Review

http://dx.doi.org/10.1590/1981-86372024004520240037

Revista Gaúcha de Odontologia

Caries disease in childhood cancer patients: a literature review

Doença cárie em pacientes com câncer infantojuvenil: revisão de literatura narrativa

Julia Pianezzer **Miquelão**[1] 0009-0005-5351-101X
Julia Funez **Barros**[1] 0009-0002-3719-1720
Bruna Cristina **Longo**[1] 0000-0002-9498-3743

ABSTRACT

This study aims to present the prevalence of dental caries in childhood cancer patients, emphasizing the effects of antineoplastic therapy. To carry out the study, a search strategy was adopted that covered books from 2017 to 2022 and articles available in databases, published between 1997 and 2021, in English and Portuguese. In recent years, there has been an increase in the incidence of malignant neoplasms in pediatric patients. The most common are leukemias, lymphomas, and tumors of the central and sympathetic nervous systems. The treatment of these diseases is antineoplastic therapy, which aims to combat cancer cells. However, it can cause unwanted effects such as systemic, craniofacial, and dental changes. The most common oral manifestations are caries, microdontia, hypodontia, root changes and taurodontism. The relationship between tooth decay and childhood cancer is still not well understood, as factors such as diet and oral hygiene can play a confounding role in the development of tooth decay. Antineoplastic therapy increases the

How to cite this article

Miquelão JP, Barros JF, Longo BC. Caries disease in childhood cancer patients: a literature review. RGO, Rev Gaúch Odontol. 2024;72:e20240045. http://dx.doi.org/10.1590/1981-86372024004520240037

[1] Centro Universitário Univel, Faculdade de Odontologia. Av. Tito Muffato, 2317, Santa Cruz, Cascavel, PR, Brasil. Correspondência para/Correspondence to: JP Miquelão. E-mail: <julia_pianezzer@hotmail.com>.

patient's risk of developing caries disease, however, it has not yet been proven to be a disease-modifying factor, so additional studies must be carried out.

Indexing terms: Dental caries. Dental plaque. Surviving cancer.

RESUMO

O presente estudo busca mostrar os índices de prevalência da cárie em pacientes pediátricos com câncer, enfatizando os efeitos da terapia antineoplásica e investigar suas consequências no desenvolvimento dentário. Para a realização do estudo, a estratégia de busca foi baseada em pesquisas no MEDLINE via Pub Med no período de 2017 até janeiro 2024, sendo prolongadas às bases de dados eletrônicas como Biblioteca Cochrane, Biblioteca Brasileira de Odontologia, LILACS, Scopus e Web of Science, publicados entre os anos de 1997 e 2021, tanto em inglês quanto em português. Nos últimos anos, houve um aumento na incidência de neoplasias malignas em pacientes pediátricos. Sendo os mais comuns, leucemias, linfomas e tumores do sistema nervoso central e simpático. O tratamento dessas doenças é a terapia antineoplásica que tem por objetivo combater as células cancerígenas. Contudo, pode causar efeitos indesejados como alterações sistêmicas, craniofaciais e dentárias. As manifestações bucais mais comuns são a cárie, microdontia, hipodontia, alterações radiculares e taurodontismo. A relação entre a cárie dentária e o câncer infantojuvenil ainda não é bem esclarecida, visto que fatores como dieta e higiene bucal podem desempenhar um papel confundidor no desenvolvimento da cárie. A terapia antineoplásica aumenta o risco do paciente desenvolver doença cárie, no entanto, ainda não foi comprovado ser um fator modificador da doença, por isso estudos adicionais devem ser realizados.

Termos de indexação: Cárie dentária. Placa dentária. Sobreviventes de câncer.

INTRODUCTION

The occurrence of malignant neoplasms has shown a significant increase in recent years in pediatric patients [1]. Childhood cancer (CC) is the name used when these diseases affect patients between 0 to 19 years old. In 2020, the National Cancer Institute estimated that there would be around 8.460 new cases of CC in Brazil [2]. Leukemias, lymphomas, central and sympathetic nervous system tumors, bone and soft tissue sarcomas, and renal sarcomas are the most common cancer types in this age group [3]. These diseases can be treated through antineoplastic therapy (AT) which may include chemotherapy, radiotherapy, surgery, and/or bone marrow transplant [2].

Both CC and AT can cause systemic, craniofacial, and dental alterations, and some of these effects may be irreversible [4]. About the oral cavity, salivary changes, oral infections, and changes in tooth development are some of the AT consequences, such as caries, microdontia, hypodontia, root changes, and taurodontism [1,4-7]. A study suggests that children undergoing chemotherapy have twice the risk of developing cavities and gingivitis compared to children not exposed to this treatment, considering the same age group and cariogenic risk [6].

However, the relationship between caries development and AT is still unclear. Some studies show the relationship between cavities and cancer because of treatment, diet, and poor oral hygiene. Furthermore, authors suggest that some factors like low immunity during the AT, acidic pH saliva, a high caloric diet, and dental hygiene difficulty due to the presence of oral lesions may increase the risk of dental caries [4-6,8-11]. On the other hand, other studies suggest the correlation presented is not a consequence of the AT, but rather a lack of follow-up at the dentist [12-14].

In this sense, the present study aims to present the prevalence of dental caries in pediatric cancer patients. Pointing out AT as a primary factor, investigating its effects and consequences on dental development in CC survivors.

METHODS

The search strategy was firstly defined for the MEDLINE database via PubMed using a controlled vocabulary (MeSH terms) for research published until January 3, 2024, and free keywords for each concept of the PECO question:

- Population (P): Children and adolescents with cancer up to 19 years old at diagnosis;
- Exposure (E): Antineoplastic therapy;
- Comparison (C): Healthy patients;
- Outcomes (O): Dental caries.

The basic MeSH terms used were “dental caries” AND “childhood cancer”. The MEDLINE search strategy was adapted to other electronic databases: Cochrane Library, Brazilian Library in Dentistry, Latin American and Caribbean Health Sciences Literature database (LILACS), and citation databases (Scopus and Web of Science). Additionally, gray literature was investigated and the reference lists of all primary and eligible studies of this systematic review were hand-searched for additional relevant publications. Studies were not restricted based on publication date and language.

Eligibility Criteria

Observational studies (OS) that compared oral alterations in childhood cancer patients submitted to antineoplastic therapy and healthy patients were included.

Study Selection and Data Collection Process

The articles retrieved by the literature search were revised in three phases. All studies were initially scanned for relevance by title; the next step was the evaluation of the abstract, and finally, by full-text retrieval. In case of doubts in any of these phases, the study was kept to the next phase. The full texts were read by two reviewers (JFB and JPM) to check if they met the inclusion criteria. In disagreement, a decision was reached by consulting a third reviewer (BCL).

RESULTS

In this review, 10 comparative studies were used. Of these, 7 reported statistically significant differences between groups, while 3 showed no such differences. Five studies exclusively evaluated permanent teeth, while the other five analyzed both permanent and primary teeth. Table 1 presents the main findings of the studies analyzed.

Table 1. Summary of results found.

Author, Year	Number of patients evaluated (CC/ healthy)	Assessment method	Statistical difference between groups	Results
Duggal et al. [12], 1997	46/46	DMFT	Yes	The authors believe that this result was because the CC did not visit the dentist regularly. They also suggest that many professionals are unprepared to care for these patients. In addition, diet changes in this group can increase dental caries.
Alpaslan et al. [8], 1999	30/20	DMFT/ dmft	No	The researchers obtained the following results: patients who underwent radiotherapy treatment have a greater risk of developing dental caries, due to the increase in bacterial species like ***Streptococcus mutans*** and ***lactobacillus***. However, they did not observe a statistical difference between the groups and suggest that this result may have been influenced by the frequent use of mouthwashes, such as 0.12% chlorhexidine, and dietary restrictions in CC.
Oguz et al. [9], 2004	36/36	deft/DMFT	No	The following conclusions were obtained: there was no significant difference between the test and control group, which may be related to the restriction of sugary foods, oral hygiene care during the AT, and prescription of 0.12% chlorhexidine in the CC group.

Table 1. Summary of results found.

Author, Year	Number of patients evaluated (CC/ healthy)	Assessment method	Statistical difference between groups	Results
Avsar et al., 2007	96/96	DMFT	Yes	Despite the difference between groups, the authors suggest that chemotherapy alone does not appear to cause adverse effects on dental caries. They suggest the difference is possible because of a period of mixed dentition, poor oral hygiene, oral flora changes, and ingestion of cariogenic foods.
Çubukçu & Sevinir [10], 2008	62/62	DMFT/ dmft	Yes	The study data, it was observed that there is a higher prevalence of dental caries in patients who underwent head/ neck irradiation and should therefore have periodic monitoring, as well as a deficiency in the oral health care of deciduous teeth compared to permanent teeth, which may be associated with poor oral hygiene and xerostomia.
Hegde et al. [11], 2011	90/30	DMFT/ DMF	Yes	Those authors believe that the increase in inflammation of the oral mucosa contributed to a deficiency in oral hygiene and, consequently to the increase in dental caries.
Nemeth et al. [13], 2013	38/40	DMFT	Yes	Despite the statistical difference between the groups, the authors reached the following conclusion that the increase in dental caries in the group with cancer is not related to AT, but rather to the lack of oral hygiene care.

Table 1. Summary of results found.

Author, Year	Number of patients evaluated (CC/ healthy)	Assessment method	Statistical difference between groups	Results
Çetiner et al. [4], 2018	53/40	DMFT/def	No	The research identified that there is no correlation between AT and the presence of dental caries. The authors believe that the results can be attributed to the continuous use of chlorhexidine rinses and the dietary restrictions of the CC.
Proc et al. [14], 2019	41/150	DMFT	Yes	The results of the study indicate that socioeconomic factors influence the prevalence of dental caries, as well as there is a need for cooperation between oncologists and dentists to prevent oral diseases resulting from AT since their caries process is more active compared to their healthy peers.
Shayani et al. [6], 2021	23/46	DMFT	Yes	Researchers understand that changes in oral microflora, reduced salivary flow, consumption of sugary foods, vomiting episodes that cause demineralization of the structure, and chemotherapy agents are predisposing factors for dental caries in CC.

Note: **AT**: antineoplastic therapy; **CC**: childhood cancer; **DMFT**: permanent teeth index, **D**: decayed, **M**: missing, **F**: filled, **T**: teeth, deft: decíduos teeth index, **d**: decayed, **m**: missing, **f**: filled, **t**: teeth.

DISCUSSION

As previously discussed, determining factors such as host, diet, biofilm, social/economic, and behavioral aspects affects the development of dental caries [14-16], making it difficult to isolate these

factors to evaluate the influence of AT alone in the development of dental caries in CC. In this sense, some researchers have been investigating this group of patients and comparing them with healthy patients (control group). Table 1 presents a summary that highlights these elements correlated with the presence of dental caries and AT. Some authors found a significant statistical difference between the groups [5,6,10-14], while others did not observe this difference [4,8,9]. Therefore, this literature review will discuss the relationship between dental caries and AT.

AT is an invasive and aggressive procedure, which significantly affects the functioning and development of several systems, especially the stomatognathic system [4]. Some researchers suggest that dental caries risk in the CC group may be due to AT indirect factors such as poor hygiene [5,10,11,13], not visiting a dentist regularly [12], mixed dentition [5], and intake of cariogenic foods [5,6], because they can also be rewarded with sweets after medical procedures [4]. In addition, because of the difficulty in eating, cancer patients depend on a diet with high-calorie content and deficiency in oral care explains this result, due to the accumulation of dental plaque after the consumption of cariogenic foods [4.10].

Furthermore, changes in oral microflora can also influence these conditions [5,6]. It is also suggested that AT may cause xerostomia [6,10]. Among the authors, despite the absence of statistical difference, they suggest the treatment causes changes in the oral flora, making the saliva pH more acidic and favoring the presence of Streptococcus mutans and lactobacillus, creating an environment favorable to the development of dental caries [8].

Proc and collaborators in 2019 found higher caries rates in the CC group and suggested that socioeconomic factors influence the prevalence of this disease. Furthermore, the authors suggest that cooperation between oncologists and dentists is necessary to prevent oral diseases resulting from AT since the dental caries process in CC is more active compared to healthy patients. In addition, patients who have good oral health and strict oral hygiene during AT, present lower cases of inflammatory changes due to the effective reduction in dental plaque accumulation than those who do not maintain good hygiene conditions [4].

On the other hand, other studies suggest that AT is not associated with the dental caries risk, and propose the results were associated with the reduction of cariogenic foods, such as chocolate drinks, sugary medicines, and sweets, as well as the maintenance of oral hygiene during treatment [9].

It is important to highlight that the interconnection between dental caries and CC is influenced by many factors such as immunosuppression, changes in pH, poor oral hygiene, and changes in the microflora composition [6]. Lack of effective oral hygiene, and high-calorie/cariogenic diet, in addition to xerostomia, are factors that contribute to the progression of dental caries in patients undergoing AT. Therefore, the need for longitudinal studies can evaluate dental caries and follow up the disease evolution is evident. In addition, there are important studies that analyze all these elements when association between AT and dental caries.

CONCLUSION

Among the ten studies evaluated, seven studies (70%) observed a significant statistical difference between the CC group and the control group, suggesting a greater risk of developing dental caries in CC. However, the multifactorial etiology of dental disease is evident and several researchers suggest that AT can modify some of them, such as oral hygiene, pH changes, and xerostomia, and thus increase the dental caries risk. It is suggested that additional longitudinal studies should be carried out to monitor the patient

in the long term, as well as evaluate all factors related to dental caries development in these patients, to prove AT as a risk factor for the disease.

Collaborators

JP Miquelão evaluated and interpreted the results of bibliographical research, in addition to preparing the manuscript. JF Barros helped with writing the manuscript. BC Longo prepared, organized and supervised the literature review, in addition to carrying out a critical edition of the manuscript.

REFERENCES

1. Quispe RA, Rodrigues ACC, Buaes AMG, Capelozza ALA, Rubira CMF, Santos PSDS. A case-control study of dental abnormalities and dental maturity in childhood cancer survivors. Oral Surg Oral Med Oral Pathol Oral Radiol. 2019;128(5):498-507.e3. http://dx.doi.org/10.1016/j.oooo.2019.07.005
2. Instituto Nacional do Câncer (INCA). Tipos de câncer: Câncer infantojuvenil, (2022). [citado 2024 maio 30];]. Disponível em: <https://www.inca.gov.br/tipos-de-cancer/cancer-infantojuvenil>.
3. Pedersen LB, Clausen N, Schrøder H, Schmidt M, Poulsen S. Microdontia and hypodontia of premolars and permanent molars in childhood cancer survivors after chemotherapy. Int J Paediatr Dent. 2012;22(4):239-43. http://dx.doi.org/10.1111/j.1365-263X.2011.01199.x.
4. Çetiner D, et al. Oral and dental alterations and growth disruption following chemotherapy in long-term survivors of childhood malignancies. Support Care Cancer. 2019;27(5):1891-1899. http://dx.doi.org/10.1007/s00520-018-4454-0
5. Avşar A, Elli M, Darka O, Pinarli G. Long-term effects of chemotherapy on caries formation, dental development, and salivary factors in childhood cancer survivors. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;104(6):781-9. http://dx.doi.org/10.1016/j.tripleo.2007.02.029
6. Shayani A, Aravena PC, Rodríguez-Salinas C, Escobar-Silva P, Diocares-Monsálvez Y, Angulo-Gutiérrez C, et al. Chemotherapy as a risk factor for caries and gingivitis in children with acute lymphoblastic leukemia: A retrospective cohort study. Int J Paediatr Dent. 2022 Jul;32(4):538-545. http://dx.doi.org/10.1111/ipd.12932
7. Cubukcu CE, Sevinir B, Ercan I. Disturbed dental development of permanent teeth in children with solid tumors and lymphomas. Pediatr Blood Cancer. 2012 Jan;58(1):80-4. http://dx.doi.org/10.1002/pbc.22902
8. Alpaslan G, Alpaslan C, Gögen H, Oğuz A, Cetiner S, Karadeniz C. Disturbances in oral and dental structures in patients with pediatric lymphoma after chemotherapy: a preliminary report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;87(3):317-21. http://dx.doi.org/10.1016/s1079-2104(99)70215-5
9. Oğuz A, Cetiner S, Karadeniz C, Alpaslan G, Alpaslan C, Pinarli G. Long-term effects of chemotherapy on oriental structures in children with non-Hodgkin's lymphoma. Eur J Oral Sci. 2004;112(1):8-11. http://dx.doi.org/10.1111/j.0909-8836.2004.00094.x
10. Cubukçu CE, Sevinir B. Dental health indices of long-term childhood cancer survivors who had oral supervision during treatment: a case-control study. Pediatr Hematol Oncol. 2008;25(7):638-46. http://dx.doi.org/10.1080/08880010802237849
11. Hegde AM, Joshi S, Rai K, Shetty S. Evaluation of oral hygiene status, salivary characteristics and dental caries experience in acute lymphoblastic leukemic (ALL) children. J Clin Pediatr Dent. 2011;35(3):319-23. http://dx.doi.org/10.17796/jcpd.35.3.u5kx28q33m760834
12. Duggal MS, Curzon ME, Bailey CC, Lewis IJ, Prendergast M. Dental parameters in the long-term survivors of childhood cancer compared with siblings. Oral Oncol. 1997 Sep;33(5):348-53. http://dx.doi.org/10.1016/s1368-8375(97)89103-8
13. Nemeth O, Hermann P, Kivovics P, Garami M. Long-term effects of chemotherapy on dental status of children cancer survivors. Pediatr Hematol Oncol. 2013;30(3):208-15. http://dx.doi.org/10.3109/08880018.2013.763391
14. Proc P, Szczepańska J, Herud A, Zubowska M, Fendler W, Młynarski W. Dental caries among childhood cancer survivors. Medicine (Baltimore). 2019;98(6):e14279. http://dx.doi.org/10.1097/MD.0000000000014279
15. Corrêa MSNP. Odontopediatria na primeira infância: uma visão multidisciplinar. 4. ed. São Paulo: Quintessence; 2017.
16. Associação Brasileira de Odontopediatria. Diretrizes para Procedimentos Clínicos em Odontopediatria. São Paulo: Santos Publicações; 2021.

17. Little J. Epidemiology of childhood cancer. IARC Scientific Publications, 1999.

18. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. CA Cancer J Clin. 2014;64(2):83-103. http://dx.doi.org/10.3322/caac.21219

19. Longo BC, Popiolek IM, Vale NG, Rangel ALCA, Souza MDB. Estudo epidemiológico do câncer infantojuvenil no Hospital de Câncer de Cascavel Uopeccan entre os anos 2000 e 2014. Rev Bras Cancer. 2021;67(3):e-201224.

20. American Cancer Society. Cancer Facts & Figures 2016. Atlanta 2016 [citado 2024 maio 30]. Disponível em: <https://www.cancer.org/research/cancer-facts-statistics/all-cancer- facts-figures/cancer-facts-figures-2016.html>.

21. Oeffinger KC, Mertens AC, Sklar CA, Kawashima T, Hudson MM, Meadows AT, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355(15):1572-82. http://dx.doi.org/10.1056/NEJMsa060185

Received on: 13/6/2024
Approved on: 19/9/2024

Assistant editor: Luciana Butini Oliveira