ORIGINAL ARTICLE

# EVALUATION OF THE ORAL HEALTH OF CHILDREN AND ADOLESCENTS WITH LEUKEMIA TREATED AT HEMORIO

## *AVALIAÇÃO DA SAÚDE BUCAL DE CRIANÇAS E ADOLESCENTES COM LEUCEMIA ATENDIDAS NO HEMORIO*

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## ABSTRACT

This study aimed to evaluate the oral health of child and adolescent participants diagnosed with leukemia, assisted by dentistry. The research was configured as cross-sectional, descriptive and observational. All children and adolescents enrolled in the hematological reference center, aged 3 to 18 years, diagnosed with leukemia, treated by the institution, between June 2022 and January 2023 were included. Sociodemographic, medical, dental and laboratory data were collected; followed by a clinical dental evaluation and photographic recording. To assess the prevalence of caries, the index of decayed, missing, filled teeth per tooth and the index of decayed primary teeth, indicated for extraction and filling, were used. The evaluation of oral manifestations was carried out according to the World Health Organization protocol. The research included 25 participants, 14 male and 11 female and the average age was 10.12 years (SD = 4.8). Acute lymphoblastic leukemia was the most prevalent (80%). Regarding the caries index, the majority of participants had zero (60%) and oral side effects were diagnosed in 60% of them, the most frequent being: change in taste (24%), mucositis (16%) and xerostomia (12%). Participants also had a high incidence of oral manifestations, unsatisfactory oral hygiene, but a low rate of caries. Furthermore, it is important for dental surgeons to know the oral manifestations most commonly found in children with leukemia, the need for quality oral hygiene, as well as the oral health condition as a whole, seeking to ensure that the mouth is not a source of infection, which harms the general health condition and cancer treatment.

**Keywords:** Leukemia, Leukemia Lymphoid, Medical Oncology, Oral Manifestations, Dental Caries, Pediatric Dentistry.

## RESUMO

Esta pesquisa transversal, descritiva e observacional objetivou avaliar a saúde bucal dos participantes infantojuvenis diagnosticados com leucemia, assistidos pela odontologia. Foram incluídas todas as crianças e adolescentes de 3 a 18 anos matriculadas no centro de referência hematológico e diagnosticados com leucemia, atendidos pela instituição, entre junho/2022 e janeiro/2023. Foram coletados os dados sociodemográficos, médicos, odontológicos e laboratoriais, seguidos de uma avaliação clínica odontológica e registro fotográfico. Para avaliação da prevalência de cárie utilizou-se o índice de dentes cariados, perdidos, obturados, por dente e o índice de dentes decíduos cariados, indicado a extração e obturado. A avaliação das manifestações orais foi realizada conforme protocolo da Organização Mundial de Saúde. Compuseram a pesquisa 25 participantes, 14 masculinos e 11 femininos, a média de idade foi de 10,12 anos (d.p. = 4,8). A leucemia linfoide aguda foi a mais prevalente (80%), a maioria dos participantes apresentou índice de cárie zero (60%), as manifestações orais foram diagnosticadas em 60% deles, sendo as mais frequentes: alteração de paladar (24%), mucosite (16%) e xerostomia (12%). Os participantes também apresentaram alta incidência de manifestações orais, condição de higiene bucal insatisfatória, porém baixo índice de cárie. Outrossim, observa-se a importância de os cirurgiões dentistas conhecerem as manifestações orais mais encontradas em crianças com leucemia, a necessidade da higiene bucal de qualidade, bem como a condição de saúde bucal total, buscando garantir que a boca não seja uma fonte de infecção que prejudique a condição de saúde geral e o tratamento oncológico.

**Palavras-chave:** Leucemia, Leucemia linfoide, Oncologia, Manifestações bucais, Cárie dentária, Odontopediatria.

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**How to cite this article:** Félix ECGC, Ferraro CTL, Pinheiro RS. Evaluation of the oral health of children and adolescents with leukemia treated at Hemorio. Nav Dent J. 51(1): 04-10.

Received: 19/12/2024
Accepted: 05/04/2024

## INTRODUCTION

Blood cells originate in the bone marrow, produced by hematopoietic stem cells, and the condition of leukemia is determined when these immature cells undergo disordered proliferation. According to the National Cancer Institute of Brazil (INCA), leukemia is a malignant disease of generally unknown origin and one of the main diseases affecting hematological patients. According to the institute, more than 11,000 cases will be diagnosed in Brazil between 2023 and 2025, with the most frequent tumors being in children and adolescents, affecting the central nervous system and lymph nodes (1,2,3,4,5).

Leukemias can be classified into 12 types, combining several classifications, such as based on speed (acute and chronic); based on the precursor cells affected (lymphoid or myeloid); those affecting lymphoid cells (lymphoid, lymphocytic or lymphoblastic); and those affecting myeloid cells (myeloid or myeloblastic). The four most common types of leukemia are chronic lymphoid leukemia (CLL), chronic myeloid leukemia (CML), acute lymphoid leukemia (ALL) and acute myeloid leukemia (AML), with ALL being the most common category in children under 15 years old, while CLL and AML have a higher incidence in older people (3).

Treatment depends on the type of leukemia, with the aim of destroying the leukemia cells to ensure the functioning of the bone marrow and re-establish the production of normal cells. Possible treatments include chemotherapy, bone marrow transplantation, target therapy, immunotherapy and the use of monoclonal antibodies, while the local treatments of surgery and radiotherapy are used infrequently (3).

The appearance of oral manifestations can occur in the initial phase of leukemia due to immunosuppression, or because of treatment, since the dose and type of medication influence the worsening and intensity of these manifestations (6). Specifically, the oral manifestations linked directly to the disease that most affect children with leukemia are a depapillated and ulcerated tongue, mucosal pallor, gingival hypertrophy, and gingival bleeding; while those resulting from treatment include dental caries, mucositis, xerostomia, and ulcerations, in addition to opportunistic infections such as candidiasis and herpes (7).

As the oral health can interfere with systemic health condition, especially in immunocompromised patients undergoing chemotherapy treatment, this study proposed to evaluate the oral health of pediatric and adolescent patients diagnosed with leukemia who receive dental care at a hematology referral center in Rio de Janeiro.

## METHODOLOY

This cross-sectional, descriptive, and observational study included all children and adolescents enrolled at the State Institute of Hematology “ARTHUR DE SIQUEIRA CAVALCANTI” (HEMORIO, Rio de Janeiro, Brazil), aged between 3 and 18 years, with a diagnosis of leukemia, either hospitalized or in outpatient care. Participants who had outdated institutional registration data due to communication impediments were excluded, as were participants diagnosed with leukemia who had some kind of disturbance of consciousness, dementia, delirium, psychosis, mental disorder or mental illness. The study took place from June 2022 to January 2023, in the dental outpatient clinic of the reference center for hematological treatment and in the pediatric hospital and was approved by the Ethics and Research Committee of the reference center for hematological treatment, by the number 5825156 of 2022.

The participants’ sociodemographic data and medical history, such as definitive diagnosis of leukemia (ALL, CLL, AML, CML), treatment phase (induction, consolidation and maintenance), use of medication and laboratory tests (last blood count collected closest to the time of the clinical dental evaluation) were obtained from the electronic system of the reference center for hematological treatment and from the participant’s medical records, and the anamnesis was taken with the caregiver and the participant. A clinical dental assessment was then carried out, followed by a photographic record. The clinical examination was carried out by a single dentist specializing in pediatric dentistry, after being calibrated by an experienced specialist. To check intra-examiner calibration, a second clinical examination was carried out on 10% of the sample after 2 weeks, with a kappa coefficient of 0.93. It was carried out under a natural light source, using a mirror, gauze and personal protective equipment (PPE). Alterations to the labial commissures, nose, cheek and chin were assessed, as well as alterations to the lymph nodes in the extraoral region. During the intraoral examination, the dental elements, tongue, floor of the mouth, gums, jugal mucosa, hard and soft palates, tonsils and mucous membranes were assessed (8).

To assess the prevalence of caries, the decayed, missing and filled teeth per tooth (DMFT) index and the decayed primary teeth, indicated for extraction and filling index (dmft) were used . The DMFT index measures the mean index of decayed, missing, and filled permanent teeth, as indicated in Table 1, while the dmft index is the dental index for counting the quantity of deciduous elements with indication for extraction, decayed, and filled (9,10,11).

## TABLE 1: DMFT INDEX

| Average DMFT value | Caries prevalence in the population |
|---|---|
| 0 to 1.1 | Very low |
| 1.2 to 2.6 | Low |
| 2.7 to 4.4 | Moderate |
| 4.5 to 6.5 | High |
| 6.6 or higher | Very high |

Source: World Health Organization – WHO (9)

Oral manifestations were assessed according to the World Health Organization (WHO) protocol (8).The hematological data classifications of thrombocytopenia and neutropenia were considered by the absolute neutrophil count (ANC), which measures the number of neutrophil granulocytes present in the blood, and thrombocytopenia was defined by the platelet count (12).

## TABLE 2: CLASSIFICATION OF NEUTROPENIA AND THROMBOCYTOPENIA

| Neutropenia (cells/mm³) |
|---|
| Normal (highest 1500) |
| Mild (1000 to 1500) - minimal risk of infection |
| Moderate (500 to 1000) - moderate risk of infection |
| Severe (under 500) - serious risk of infection |
| **Thrombocytopenia (thousand fragments/mm³)** |
| Normal (greater 150 to 450) |
| Light (100 to 150) |
| Moderate (50 to 99) |
| Severe (under 50) |

Source: Hemograma: manual de interpretação, 2003 (12)

As a data collection tool, we used forms produced by the researcher, comprising: two record forms (examiner's form and anamnesis), a clinical assessment form (examiner's form) and three record form templates, according to the stage of dentition (deciduous, mixed, and permanent dentition). Statistical analyses were carried out using the PlanMaker for Windows 11 program. Frequency distribution was assessed using absolute (n) and relative (%) data.

## RESULTS

Twenty-five participants took part in the survey, 14 of whom were male (56%) and 11 female (44%). The average age was 10.12 years (Standard Deviation - SD = 4.8), with a minimum age of 4 and a maximum age of 17. Of the total number of participants, 12 were hospitalized, while 13 had an outpatient approach. In terms of sociodemographic characterization, 15 were residents of the state of Rio de Janeiro, while 10 lived in the capital city. As for the participants' level of education, 16 were studying and the highest level of education attained was incomplete primary education. As for the caregivers, 39% had completed high school. In terms of employment, 67% of the caregivers were employed.

Regarding the oncological and laboratory aspects: of the 25 participants, 16 (64%) were recently diagnosed (between 2021 and 2022), while the others have been dealing with the disease for a longer period (from 2010 to 2020). There were 20 cases of ALL (80%), 3 of AML (12%) and 2 of CML (8%). As for chemotherapy treatment, the AIEOP/BFM 2009 protocol, version 2013, was the most commonly used treatment method. As informed by the blood center's hematologists, this protocol uses the stratification of patients according to risk groups for recurrence. With regard to the treatment phase, 12 participants were in the induction phase, three in the consolidation phase, three in the maintenance phase, six in control and one in post-hematopoietic stem cell transplant (HSCT) follow-up. The clinical data found is shown in Table 3.

## TABLE 3: CLINICAL AND LABORATORY DATA

| Clinical Data | |
|---|---|
| **Diagnosis** | |
| Type | % (n) |
| ALL | 80 (20) |
| AML | 12 (3) |
| CML | 8 (2) |
| Treatment | |
| Phase | % (n) |
| Induction | 48 (12) |
| Consolidation | 12 (3) |
| Maintenance | 12 (3) |
| Control | 24 (6) |
| Post-HSCT follow-up | 4 (1) |
| Chemotherapy use % (n) | |
| Yes | 68 (17) |
| No | 32 (8) |
| Neutrophill count % (n) | |
| Normal | 60 (15) |
| Mild Neutropenia | 0 (0) |
| Moderate Neutropenia | 4 (1) |
| Severe Neutropenia | 36 (9) |
| Platelet count % (n) | |
| Normal | 56 (14) |
| Mild thrombocytopenia | 12 (3) |
| Moderate thrombocytopenia | 4 (1) |
| Severe thrombocytopenia | 28 (7) |

Source: Hemograma: manual de interpretação, 2003 (12)

In the clinical evaluation, the presence of biofilm was observed in the majority of participants (84%); tongue coating was observed in almost half (44%); and calculus, gingival bleeding and gingivitis in smaller proportions (20%, 8% and 4%, respectively). As for the DMFT/dmft index, 60% of the participants had an index equal to 0, with a mean of 1.92 and a standard deviation of 3.82. According to the WHO DMFT index, this group of participants has a low DMFT prevalence.

Considering the clinical analysis and the DMFT/ dmft value, it was observed that 84% (n=21) of the participants had biofilm and needed dental follow-up. When considering participants with a DMFT/ dmft greater than 0, bleeding, gingivitis and/or calculus, 52% (n=13) required dental intervention. As a result, 92% (n=23) of the participants needed dental follow-up or intervention (among the necessary interventions, oral hygiene guidance and periodontal care stand out).

Oral manifestations were found in 60% (n=15) of the total sample studied, including dry lips, altered taste, xerostomia, mucositis, gingival hypertrophy, primary herpetic gingivostomatitis and angular cheilitis, the incidences of which are shown in Table 4. Nausea was also observed in 44% (n=11) of the participants.

**TABLE 4: PREVALENCE OF ORAL MANIFESTATIONS**

| Oral manifestations % (n) | |
|---|---|
| Dry lips | 28 (7) |
| Change in taste | 24 (6) |
| Mucositis | 16 (4) |
| Xerostomia | 12 (3) |
| Gingival hypertrophy | 4 (1) |
| Primary herpetic gingivostomatitis | 4 (1) |
| Angular cheilitis | 4 (1) |

With regard to oral manifestations in the last 30 days, the data collected from the medical records revealed mucositis (16%), primary herpetic gingivostomatitis (8%), pericoronaritis (4%) and angular cheilitis (4%). Dental anomalies were found in 24% (n=6) of the participants. The anomalies observed included dental crowding (16.7%), prolonged retention (16.7%), late eruption (16.7%) and gyroversion (8.3%). Dental anomalies included hypodontia 16.7% (n=2), microdontia 16.7% (n=2), and twinning/fusion 8.3% (n=1). Low-power laser photobiomodulation therapy was performed in 44% (n=11) of the patients and the indications for this type of treatment are listed in Table 5.

**TABLE 5: INDICATIONS FOR PHOTOBIOMODULAR THERAPY**

| Indication | % (n) |
|---|---|
| Prophylactic protocol | 45.4 (5) |
| Mucositis | 36.4 (4) |
| Angular cheilitis | 9.1 (1) |
| Herpes | 9.1 (1) |

## DISCUSSION

The participants in the study had unsatisfactory oral hygiene, as seen in the presence of biofilm in 84% of the sample. This condition tends to make them more susceptible to colonization by multidrug-resistant microorganisms, due to their immunocompromise (14). In this study, immunosuppression was observed in 40% of the participants (represented by the neutrophil count), thus showing susceptibility to colonization by microorganisms in the group of participants studied. In this context, preventive treatment and educational work should be reinforced, avoiding infections that could increase hospitalization time and costs, as well as interrupting treatment (15).

The results of the DMFT/dmft indices showed that 40% of the participants had caries disease. In 2020, Afshar *et al*. evaluated 50 children with ALL and observed a mean DMFT of 4.01 (SD = 3.60) 16. In 2019, De Oliveira *et al*., in a study of 61 children and adolescents with malignant neoplasms, observed a mean dmft and DMFT of 2.8 (±3.3) and 1.7 (±1.5) (17). These data corroborate the research findings, with a mean DMFT = 1.92 (SD = 3.82) in all the individuals surveyed and a mean DMFT = 1.85 (SD = 4.20) in the participants with ALL.

It was found that 92% of the child and adolescent cancer patients treated at the reference center for hematological treatment needed dental follow-up or intervention, in addition to the presence of caries, bleeding, gingivitis, calculus and biofilm. The regularity and form of brushing, when not performed correctly, can increase caries rates, and this unsatisfactory oral condition tends to accentuate the development of infections during the myelosuppression process (18). Odontogenic infections can be the source of systemic infections during periods of myelosuppression, as well as causing secondary infections related to central venous access, and it is important to eliminate them or minimize their risks (19,21).

Chemotherapy is a widely used antineoplastic treatment and it is important to understand the protocols used in the treatment of leukemia due to the possible side effects of these drugs. This form of treatment can be administered alone or in combination with other medications. Administration takes place at regular intervals which vary according

to the protocol used (20). The most commonly used protocol among the participants surveyed was the BFM (Berlin-Frankfurt-Munich) protocol, which uses reinduction therapy during the consolidation phase, reusing the same medications administered during the induction phase (22).

The drugs used in chemotherapy are divided into groups of alkylating agents, antitumor antibiotics, mitotic inhibitors, antimetabolites, corticosteroids (prednisone, prednisolone, dexamethasone) and asparaginase, among others. These medications can cause side effects such as nausea and vomiting (20). These effects were reported by 44% of patients, who may have their oral hygiene affected by avoiding brushing or mouthwash.

Leukemia is characterized by a high incidence of oral complications at the time of diagnosis and during treatment. On some occasions, patients with leukemia may come to dental care before the medical diagnosis, for routine care or for some oral manifestation of leukemia, such as gingival hyperplasia and gingivitis (7,23). A detailed anamnesis combined with laboratory tests can highlight to the dentist the possibility of blood dyscrasia, requiring attention for a differential diagnosis and referral of the patient to a hematologist.

Oral manifestations can be divided into three groups based on the causative agent. Primary lesions are induced by the infiltration of malignant cells into oral structures: gingival infiltration and infiltration into bony oral structures. Secondary lesions result from the myeloid nature of the disease and this group includes signs and symptoms as anemia, increased bleeding tendency and increased susceptibility to infections. On the other hand, tertiary complications are usually due to the complex interaction of the therapy itself, its side effects or a systemic condition resulting from the therapy. Such lesions and complications include ulcerations, mucositis, altered taste, candidiasis, gingival bleeding, xerostomia, dysphasia, opportunistic infections and trismus (24).

Chemotherapy acts on cells with a high rate of renewal, such as the cells of the oral mucosa, generating alterations in the integrity of these cells, causing changes in the oral microbiota, salivary flow and biochemistry and epithelial maintenance (7,20). Some chemotherapy drugs such as cytarabine, mitoxantrone and methotrexate are used in pediatric oncology and are closely related to the onset of mucositis (20).

All the participants were undergoing chemotherapy (68%) or post-chemotherapy (32%). Thus, the primary oral/dental manifestations (primary lesions) were not identified, because there were no participants before cancer treatment. Among the secondary oral manifestations, gingival bleeding was observed in 8% of the participants, herpetic gingivostomatitis in 4% and angular cheilitis in 4%. Lopes apud Caldas *et al*., in 2021, found a percentage of 25% of gingival bleeding in the sample of a study involving 24 children aged between 6 and 12 with an oncological diagnosis, 50% of whom had leukemia. Although the sample size of Lopes and the present study was similar, there was a significant difference in these findings, probably because they assessed other types of cancer (21).

In a 2018 study of 71 children and adolescents with ALL, Pinto *et al*. found that 4.9% had gingival bleeding, 3.3% had herpetic gingivostomatitis and 1.6% had angular cheilitis. Apart from the result of herpetic gingivostomatitis, which is similar to the result of the present study, the other values are divergent and this may be related to the difference in sample size in the two studies, the difference in protocols used or the quality of the oral health and/or clinical condition of those interviewed (25).

As for tertiary manifestations, xerostomia was found in 12% and mucositis in 16% of the sample. Pias *et al*. (2020), after evaluating 162 medical records of children with leukemia, found an incidence of 6.17% of xerostomia. This difference may be associated with the difference in sample size, for having covered other types of hematological cancers, or for different chemotherapy treatment protocols (26).

Regarding mucositis, Lopes apud Caldas *et al*., in 2021, found that in a total of 24 children, 62.5% had mucositis (21). Pinto *et al*. in 2018 detected the oral alteration of mucositis in 72.1% of 71 children and adolescents (24), while Lima *et al*. in 2022, when studying 117 children undergoing antineoplastic therapy, observed the appearance of mucositis in 66.7% of the participants surveyed (27). The differences in the authors' percentages in relation to this study may be due to the difference in sample size, the difference in treatment protocol or the fact that most of the patients at the reference center for hematological treatment were undergoing prophylactic photobiomodular treatment.

Altered taste is one of the side effects of chemotherapy, due to changes in the salivary glands, and can be mild or more complex, involving all four types of taste (28). Fernandes and Spinelli, in 2020, carried out a cross-sectional study with 17 family members of children undergoing cancer treatment (57.9% referring to children undergoing cancer treatment for leukemia) and found 63.2% reported changes in taste (29). In the present study, a lower percentage (24%) of patients declared alterations in taste.

One adolescent had microdontia, prolonged retention and delayed eruption. As well as receiving chemotherapy as an anti-neoplastic treatment, he

underwent radiotherapy at the age of three years-old. The treatment data was obtained by interviewing the caregiver, without access to the records of the drugs used and the dosage of radiotherapy applied at the time. The literature shows that chemotherapy drugs, and especially radiotherapy drugs in the head and neck region, can interfere with odontogenesis and can result in dental alterations such as agenesis and hypodontia when applied before the morphodifferentiation phase of the ameloblasts. If it occurs later in tooth development, microdontia, hypoplasia and root malformation are expected side effects. In addition, alkylating agents such as cyclophosphamide can cause tooth agenesis and microdontia, while vincristine and doxorubicin can affect the development of odontogenic tissues (20,30).

The participants in the study are being treated for an acute life-threatening illness. The discovery of cancer also alters the routine of their families, who begin to experience suffering plus worries and demands (31). Treatment should be carried out by a multi-professional team, starting with qualified and empathetic listening, with the aim of prevention and health promotion. The dental surgeon on this team should raise awareness among caregivers and children about the importance of oral health, encourage greater adherence to treatment, promote the adaptation of the oral environment and reduce the likelihood of invasive treatments, as infectious foci are a severe threat to the health of immunosuppressed patients. Dental care for this group of participants should be carried out before, during and after cancer treatment (13,32).

In addition, the main limitations to conducting this research were the number of participants seen during the period, their attendance at appointments and the difficulty in communicating with the participants and their guardians. Further studies on this subject are suggested in order to reach a larger number of participants.

Despite the limitations presented, this study is of great scientific relevance, as it demonstrates that the dental surgeon can be the first to observe a clinical manifestation of leukemia. In addition, in the stages of treatment with significant immunosuppression, this professional acts in the prevention and treatment of oral manifestations, providing an ideal hygiene condition to avoid complications arising from a poor oral condition.

## CONCLUSION

Children and adolescents with leukemia who receive dental care at a reference center for hematological treatment have a high percentage of oral manifestations and unsatisfactory oral hygiene, making them more susceptible to infections. This reinforces the need for the dental surgeon to continuously monitor patients during all phases of antineoplastic treatment, reinforcing their importance in the multidisciplinary team that treats this group of patients.

The authors declare that there is no conflict of interest and that they have no economic or other interests that could cause embarrassment if known after the article has been published.

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## REFERENCES

1. CANCER.ORG. What Is Acute Myeloid Leukemia (AML)?. [S. l.], 21 ago 2018 (Accessed on Mar 13rd, 2022). Available at: https://www.cancer.org/cancer/acute-myeloid-leukemia/about/what-is-aml.html.
2. Peixoto LSB, Gomes JO. Atuação do cirurgião dentista no tratamento de pacientes com câncer no Brasil de 2013 à 2023. REASE. 2023;9(10):1686-701.
3. Instituto Nacional de Câncer. TIPOS de câncer: Leucemia. [S. l.], 20 ago 2021 (Accessed on Mar 20th, 2022). Available at: https://www.inca.gov.br/tipos-de-cancer/leucemia#:~:text=A%20leucemia%20%C3%A9%20uma%20doen%C3%A7a,substituem%20as%20c%C3%A9lulas%20sangu%C3%ADneas%20normais.
4. Hemorio. Manuais. In: Manuais. [S. l.], 2014 (Accessed on Mar 20th, 2022). Available at: http://www.hemorio.rj.gov.br/.
5. Instituto Nacional de Câncer. Estimativa 2023: incidência de câncer no Brasil. Rio de Janeiro: INCA; 2022 (Accessed on Jan, 31st, 2023). Available at: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//estimativa-2023.pdf.
6. Teixeira AM, Perez JMP, Pereira VAS. Manifestações orais em pacientes submetidos a quimioterapia e radioterapia. Diálogos em Saúde. 2022;4(2):72-83.
7. Pereira EML, Gomes IA, de Sousa ACC, Ferreira GLC. Pacientes oncológicos pediátricos: Manifestações orais decorrentes da terapia antineoplásica. Revista de Estudos Multidisciplinares UNDB. 2023;3(1).
8. World Health Organization. Oral health surveys: basic methods - 5th edition. World Health Organization; 2013. ISBN 978-92-4-154864-9.
9. World Health Organization. International Classification of Functioning, Disability, and Health: Children & Youth Version: ICF-CY. World Health Organization; 2007.

10. Agnelli PB. Variação do índice CPOD do Brasil no período de 1980 a 2010. Rev Bras Odontol. 2016;72(1/2):10-5.
11. Han L, Wang Qi. Associations of brominated flame retardants exposure with chronic obstructive pulmonary disease: A US population-based cross-sectional analysis. Front Public Health. 2023;11:1138811.
12. Lupp JS, Silva LAA. The importance of interpreting complementary laboratory tests in routine dentistry: A brief review. Int J Health Res. 2023;2(6):1533-45.
13. de Andrade LC, Gomes SL, Santos TB. Papel do Cirurgião Dentista nos cuidados paliativos multidisciplinares com pacientes oncopediatricos: revisão integrativa. Res Soc Dev. 2022;11(6):e27911629189.
14. Tejo NP, Andrade KS, Ferreira AFM. Condição oral de pacientes imunocomprometidos internados em Unidade de Terapia Intensiva. Arch Health Invest. 2021;10(4):674-9.
15. Farias GLC, Sousa HMM, Pereira LS, de Carvalho ALA, de Melo Júnior WA. Laserterapia e Ações Educativas Transdisciplinares na Oncologia Pediátrica. Caderno Impacto em Extensão. 2023;3(1):1-4.
16. AFSHAR MK, Farahmandinia Z, Parizi MT, Parivar F. Oral Health Status of South-Eastern Iranian Children with Acute Lymphoblastic Leukemia. JJ Evol Med Dent Sci. 2020;9(2):86-91.
17. Ponte YO, Ximenes RDA, Vasconcelos AA, Girão DC. Saúde bucal em crianças com câncer: conhecimentos e práticas dos cuidadores. Revista da Faculdade de Odontologia-UPF. 2019;24(2):183-91.
18. Rosso MLP, Neves MD. de Araújo PF, Ceretta LB, Simões PW, Sônego FGF, *et al*. Análise da condição bucal de pacientes pediátricos e adolescentes portadores de neoplasias na instituição Casa Guido na Cidade de Criciúma (SC). Revista de Odontologia da Universidade Cidade de São Paulo. 2015;27(3):210-9.
19. Buzetto JC, Brito RCM, Imparato JCP. Há um protocolo odontológico para prevenção e tratamento de doenças bucais em crianças submetidas ao tratamento oncológico? Revisão integrativa. Res Soc Dev. 2023;12(2):e15512240100.
20. de Souza JLR, de Araújo ACS, do Nascimento FSL. O Papel do Farmacêutico na Adesão De Pacientes em Uso de Antineoplásicos Orais. Revista Eletrônica da Estácio Recife. 2019;5(2):1-12.
21. Caldas LHTA, Ricarte RG, Souza e Souza SR, Néri JSV, Dantas JBL. Alterações orais da quimioterapia em pacientes infantojuvenis com leucemia linfoide aguda: uma revisão de literatura. Revista Brasileira de Saúde Funcional. 2021;9(2):133-50.
22. Tessmann L, Medeiros-Souza P, Códoba JCM, Tavares NUL, Abílio VM. Matos DO, *et al*. Partição de Comprimidos Antineoplásicos Utilizados no Tratamento de Leucemias Agudas em Crianças e Adolescentes. Revista Brasileira de Cancerologia. 2020;66(2):e-01764.
23. Araújo NS, Cezário LRA, Gois CMB, Araújo AB, de Araújo DVA, de Alburquerque SAV, *et al*. Condições bucais e o impacto na qualidade de vida de crianças e adolescentes em tratamento antineoplásico. Braz J Develop. 2023;9(2):7014-31.
24. Silveira ACAS, Coutinho LN, Correa GTB. Manifestações orais em pacientes pediátricos com Leucemia Linfoide Aguda. Res Soc Dev. 2022;11(7):e27711730119.
25. Pinto ETF, Queiroz SIML, Gonçalves P, Gurgel BCV. Avaliação retrospectiva das alterações orais em crianças com leucemia linfoblástica aguda. Revista Portuguesa de Estomatologia, Medicina Dentaria e Cirurgia Maxilofacial. 2018;59(1):30-5.
26. Pias MCM, Neto GOP, Ferreira CMB, Libório-Kimura TN. Manifestações bucais da leucemia linfoblástica: estudo clínico em centro de referência hematológico no Amazonas. Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial. 2020;61(3):128-34.
27. de Lima AKMMN, Paulo AC, Duarte DA. Qualidade de Vida e Saúde Bucal em Crianças Submetidas à Terapia Antineoplásica. RBC. 2022;68(2):e-202164.
28. Hernandes CO, de Carvalho MM, Simonato LE. Manifestações bucais em pacientes com leucemia Oral manifestation in patients with leukemia. Braz J Dev. 2021;7(12):110930-43.
29. Fernandes RCS, Spinelli MGN. Percepção de pais e responsáveis por crianças diagnosticadas com câncer: a gastronomia hospitalar em foco. Nutr Clín Diet Hosp. 2020;40(1):20-4.
30. Bendoraitiene EA, Andruskeviciene V, Kscenaviciute G, Srebaliene E, Maciulaityte I. Peculiarities of dental treatment among paediatric oncological patients: A case report. J Oral Maxillofac Res. 2020;11(3):e5.
31. dos Santos PA, Serralta FB. Narrativas sobre o câncer: um estudo clínico-qualitativo em cuidados paliativos. Revista da Sociedade Brasileira de Psicologia Hospitalar. 2019;22(2):301-24.
32. da Silva MVI, de Lima RO, Monteiro VMC, dos Santos SEN, Gaines APL, Rocha LMBM, *et al*. Câncer bucal e o papel do Cirurgião-Dentista no diagnóstico precoce: Revisão integrativa. Res Soc Develop. 2023;12(13):e75121344156.