Clinical

http://dx.doi.org/10.1590/1981-86372024002220230118

Revista Gaúcha de Odontologia

Health-related quality of life of a child with Trisomy 21 and Acute Myeloid Leukemia: Case report

Qualidade de vida relacionada à saúde de uma criança com Trissomia 21 e Leucemia Mieloide Aguda: relato de caso

Anna Vitória Mendes Viana **Silva**[1] 0000-0002-1867-2126
Isabel Zanforlin **Freitas**[1] 0000-0003-0468-5863
Alice Machado Carvalho **Santos**[1] 0000-0002-6864-246X
Priscila Cezarino **Rodrigues**[2] 0000-0002-7986-9272
Saul Martins **Paiva**[1] 0000-0002-3968-1638

ABSTRACT

Trisomy 21 (Down syndrome) is a genetic condition arising from the presence of three chromosomes at position 21. Individuals diagnosed with this syndrome have a greater likelihood of developing systemic problems, as well as cognitive, developmental, and psychiatric disorders. This paper reports a case of a child with Down syndrome under treatment for acute myeloid leukemia, emphasizing its impact on quality of life. The mother' perception on health-related quality of life (HRQoL) was measuredby the Pediatric Quality of Life Inventory (PedsQL), Generic Core and Cancer Module Scales. The mother's perception shown that physical and functional functioning indicated a higher negative impact on the child's life. The

How to cite this article

Silva AVMV, Freitas IZ, Santos AMC, Rodrigues PC, Paiva SM. Health-related quality of life of a child with Trisomy 21 and Acute Myeloid Leukemia: Case report. RGO, Rev Gaúch Odontol. 2024;72:e20230118. http://dx.doi.org/10.1590/1981-86372024002320230118

[1] Universidade Federal de Minas Gerais, Faculdade de Odontologia, Departamento de Saúde Bucal da Criança e do Adolescente. Av. Antônio Carlos, 6627, Pampulha, Belo Horizonte, MG, Brasil. Correspondence to: AVMV Silva. E-mail: <annavitoriavitoriamendes@gmail.com>.
[2] Universidade Federal de Minas Gerais, Faculdade de Medicina, Departamento de Clínica Médica. Av. Prof. Alfredo Balena, 190, Santa Efigênia, Belo Horizonte, MG, Brasil.

lowest scores were in the domains nausea and anxiety about the procedure. Intraoral examination revealed an incomplete primary dentition with ectopic eruption. The child has had a multidisciplinary health care approach (pediatrician, hematologist, gastroenterologist, cardiologist, physiotherapist and dentist). Therefore, it is essential that health professionals, including dentists, to incorporateinto their practice the knowledge on the difficulties and emotional aspects of this population, providinga patient-centered humanized care.

Indexing terms: Patient-centered care. Leukemia, monocytic, acute. Quality of life. Down syndrome.

RESUMO

A trissomia 21 (síndrome de Down) é uma condição genética decorrente da presença de três cromossomos 21. Indivíduos diagnosticados com essa síndrome apresentam maior probabilidade de desenvolver problemas sistêmicos, além de distúrbios cognitivos, de desenvolvimento e psiquiátricos. Este artigo relata o caso de uma criança com síndrome de Down em tratamento para leucemia mieloide aguda, enfatizando seu impacto na qualidade de vida. A percepção da mãe sobre a qualidade de vida relacionada à saúde (QVRS) foi mensurada pelo Pediatric Quality of Life Inventory (PedsQL), Escalas Genéricas Core e Módulo Câncer. A percepção da mãe mostrou que o funcionamento físico e funcional indicava maior impacto negativo na vida da criança. Os menores escores foram nos domínios náusea e ansiedade em relação ao procedimento. O exame intraoral revelou dentição decídua incompleta com erupção ectópica. A criança teve abordagem multidisciplinar de saúde (pediatra, hematologista, gastroenterologista, cardiologista, fisioterapeuta e dentista). Portanto, é fundamental que os profissionais de saúde, inclusive os cirurgiões-dentistas, incorporem em sua prática o conhecimento sobre as dificuldades e aspectos emocionais dessa população, proporcionando um cuidado humanizado centrado no paciente.

Termos de indexação: Assistência centrada no paciente. Leucemia monocítica aguda Qualidade de vida. Síndrome de Down.

INTRODUCTION

Trisomy 21 (Down syndrome) is a genetic condition arising from the presence of three chromosomes at position 21. The global incidence is one in every 1000 live births. In Brazil, this incidence is one in every 700 live births.Individuals with Down syndrome (DS) have specific oral and craniofacial characteristics [1,2]. Additionally, these individuals are more likely to develop heart disease, respiratory disorders, and leukemia [1,3].

Acute myeloid leukemia (AML), specifically the megakaryoblastic subtype (AML-M7), is a frequent form of leukemia found in children with DS. Studies indicate that the occurrence of the disease in this population is related to the mutation of the GATA-1s gene. Under normal conditions, this gene functions as a hematopoietic regulator, but is often altered in DS.Besides the predisposition to systemic problems, children with DS often also present cognitive, developmental, behavioral and psychiatric disorders, which can exert a direct effect on health-related quality of life (HRQoL) [3].Individuals with DS who are diagnosed with leukemia face additional challenges regarding quality of life (QoL) due to the side effects of treatment [4].

Children with DS have historically been excluded from survival analyses in studies that evaluate QoLfollowing treatment for cancer, which limits the understanding of the medical and psychosocial difficulties that these children and their families face during and after treatment [3,4]. Traditionally, patient care was

based on the paternalist model, in which the healthcare provider asks patients about their health state and makes treatment decisions based on this information. However, this situation has begun to change at services focused on health promotion and the humanized patient-centered care model is gradually gaining ground [5].

Patient-centered care enhances the satisfaction of the patient and family with treatment, leading to better results [6]. Patient-reported experience measures (PREMs) and patient-reported outcome measures (PROMs) provide tools for measuring the benefits and risks of an intervention by assessing how patients feel with regards to their own health [7,8]. These measures give patients a voice at healthcare services, enabling them to contribute to decision-making processes in the establishment of public health policies [6].

A patient-centered assessment can be adopted for different intervention methods and health-related outcomes [2]. HRQoL is one of the most widely investigated concepts in patient-centered approaches and constitutes a multidimensional construct. With this, understanding perceptions about HRQoL can contribute to the knowledge of caregivers, health professionals and policy makers about the needs of children diagnosed with DS and leukemia, who constitute a population full of difficulties. Therefore, the objective of the present study was to report the case of a child with DS undergoing treatment for AML with a genetic risk factor, emphasizing the repercussions on the QoL of the child and the family.

CASE REPORT

A male child, one year and seven months of age, with Down syndrome, resident of the city of Contagem, Brazil. The pregnancy had occurred without complications. The mother, 36 years of age, reported having undergone medical follow-up throughout the pregnancy and developed preeclampsia at the end of the pregnancy. The child was born through natural childbirth and was not the product of a consanguine marriage. Healthy father, mother and half-sister (22 years of age). Twelve-year-old sister has DS and had undergone treatment for AML-M7 diagnosed at the age of one year and six months. The mother signed the Free and Informed Consent Form (FICF) before the start of the case report study, authorizing the collection and use of data for research and publication purposes.

The diagnosis of DS occurred after childbirth. At one year and three months of age, thrombocytopenia was diagnosed during a routine exam (March 2021). The patient had been vaccinated for yellow fever the previous month (February 2021). The patient was in follow-up with the pediatrician and awaited a consultation with a hematologist due to the persistence of thrombocytopenia. In August 2021, at one year and four months of age, the child presented edema in the lower limbs and eyelids with no other associated symptoms. New exams revealed the presence of atypical cells, which led to the diagnosis of AML-M7. Chemotherapy treatment was carried out in three cycles: induction, consolidation and maintenance, with the child receiving treatment until June 2022. Patient had no allergies or history of previous hospitalizations.

The patient presents some phenotypic findings, such as brachycephaly, muscle hypotonia, short, broad neck, slanted eyes, flat occipital region, joint hyperextension and broad hands with short fingers (figure 1). The intraoral examination revealed an incomplete primary dentition with ectopic eruption, the absence of carious lesions, presence of dental biofilm and inflamed gingiva with sporadic gingival bleeding upon brushing (figure 2) and absence of mucositis and candidiasis. The child is in follow-up with a multidisciplinary team (pediatrician, hematologist, gastroenterologist, cardiologist, physiotherapist and dentist).

Figure 1. Phenotypic characteristics of Down syndrome: muscle hypotonia; short stature; small, broad hands; wide, flat face; eyes spaced far apart; small nose with flat nasal base; low position of ears; hypotonic tongue.

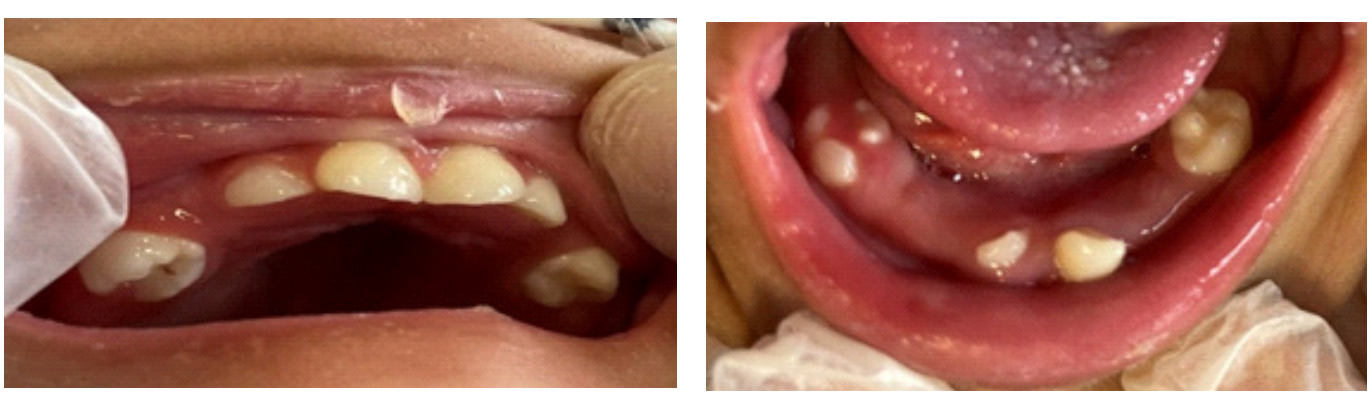

Figure 2. Oral characteristics of Down syndrome. Children one year and seven months of age presenting incomplete primary dentition with ectopic eruption, absence of carious lesions, presence of dental biofilm and inflamed gingiva.

The perceptions of the mother regarding HRQoLwere collected using the Brazilian versions of the *Pediatric Quality of Life Inventory* (*PedsQL*), *Version 4.0 Generic Core Scales* [9,10] and *PedsQL 3.0 Cancer Module* [10,11]. This questionnaire was intended for the guardian and contained the items (0 = never; 1 = almost never; 2 = sometimes; 3 = often; 4 = almost always). Children aged 1 to 4 years do not respond to the

instrument, so only the guardian's report is required. They were administered individually; the researcher was available to read the questions to the investigators, allowing them to mark the answer sheet or also instruct the researcher to do so. The items were scored inversely and linearly transformed to a scale from 0 to 100 (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), so that higher scores indicate better HRQoL. Scale scores are calculated as the sum of the items divided by the number of items answered.

Table 1 displays the score of the domains of the PedsQL 4.0.The lowest scores were in the Physical Functioning (18.75 points) and Emotional Functioning (50.0 points) domains, indicating greater negative impact. Table 2 displays the scores of the PedsQL 3.0 domains. The lowest scores were found for Nausea (20.00 points) and Procedural Anxiety (41.7 domains),

Table 1. Scores on domains of *PedsQL 4.0 Generic Cor*e.

DOMAIN	***PedsQL 4.0 generic scale*** **(*)**
Physical functioning	18.75
Emotional functioning	50
Social functioning	100
School functioning	100
TOTAL SCORE	67.20

Note: * Pediatric quality of life scale, Generic Scale – Version 4.0 –Portuguese (Brazil)- Parental report about child.

Table 2. Scores on domains of *PedsQL 3.0 Cancer Module*.

DOMAIN	***PedsQL 3.0 Cancer Module*** **(*)**
Pain and Hurt	62.50
Nausea	20
Procedural anxiety	41.70
Treatment anxiety	58.4
Worry	84
Cognitive Problems	100
Perceived Physical Appearance	100
Communication	100
TOTAL SCORE	70.82

Note: * Pediatric quality of life scale, Cancer Module – Version 3.0 – Portuguese (Brazil) – Parental report about child.

DISCUSSION

Children with DS are 10 to 20 times more likely to develop acute leukemia compared to those without DS, with a greater incidence of the AML-M7 subtype [12,13]. Epidemiological studies have been conducted to identify the possible cause for the increase in the incidence between these two conditions. However, no associations were found between the risk of developing acute leukemia in children with DS and infection, maternal or paternal exposure to pre-conceptional irradiation or the presence of congenital anomalies [12]. The risk of developing AML-M7 is estimated to be 400 times higher in children with DS less than four years of age [14]. The patient in the present report fits this description, as AML-M7 was diagnosed in the second year of life.

The etiology of leukemia has not yet been established, although the following factors have been considered as possible causes: effects of radiation, exposure to anti-cancer drugs, associated genetic and immunological factors and exposure to some viruses [14]. Moreover, the hypothesis of a relation between a family history of cancer and the risk of acute childhood leukemia has been suggested, especially in cases of AML [15]. Two studies found this association in first-degree and second-degree relatives [15,16]. Regarding siblings, evidence suggests a greater risk in identical twins and not siblings with different ages [17]. In the present case, the patient's older sister also with DS had a history of treatment for AML-M7, which was diagnosed when she was one year and six months of age. The prevalence of DS in two non-twin siblings is not clear in the scientific literature, suggesting that the occurrence in the siblings in the present study may be a rare condition. However, two individuals with DS presenting leukemia may occur with greater frequency, as DS is a risk factor for AML [14].

Children with DS have a characteristic craniofacial phenotype that is easily identified. The midface has hypoplastic development, which gives rise to the underdevelopment of the paranasal sinuses, resulting in an inclined forehead and flat facial features [18]. These patients generally have cardiovascular complications. The clinical manifestations described in the present case are compatible with such characteristics and the patient had a heart murmur.

Regarding oral health, numerous studies have reported poor oral hygiene and periodontal disease in patients with DS [18,19]. Gingivitis is also common. Therefore, daily oral hygiene and careful dental follow-up should be performed to avoid irreversible harm and morbidity [20]. Patients with DS have primary medical problems that interfere with oral hygiene [21], posing a risk to oral health. Dental biofilm and gingival inflammation were observed in the present case, with sporadic bleeding upon brushing. This may be explained by the difficulty that the mother had in performing oral hygiene due to the child's limited mouth opening and use of an enteral feeding tube.

Although there are many well-established studies and evidence showing that dental agenesis is present in a significant portion of people with t21, there are few studies that specifically address the relationship between DS, onco-chemotherapeutic treatment and the absence of dental agenesis. Some report of rate of 25 to 30% in this population without considering third molars [22,23]. Others found a rate of around 60% in 70 and 114 individuals with DS and 65%in 46 individuals with DS [24]. Considering these substantial percentages, dental agenesisseems to be a peculiar condition in this population. Delayed tooth eruption is also common in DS, affecting mainly the primary maxillary and mandibular central and lateral incisors, canines and first molars [23,24]. The oral examination in the present study revealed ectopic eruption – the teeth presented deviations from the normal eruption pattern, erupting in atypical order and position, which may be directly related to biological and morphological factors in this individual. It is

important for children with cancer to have adequate oral health care and treatment. Interdisciplinary care with cooperation between the dental and medical teams is fundamental in all phases of care for children diagnosed with cancer and DS.

According to the literature, children with DS are at high risk of acute leukemia, including acute lymphoblastic leukemia (ALL) and AML (generally the AML-M7 subtype) [24]. However, the survival rate for children with AMLand DS is higher than that for children with AMLand without DS, which is believed to be due to the greater sensitivity to chemotherapy in children with DS, resulting in a better response to treatment [3]. Despite this, children with DS and leukemia face additional challenges affecting QoL. A study conducted in 2017evaluated the HRQoLof children with SD who survived AMLin comparison to children without DS who survived AML. The authors found worse HRQoLin terms of physical and psychosocial aspects in the population with SD in comparison to the general population. However, differences in comparison to the children without DS who survived AMLwere non-significant [25].

HRQoL was assessed in the present study using the PedsQL 4.0 Generic Core) [9,21] and PedsQL3.0 Cancer Module [10,12]. Although the PedsQLis normalized for parents of children two to 18 years of age, the questionnaire was administered taking into consideration that the child developed all actions addressed on the questionnairedespite not having reached two years of age. Lower scores (denoting poorer QoL) were found for emotional functioning (50.00 points), physical functioning (18.75 points), nausea (20.00 points) and procedural anxiety (41.7 points). These results are consistent with findings described in previous studies [25] and were expected, as children with DS have development deficits as well as behavioral and emotional problems.

The interest in a holistic approach to health has been growing. Studies have revealed that including the patient and family in the decision-making process with regards to treatment leads to promising results in terms of the clinical status of the patient as well as the treatment itself [6] PROMs and PREMs are suitable in situations such at that reported in the present case, in which the expectations of the mother regarding the treatment of her son were valued and the impact of the disease and treatment on the family were considered. The perceptions of parents are useful in guiding health services to more humanized care that values each family as unique.

The difficulties faced by individuals with DS and leukemia require the support of a multidisciplinary health team. The present case demonstrates the need for care centered on the patient and family, making these individuals active participants with regards to treatment decisions and more likely to express their needs and opinions to healthcare providers [9]. Patient-centered clinical methods can result in greater patient satisfaction and better adherence to treatment while also providing a greater sense of satisfaction for healthcare providers. Thus, studies should be conducted to assess the QoLof the population with SD and instruments should be developed to measure the QoLof these individuals, contributing to the acquisition of knowledge on the part of caregivers, healthcare providers and policy formulators regarding the needs of children with a diagnosis of DS. However, this study has significant limitations, such as the lack of follow-up until the end of treatment. Without this follow-up, it is difficult to fully assess the effectiveness of the treatment and the long-term impacts on quality of life.

CONCLUSION

According to the mother's perception, physical and functional functioning indicated a higher negative impact on the child's life. Regarding the impact of the disease and cancer treatment on HRQoL, the lowest

scores were in the domains'nausea' and 'anxiety' about the procedure.Although self-report of HRQoL is ideal, mothers' reports in various situations are important to assess HRQoL when the child is not able to respond.While the oral health status was described as fair, intraoral examination revealed an incomplete deciduous dentition with ectopic eruption, as is often the case in children with Down syndrome. Additional considerations are needed to segregate different factors that caused their HRQoL.

Considering the limitations and systemic condition of individuals with Down syndrome, the investigation of their quality of life is essential, especially when such individuals also have a diagnosis of leukemia. An increase in the number of studies on this issue could enable the establishment of measures for improving the quality of life of affected individuals and their families.

Collaborators

AVMV Silva led the collection of the case report, analyzed and interpreted the results and wrote the manuscript, writing - first draft. IZ Freitas conducted data collection with participants and assisted in writing the manuscript. AMC Santos conducted data collection with participants and helped with writing the manuscript. PC Rodrigues, responsible for the patient, supervised and conducted the case report data. SM Paiva conceived, designed and supervised the case report and critically edited the manuscript.

REFERENCES

1. Lisboa KF, Pina RS, Matias CF, Oliveira LAM, Carvalheiro PC, Ferreira TZ, et al. Alterações citomorfológicas na neoplasia de células dendríticas plasmocitoides blásticas: relato de caso. Hematol Transfus Cell Ther. 2020; 42, Sup 2: 139-140. https://doi.org/10.1016/j.htct.2020.10.236
2. Kaczorowska N, Kaczorowski K, Laskowska J, Mikulewicz M. Down syndrome as a cause of abnormalities in the craniofacial region: A systematic literature review. Adv Clin Exp Med. 2019; 28(11):1587-1592. https://doi.org/10.17219/acem/112785.
3. Mustacchi Z, Peres S. Genética baseada em evidências: síndromes e heranças. São Paulo: CID Editora; 2000.
4. Choo CC, Chew PKH, Tan P, Choo JQ, Choo AMH, Ho RC, et al. Health-Related Quality of Life in Pediatric Patients with Leukemia in Singapore: A Cross-Sectional Pilot Study. Int J Environ Res Public Health. 2019; 16(12):2069. https://doi.org/10.3390/ijerph16122069
5. Bao L, Shi C, Lai J, Zhan Y. Impact of humanized nursing care on negative emotions and quality of life of patients with mental disorders. Am J Transl Res. 2021; 13(11):13123-13128.
6. Perazzo MF, Serra-Negra JM, Firmino RT, Pordeus IA, Martins-Junior PA, Paiva SM. Patient-centered assessments: how can they be used in dental clinical trials? Braz Oral Res. 2020;34 Suppl 2:e075. https://doi.org/10.1590/1807-3107bor-2020.vol34.0075
7. Miller D, Steele Gray C, Kuluski K, Cott C. Patient-centered care and patient-reported measures: let's look before we leap. Patient. 2015;8(4):293-299. https://doi.org/10.1007/s40271-014-0095-7
8. Santana MJ, Haverman L, Absolom K, Takeuchi E, Feeny D, Grootenhuis M, et al. Training clinicians in how to use patient-reported outcome measures in routine clinical practice. Qual Life Res. 2015; 24(7):1707-1718. https://doi.org/10.1007/s11136-014-0903-5
9. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr. 2003;3(6):329-341. https://doi.org/10.1367/1539-4409
10. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL in pediatric cancer: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, multidimensional fatigue scale, and cancer module. Cancer. 2002; 94(7):2090-2106. https://doi.org/10.1002/cncr.10428.
11. Carrada CF, Scalioni FAR, Abreu LG, Ribeiro RA, Paiva SM. Impact of oral conditions of children/adolescents with Down syndrome on their families' quality of life. Spec Care Dentist. 2020; 40(2):175-183. https://doi.org/10.1111/scd.12444
12. Scarpelli AC, Paiva SM, Pordeus IA, Ramos-Jorge ML, Varni JW, Allison PJ. Measurement properties of the Brazilian version of the Pediatric Quality of Life Inventory (PedsQL) cancer module scale. Health Qual Life Outcomes. 2008;6:7. https://doi.org/10.1186/1477-7525-6-7

13. Goldsby RE, Stratton KL, Raber S, Ablin A, Strong LC, Oeffinger K, et al. Long-term sequelae in survivors of childhood leukemia with Down syndrome: a childhood cancer survivor study report. Cancer. 2018; 124(3):617-625. https://doi.org/10.1002/cncr.31065

14. Saida S. Evaluation of myeloid leukemia in children with Down syndrome. Int J Hematol. 2016; 103: 365-372. https://doi.org/10.1007//s12185-016-1959-5

15. Mast KJ, Taub JW, Alonzo TA, Gamis AS, Mosse CA, Mathew P, et al. Pathologic features of down syndrome myelodysplastic syndrome and acute myeloid leukemia: a report from the children's oncology group protocol AAML0431. Arch Pathol Lab Med. 2020; 144(4): 466-472. https://doi.org/10.5858/arpa.2018-0526-OA

16. Santos de Faria AB, Silva IH, de Godoy Almeida R, Silva SP, Carvalho AT, Leão JC. Seroprevalence of herpes virus associated with the presence and severity of oral mucositis in children diagnosed with acute lymphoid leukemia. J Oral Pathol Med. 2014; 43(4):298-303. https://doi.org/10.1111/jop.12138

17. Ripert M, Menegaux F, Perel Y, Méchinaud F, Plouvier E, Gandemer V, et al. Familial history of cancer and childhood acute leukemia: a French population-based case-control study. Eur J Cancer Prev. 2007;16(5):466-470. https://doi.org/10.1097/01.cej.0000243849.82232.cb

18. Westergaard T, Andersen PK, Pedersen JB, Olsen JH, Frisch M, Sørensen HT, et al. Birth characteristics, sibling patterns, and acute leukemia risk in childhood: a population-based cohort study. Natl Cancer Inst. 1997; 89(13): 939-947. https://doi.org/10.1093/jnci/89.13.939

19. Suh E, Stratton KL, Leisenring WM, Nathan PC, Ford JS, Freyer DR, et al. Late mortality and chronic health conditions in long-term survivors of early-adolescent and young adult cancers: a retrospective cohort analysis from the Childhood Cancer Survivor Study. Lancet Oncol. 2020; 21(3): 421-435. https://doi.org/10.1016/S1470-2045(19)30800-9

20. Goud EVSS, Gulati S, Agrawal A, Pani P, Nishant K, Pattnaik SJ, et al. Implications of Down's syndrome on oral health status in patients: A prevalence-based study. J Family Med Prim Care. 2021;10(11):4247-4252. https://doi.org/10.4103/jfmpc.jfmpc_885_21

21. Shukla D, Bablani D, Chowdhry A. Dentofacial and cranial changes in down syndrome. Osong Public Health Res Perspect. 2014; 5(6):339-344. https://doi.org/10.1016/j.phrp.2014.09.004

22. Abanto J, Ciamponi AL, Francischini E, Murakami C, de Rezende NP, Gallottini M. Medical problems and oral care of patients with Down syndrome: a literature review. Spec Care Dentist. 2011; 31:197–203. https://doi.org/10.1111/j.1754-4505.2011.00211.x

23. Anders PL, Davis EL. Oral health of patients with intellectual disabilities: a systematic review. Spec Care Dentist. 2010; 30:110-117. https://doi.org/10.1111/j.4505

24. Suri S, Tompson BD, Atenauf E. Prevalence and pattern of permanent tooth agenesis in Down syndrome and their association with craniofacial morphology. Angle Orthod. 2011; 81: 260-269. https://doi.org/10.2319/070910-391.1

25. Abildgaard L, Ellebaek E, Gustafsson G, Abrahamsson J, Hovi L, Jonmundsson G, et al. Optimal treatment intensity in children with Down syndrome and myeloid leukaemia: data from 56 children treated on NOPHO-AML protocols and a review of the literature. Ann Hematol. 2006; 85(5):275-280. https://doi.org/10.1007/s00277-005-0045-5

Received on: 22/1/2024
Final version resubmitted on: 11/6/2024
Approved on: 27/6/2024

Assistant editor: Luciana Butini Oliveira