	When the signs and symptoms match with leukemia, a blood count was requested. When diagnosed, before start the chemotherapy and transfusions, the dentist should eliminate infection and address acute or potentially problems.
Guan; Firth. Australian Dental Journal.	Case report.	2015, New Zealand.	1M.	49.	Blood count, clinical oral examination and panoramic and periapical radiographs.	Gingival bleeding, gingival hyperplasia, oral mucosal pallor, periodontal pocket.	When the dentist faces a pallor mucosa, petechial hemorrhages, spontaneous bleeding, gingival hyperplasia and oral ulcers, they should request haematological tests, such as complete blood count.
Misirlioglu; Adisen; Yilmaz. Nigerian Journal of Clinical Practice.	Case report.	2015, Turkey.	1M.	30.	Blood count, clinical oral examination and radiographs.	Generalized gingival enlargement involving the buccal, palatal, and lingual regions, covering the crowns of the teeth. The gingiva was hemorrhagic, swollen, ulcerative, fragile, painful, and bled easily. The gingival color ranged from reddish to purplish. The hard and soft palatal mucosa exhibited a large area of ecchymosis. Additionally, the patient presented halitosis.	The differential diagnosis of acute leukemia and HIV infection were considered for this patient. She was urgent referred to the Hematology Department at Faculty of Medicine for blood count. There, further tests were performed, such as peripheral blood smear, bone marrow biopsy, flow cytometry and HIV infection.
Gowda *et al.* Journal of Indian Society of Periodontology.	Case report with literature review.	2013, India.	1F.	28.	Extra-oral and intra-oral examination and laboratory exams.	Swelling accompanied by pain and bleeding. On extraoral examination, mild bilateral submandibular lymphadenopathy with slight tenderness was observed. In the intraoral examination, papillary and marginal gingival enlargement was noted, along with gingival inflammation accompanied by moderate plaque deposits, calculus, and bleeding on probing. A few days later, upon the	A treatment plan was initially formulated, including prophylaxis and the use of a 2% chlorhexidine mouthwash, as the condition was suspected to be pregnancy-associated gingival enlargement. However, upon the patient's return, laboratory tests were requested, and she was asked whether she had undergone systemic treatment or chemotherapy. Following the analyses, the patient was referred to an obstetrician and an oncologist.

(continues)

						patient's return, she presented with gingival pain, severe generalized gingival hyperplasia with localized necrosis and disintegration involving the interdental papilla, and abnormal color changes of the interdental papilla, which appeared more erythematous and soft.	
Ratre *et al.* Journal of Indian Society Periodontology.	Case report.	2018, India.	1M.	51.	Laboratory exams and clinical oral examination.	On physical examination, the patient appeared pale, anemic, febrile, and cachectic, with palpable and tender submandibular lymph nodes. Intraoral examination showed generalized gingival enlargement in the buccal, palatal, and lingual regions. The gingiva was enlarged, ulcerated, painful, and hemorrhagic, with spontaneous bleeding. The gingival coloration ranged from red to bluish-red, suggesting cyanosis. Large areas of ecchymosis were also observed on the hard palate. Additionally, the patient had halitosis and poor oral hygiene.	Based on the signs of gingival enlargement, ulcers, bleeding, palatal ecchymosis, and systemic symptoms, leukemia was suspected. A complete blood count revealed elevated leukocyte levels and decreased hemoglobin and platelet counts. The patient was referred to an oncology hospital, where the diagnosis of acute myeloblastic leukemia was confirmed through peripheral blood smear and bone marrow biopsy.
Babu *et al.* Journal of Indian Society Periodontology.	Case report.	2014, India.	1F.	43.	Laboratory exams and clinical oral examination.	The extraoral examination revealed bilateral submandibular and deep cervical lymphadenopathy, with firm and tender lymph nodes. Intraorally, generalized gingival enlargement was observed in the buccal, lingual, and palatal regions, with swollen, inflamed, non-stippled, firm, edematous, painful gingiva that bled upon light touch. Although significant plaque and calculus were present, they did not account for the severity of the gingival enlargement. A complete blood count revealed elevated leukocyte levels,	The diagnosis of Acute Myeloid Leukemia is confirmed. The patient was provided with oral hygiene instructions, including the use of a soft-bristled toothbrush and a 0.2% chlorhexidine mouthwash three times a day. Scaling and root planning were postponed due to the low platelet count. The patient was referred to an oncology center, where a bone marrow biopsy confirmed the diagnosis of Acute Myeloid Leukemia, and chemotherapy was initiated.

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						reduced erythrocyte counts with decreased hemoglobin levels, and a low platelet count.	
Sharan *et al.* Journal of Indian Society Periodontology.	Case report.	2023, India.	1F.	11.	Laboratory exams and clinical oral examination.	The clinical examination revealed pale, bulbous gingiva with loss of stippling and focal hemorrhagic areas. The submandibular and submental lymph nodes were enlarged and tender upon palpation, with no involvement of cervical lymph nodes. The patient was taking antibiotics and analgesics prescribed by a local health center.	Undergo a complete blood count, flow cytometry and peripheral blood smear. She was referred to the oncologist to start the chemotherapy.
Arora; Arora; Arora. Indian Journal of Dermatology.	Case series.	2020, India.	Case 1: 1F; Case 2: 1M.	Case 1: 18; Case 2: 25.	Laboratory exams and clinical oral examination.	Case 1: The intraoral examination revealed irregular ulcers on the tip of the tongue, buccal mucosa, and gingiva, with bluish-red hemorrhagic borders and mild interdental gingival enlargement in the anterior teeth. Case 2: The patient presented with extreme pallor, enlarged submandibular lymph nodes, and generalized, spongy, non-stippled gingiva with hemorrhagic areas in the anterior region.	Differential diagnoses included aphthous stomatitis and HIV-associated oral ulcers. Hematological tests showed anemia, leukocytosis, and thrombocytopenia. The peripheral blood smear revealed atypical myeloid blast cells, suggesting Acute Myeloid Leukemia.
Fernandes *et al.* Special Care Dentistry.	Case report.	2018, Brazil.	1F.	10.	Extra-oral and intra-oral examination, imaging examination and incisional biopsy.	Gingival hyperplasia, gingival color ranged from normal coloration to dark purple. Panoramic X-ray and periapical radiographs of the jaw showed no evidence of periodontal resorption. Incisional biopsy revealed infiltration of the gingival tissue with myeloid cells.	Performed a complete clinical examination. Requested biopsy. When confirmed the suspicion of leukemia, the patient was referred to the hematologist, and then initiated chemotherapy treatment.
Ghouraba et al. Nature portfolio.	Cross-sectional.	2025, Egypt.	Leukemic group: 13F: 10 M; Control group: 12F: 11 M.	6-10.	Clinical oral examination, and imaging examination.	Gingival bleeding, oral ulcerations, gingival masses and dental mobility. Panoramic X-ray and computed tomography showed bone osteolysis, moth-eating appearance, and abnormal tooth chronology.	Detailed clinical evaluation and imaging exams. Use of dental chronology as a complementary indicator. Suggest the dentist's role in early diagnosis.

(conclusion)

						65% of the leukemic group showed grade III mobility related to permanent lower first molars while eight cases (35%) showed grade II mobility that was used as markers for tooth affection.	
Bhambal et al. Journal of Indian Society Periodontology.	Case report.	2021, India.	1M.	50.	Extra-oral and intra-oral examination and blood count.	Extra-oral examination revealed pallor on the fingers and palms, but no lymphadenopathy was elicited. Intra-oral examination showed generalized gingival hyperplasia, color appeared pale pink to red to purple, presence of pseudopockets, and gingival bleeding. Complete blood picture showed raised lymphocytic count and peripheral smear showed myeloblasts.	The dentist performed a thorough clinical evaluation, noting generalized gingival enlargement without evident local irritants or relevant systemic history. A complete blood count was requested. Based on the findings, the patient was referred to an oncology center with a final diagnosis of acute myeloid leukemia
Sukhdeo et al. International Journal of Scientific Study.	Case report.	2014, India.	1F.	15.	Intra-oral examination and blood count.	Generalized diffuse enlargement of maxillary and mandibular gingiva, gingival color appeared reddish blue with loss of stippling, oral ulcer, and palatal petechiae. Blood count showed a decrease in red blood cells with lowered hematocrit and haemoglobin levels and a low platelet count indicative of leukocytosis, anemia and thrombocytopenia.	A diagnostic hypothesis of a hematologic disorder was made despite the absence of significant prior medical history. Invasive procedures such as scaling or probing were avoided. The patient was immediately referred for medical investigation. Dental treatment included: prescription of 0.2% chlorhexidine for chemical plaque control and guidance on non-traumatic oral hygiene. Scaling and root planing were postponed due to severe thrombocytopenia. Referral and outcome: the patient was referred to a specialized pediatric hospital.
Telagi; Ahmed. Journal of Oral and Maxillofacial Pathology.	Case report.	2021, India.	1M.	53.	Extra-oral and intra-oral examination and blood count.	On extraoral examination right submandibular lymphnodes were palpable, tender, and movable. Intra-oral examination showed painful ulcers.	A complete blood count was requested due to suspicion of a hematologic disease. The patient was referred to a hematologist for confirmation of chronic myeloid leukemia

Source: Own authors.

Table 4. Blood test results along with the laboratory standard documented in the case reports.

(continues)

Study Identification	Blood count results	Laboratory standard
Aurora; Arasaretnam; Hobkirk. Bulletin of the National research Centre.	Haemoglobin: 41 g/L; White cell count: 9.7 10^9/L; Neutrophil count: 0.3 10^9/L; Platelet count: 18 10^9/L;	Haemoglobin: 115-165 g/L; White cell count: 4-10 10^9/L; Neutrophil count: 2-7 10^9/L; Platelet count: 150-410 10^9/L.
Michalak *et al.* Hematology in Clinical Practice.	White blood cells: 1.8 G/L; Lymphocytes: 1.2 G/L; Monocytes: 0.49 G/L; Neutrophils: 0.1 G/L; Platelets: 31 G/L.	White blood cells: 4.0-10.0G/L; Lymphocytes: 0.8-4.5G/L; Monocytes: 0-1.2G/L; Neutrophils: 1.6-6.5 G/L; Platelets: 150-400 G/L.
Rosa *et al.* Acta stomatol Croat.	Haemoglobin: 10.40 G/dl; Hematocrit: 30.10%; Leukocytes: 67.200/Mm; Lymphocytes: 9.408/Mm; Monocytes: 3.360/Mm; Platelets: 22.000/Mm.	Haemoglobin: 12.8-17.8 G/dl; Hematocrit: 38.8-54%; Leukocytes: 3.500-11.000/Mm; Lymphocytes: 900-3.900/Mm; Monocytes: 100-700/Mm; Platelets: 150.000-450.000/Mm.
Guan; Firth. Australian Dental Journal.	Haemoglobin: 63 g/L; Neutrophils: 0.0 10^9/L; Lymphocytes: 0.4 10^9/L; Monocytes: 0.1 10^9/L; Platelets: 23 10^9/L.	Haemoglobin: 130-175 g/L; Neutrophils: 1.9-7.5 10^9/L; Lymphocytes: 1-4 10^9/L; Monocytes: 0.2-1.0 10^9/L; Platelets: 150-400 10^9/L.
Aurora; Arasaretnam; Hobkirk. Bulletin of the National research Centre.	Haemoglobin: 41 g/L; White cell count: 9.7 10^9/L; Neutrophil count: 0.3 10^9/L; Platelet count: 18 10^9/L;	Haemoglobin: 115-165 g/L; White cell count: 4-10 10^9/L; Neutrophil count: 2-7 10^9/L; Platelet count: 150-410 10^9/L.
Michalak *et al.* Hematology in Clinical Practice.	White blood cells: 1.8 G/L; Lymphocytes: 1.2 G/L; Monocytes: 0.49 G/L; Neutrophils: 0.1 G/L; Platelets: 31 G/L.	White blood cells: 4.0-10.0G/L; Lymphocytes: 0.8-4.5G/L; Monocytes: 0-1.2G/L; Neutrophils: 1.6-6.5 G/L; Platelets: 150-400 G/L.
Rosa *et al.* Acta stomatol Croat.	Haemoglobin: 10.40 G/dl; Hematocrit: 30.10%; Leukocytes: 67.200/Mm; Lymphocytes: 9.408/Mm; Monocytes: 3.360/Mm; Platelets: 22.000/Mm.	Haemoglobin: 12.8-17.8 G/dl; Hematocrit: 38.8-54%; Leukocytes: 3.500-11.000/Mm; Lymphocytes: 900-3.900/Mm; Monocytes: 100-700/Mm; Platelets: 150.000-450.000/Mm.
Guan; Firth. Australian Dental Journal.	Haemoglobin: 63 g/L; Neutrophils: 0.0 10^9/L; Lymphocytes: 0.4 10^9/L; Monocytes: 0.1 10^9/L; Platelets: 23 10^9/L.	Haemoglobin: 130-175 g/L; Neutrophils: 1.9-7.5 10^9/L; Lymphocytes: 1-4 10^9/L; Monocytes: 0.2-1.0 10^9/L; Platelets: 150-400 10^9/L.
Gowda *et al.* Journal of Indian Society of Periodontology.	Haemoglobin: 8.4 G/dl; Hematocrit: 25.1%; Red blood count: 2.8 10^6/cmm^3; White blood cells: 48.400/cmm^3 Neutrophils: 6%; Platelets: 0.46/cmm^3.	Haemoglobin: 14-18 G/dl; Hematocrit: 42-52%; Red blood count: 4.6-6.2 10^6/cmm^3; White blood cells: 4.800-10.500/cmm^3 Neutrophils: 50-70%; Platelets: 1.4-4.4/cmm^3.
Ratre *et al.* Journal of Indian Society Periodontology.	Haemoglobin: 7.0 G/dl; Erythrocytes: 2.68 M/ µL; Platelets: 30 10^3/ µL.	Haemoglobin: 12.0-16.0 G/dl; Erythrocytes: 3.50-5.50 M/ µL; Platelets: 150-450 10^3/ µL.
Babu *et al.* Journal of Indian Society Periodontology.	Haemoglobin: 5.1 gm% Erythrocytes: 135 mm/h Platelets: 11.000; White blood cells: 1,97600; Neutrophils: 1%.	Haemoglobin: 11.5-14.5 gm%. Erythrocytes: 2-12; Platelets: 150.000-400.000; White blood cells: 4.000-10.000 Neutrophils: 45-65.

(conclusion)

Sharan *et al.* Journal of Indian Society Periodontology.	Haemoglobin: 8.5 G/dl; Red blood cells: 2.76 million/ mm^3; Hematocrit: 26.7%; White blood cells: 59.8 $10^3/mm^3$; Neutrophils: 2%; Lymphocytes: 17%; Monocytes: 5%; Platelets: 130 $10^3/mm^3$.	Haemoglobin: 11.5-15.5 G/gl; Red blood cells: 4-5.2 million/ mm^3; Hematocrit: 35-45%; White blood cells: 5-13 $10^3/mm^3$; Neutrophils: 22-90%; Lymphocytes: 11-55%; Monocytes: 2-11%; Platelets: 170-450 $10^3/mm^3$.
Sukhdeo et al. International Journal of Scientific Study.	Total leukocyte count: 107.69 $10^3/mm^3$; Erythrocyte count: 1.67 $10^6/mm^3$; Haemoglobin: 7.3 G/dl; Hematocrit: 17.74%; Platelet count: 0.16 $10^3/mm^3$.	Total leukocyte count: 4.5-11.0 $10^3/mm^3$; Erythrocyte count: 3.8-4.8 $10^6/mm^3$; Haemoglobin: 12-15 G/dl; Hematocrit: 36-46%; Platelet count: 1.5-4.5 $10^3/mm^3$.

Source: Own authors.

DISCUSSION

This scoping review aimed to explore the existing understanding of the dentist' role in the diagnosis of leukemia. Prior to conducting this scoping review, other literature reviews[16, 27, 31, 36] had been published, and their results regarding the approach and the oral manifestations aligned with the findings of the current review. Despite the availability of these literature reviews, we have chosen to pursue a scoping review to not only offer a more comprehensive perspective on the subject, but also to conduct a more rigorous review methodology. Our goal was to review the existing literature, analyze the research methodologies utilized in the oral medicine, identify knowledge gaps, and suggest directions for future investigation.

Regarding oral manifestations, the studies included in this review identified spontaneous bleeding, gingival hyperplasia, changes in soft tissue coloration, and ulcers as the most frequent findings. Although commonly observed in clinical practice, these signs warrant special attention when they appear excessively and are not associated with local factors. Bleeding and gingival hyperplasia, for instance, are typically linked to the presence of biofilm. However, when they occur in patients with good oral hygiene or do not respond to conventional periodontal treatments, clinical suspicion of systemic conditions should be raised. Similarly, such oral manifestations may arise in the oral cavity as a result of the use of certain medications. In these cases, it is essential that the dentist does not interpret these alterations as isolated findings, but rather as part of a broader systemic clinical picture that may potentially indicate hematologic malignancies.

Clinically, the patient presents with mucosal ulcerations due to the body's reduced ability to combat the oral microbiota. These lesions, commonly found on the gingival mucosa, may appear deep, perforated, and with a grayish-white necrotic base. On the other hand, the infiltration of leukemic cells into the oral soft tissues causes a diffuse and spongy swelling, which may become painful when ulcerated.[37] This clinical presentation is supported by the studies included in this review, which reported the presence of ulcers, pain, and necrosis in soft tissues, mentioned 7, 5, and 3 times, respectively.

Understanding these signs and symptoms, as well as the clinical reasoning behind them, is essential for an early diagnostic hypothesis, helping to avoid errors and delays in referral. In this context, a focused approach is recommended, including a thorough and well-structured medical history, with attention to systemic symptoms. In hematological conditions such as leukemia, there is a reduction in the production of red blood cells, resulting in decreased oxygen transport to tissues. As a consequence, the patient may report fatigue, low energy, loss of appetite, weight loss, and dysphagia.[16,36,37] Furthermore, it is crucial to perform both extraoral and intraoral examinations, ensuring that soft and hard tissues are carefully assessed, since these patients may present with enlarged submandibular and submental lymph nodes.[16-19,23] When necessary, complementary tests such as blood counts and imaging exams should be requested.

With the exception of Mester et al.[27], Fernandes et al.[32], and Ghouraba et al.[35], all studies used laboratory tests as a complement to the anamnesis. Based on the complete blood count results presented in this scoping review, all authors reported low platelet counts, elevated leukocyte levels, and reduced red blood cell counts with decreased hemoglobin levels, indicating thrombocytopenia, leukocytosis, and anemia. According to Neville et al.[37] , spontaneous bleeding, as well as the presence of ecchymoses and petechiae on the soft and hard

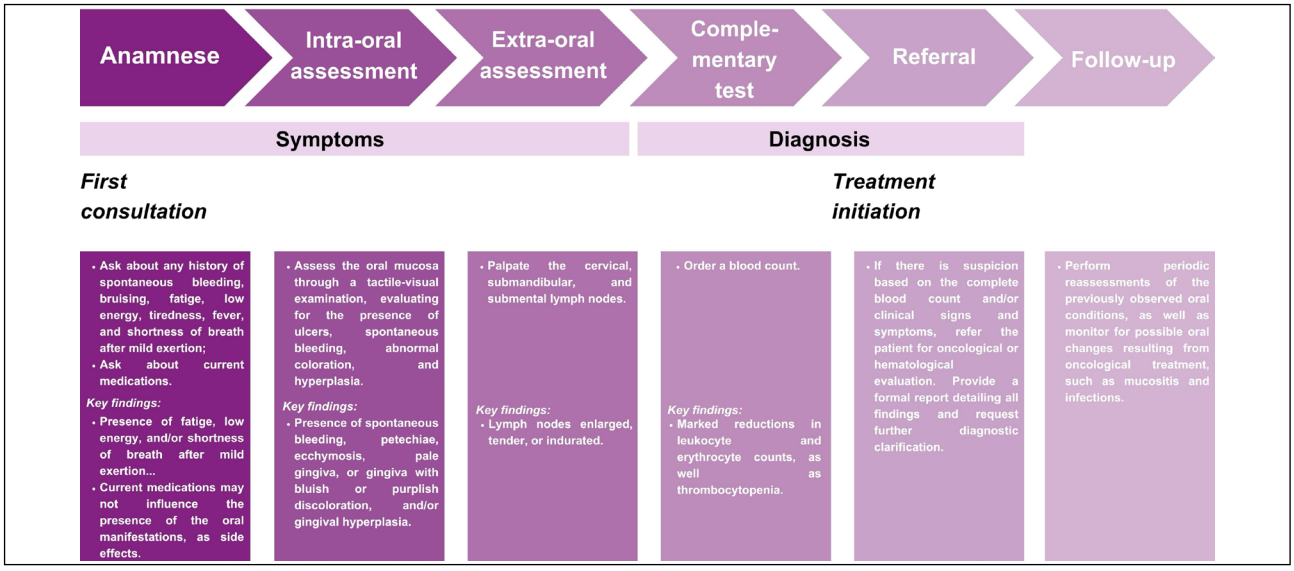
palate, are frequently associated with severe thrombocytopenia. This condition results from the replacement of normal bone marrow by immature leukemic cells, impairing platelet production, especially when levels fall below 10,000 to 20,000/mm³. This observation is confirmed by all studies included in the present review, which identified a correlation between blood count findings and these oral manifestations.

The use of imaging exams can be an alternative for investigating signs at the bone level. Accordingly, some authors used panoramic or periapical radiographs and identified cortical expansion, osteolytic areas, and severe vertical or horizontal bone loss. [25, 29, 31] In patients with certain hematological malignancies, such as leukemia, exacerbated gingival inflammation is common and, if left untreated, may progress to periodontitis.[38] This likely explains why patients with leukemia frequently present the aforementioned signs.

Interestingly, some studies reported that dentists also requested anti-HIV tests as part of the process of ruling out differential diagnoses[18,24], and in some cases, incisional biopsies revealed infiltration of immature myeloid cells[28,31,37], further reinforcing the dentist's role in the clinical suspicion of systemic diseases. Despite these contributions, a report described by Rosa et al.[30] highlighted the tragic consequences of delayed referral, as the patient died three days after being referred to the oncology service. These findings underscore the urgency of timely clinical suspicion and immediate action.

Moreover, when the clinical suspicion is supported by findings from the anamnesis, intraoral and extraoral evaluations, and complementary tests, the patient must be immediately referred to an oncologist for confirmation of the diagnostic hypothesis. In the meantime, the patient should undergo oral environment preparation, aiming to eliminate infection foci, extract non-restorable teeth, treat carious lesions, and manage acute or potential oral health issues.[25,27,29,33] Once this is completed, the multidisciplinary team can ensure a more streamlined path to treatment. A detailed overview of the dentist's role in early diagnosis is presented in Figure 5.

Figure 5. Summary of the procedures that should be conducted by the dentist.



Source: Own authors. Figure generated with Canva.com.

Given the above, a critical issue identified relates to the gap between scientific evidence and clinical practice. Many dentists do not feel prepared to formulate diagnostic hypotheses for hematologic neoplasms, request laboratory tests, nor recognize the most common oral manifestations, which are sometimes overlooked in clinical practice. This problem stems from limited academic training in stomatology, lack of clinical protocols, and low integration within multidisciplinary teams. In this context, the findings of the present review reaffirm the need for institutional support, continuing education, and foundational knowledge in stomatology, so that dentists can act with confidence and responsibility when managing similar cases.

The present study has some limitations. Although it is a scoping review on a relatively recent topic in scientific research, the authors acknowledge the limited number of included studies. Furthermore, it is not possible to provide precise data on the prevalence of oral

manifestations in these patients, despite the clear identification of common symptoms. Moreover, there was a predominance of case reports and case series, which offer lower scientific evidence, small sample sizes, and limited generalizability. Methodological biases were observed, such as selection bias, since the samples are not representative of the global population, and recall bias, as much clinical data depend on the memory and subjective reports of the involved professionals. For these reasons, further studies with representative samples and robust methods are necessary.

This review, despite its limitations, represents the first synthesis article to address oral manifestations in patients with leukemia and the role of the dentist in diagnosis and referral to oncology. The strengths of the study include a rigorous literature search across multiple databases, including gray literature, the transparent and meticulous application of scoping review methodology, and well-defined inclusion criteria that allowed the integration of various study types. Furthermore, the clinical relevance of this work lies in the practical guidance provided to dentists in performing differential diagnoses of leukemia.

CONCLUSION

This scoping review demonstrates how the dentist can play a crucial paper in the early diagnosis of leukemia. By identifying the signs and symptoms presented in this study, it is essential to request complementary tests to assist in the diagnosis and promote an intervention with higher chances of a cure.

SUPPLEMENTARY INFORMATION

The online version contains supplementary material available at https://osf.io/zpr7k/

AUTHOR CONTRIBUTION

Valder Ferreira da Silva Filho: Study Conception; Methodology; Data Analysis; Data Curation; Writing- Draft Preparation. Marina Rocha Guerra: Study Conception; Data Analysis; Writing- Draft Preparation. Letícia Rocha Dias da Motta: Study Conception; Methodology; Data Analysis; Data Curation. Heloisa Pelanda, César Henrique Alves and Clarice Luiza de Paula Ribeiro: Data Analysis. Érica Guilhen Mario and Bruno Sérgio Bahia Lopes: Supervision; Visualization; Writing – Review and Editing. All authors read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest to declare.

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A importância do cirurgião-dentista no diagnóstico precoce da leucemia: uma revisão de escopo

Objetivo: este estudo visa evidenciar como os dentistas podem contribuir para o diagnóstico precoce da leucemia por meio do reconhecimento das manifestações orais e do encaminhamento oportuno.

Métodos: realizou-se uma revisão de escopo da literatura que analisou o papel do dentista no diagnóstico precoce da leucemia, bem como suas manifestações na cavidade oral. Seguiu-se as diretrizes PRISMA-ScR. As buscas eletrônicas foram realizadas no PubMed, Embase, Web of Science, Scopus e Google Acadêmico, como fonte de literatura cinzenta.

Resultados: de um total de 3.578 artigos potencialmente elegíveis, 34 foram selecionados para avaliação metodológica do texto completo e 20 foram incluídos na revisão de escopo. As manifestações orais mais comuns sugestivas de leucemia são: úlceras, sangramento intenso, hiperplasia gengival, necrose de papilas gengivais, petéquias e alteração da cor da mucosa.

Conclusão: o cirurgião-dentista desempenha um papel crucial no diagnóstico precoce da leucemia. Ao se deparar com as manifestações orais, sinais e sintomas sistêmicos apresentados nesta revisão de escopo, é essencial solicitar prontamente exames complementares para auxiliar no diagnóstico preciso e na intervenção oportuna.

Descritores: leucemia; manifestações bucais; odontólogos.