

## REVIEW

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### Oral and Dental Health in Paediatric Oncology Patients

#### Dila Özyılkan Oral Status of on Oncology Patients

Dila Özyılkan

Department of Pediatric Dentistry, Near East University Faculty of Dentistry, Nicosia, North Cyprus

#### Abstract

It is aimed to underline the importance of recognising that paediatric cancer patients should be referred to paediatric dentists to establish preventive and restorative treatment plans before starting to cancer therapy, as they are highly susceptible to oral health issues. Oral complications are three times more common in paediatric oncology patients than adults and constitute the primary non-hematologic side effect of cytotoxic chemotherapy and radiotherapy. Children undergoing immunosuppressive oncology treatments, are susceptible to developing acute and long-term oral and dental complications. Current guidelines advise that children undergo an oral examination before commencing cancer therapy. A pre-treatment examination helps in forming a dentist-child relationship prior to the emergence of oral complications associated with cancer treatment. According to the American Academy of Paediatric Dentistry these patients are considered as in high-risk group and they should visit dentist in every 3 months. Fluoride serves as a preventive precaution against dental caries and the literature extensively documents the anticariogenic advantages of fluoride therapy. The primary target of paediatric dentist is to educate these patients and their families on preventing oral health problems.

**Keywords:** Cancer, children, healthcare

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**ORCID IDs of the authors:** D.Ö. 0000-0003-4583-0799.

**Address for Correspondence:** Dila Özyılkan

**E-mail:** dila.ozyilkan@neu.edu.tr

**ORCID ID:** orcid.org/0000-0003-4583-0799

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#### Introduction

According to definitions, cancer is the greatest cause of death in affluent countries and the second biggest cause in developing ones (1). Approximately 1 in 285 kids under the age of 20

receive a cancer diagnosis, or 150 out of every million (2). According to cancer incidence studies conducted in the Turkish Republic of Northern Cyprus (TRNC), the increase in the number of new cases emphasizes that some measures should be taken in this regard. Pervaz et al. (3) reported in their article published in 2017 that there was an increase in the number of new cases between 2007 and 2012 compared to previous years. Although no specific results were announced for children in the study, the increase in the number of cases suggests that precautions should be taken in terms of oral health before, during or after treatment. Djamgoz et al. (4) compared the incidences in cancer patients in NCTR with Northern and Southern European values. Although the cancer cases in NCTR are in a similar line with European countries, they suggested that programs for the society be prepared to raise cancer awareness. Sancar et al. (5) reported the cancer incidence in individuals aged 15 and over in their article published in 2017. The cancer types and incidences of the patients who applied to Near East University hospitals between 2010-14 were reported, and since there was no pediatric cancer unit, the age group was reported as 15 years and above.

Ministry of Health of the Turkish Republic of Northern Cyprus reported a survey in 2019 where the case distribution according to age groups (5). In the study, new cases diagnosed between 2012-16 were evaluated. Due to the report the ratio of cases in the 0-14 age group to total cases was found to be 2.3%. The distribution of this age group according to the population is 36%.

Even so, in Cyprus, where more than 1.26 million people live, the first population-based descriptive epidemiology study of childhood and adolescent cancer discovered that the country has one of the highest age-standardized incidence rates per million children and adolescents worldwide for all pediatric malignancies combined (6,7).

According to the American Academy of Paediatric Dentistry (AAPD), pediatric dentists play an important role in the diagnosis, prevention, stabilization, and management of oral and dental conditions that can impair a child's quality of life prior to, during, and following immunosuppressive treatments and/or head and neck radiation (8). Children receiving cancer therapy may have problems with their teeth and oral hygiene both during and after their treatment. Pediatric cancer patients may have dental caries that is not treated, periodontal disease, and/or pathological lesions in the oral hard and soft tissues. In addition, they could experience oral side effects from cancer treatments, show oral cancer symptoms, and experience long-term dental and orofacial problems following cancer therapy (9). For these reasons a team consisting of doctors, nurses, dentists, social workers, dietitians and other medical specialists should work together for children who will receive immunosuppressive therapy and/or head and neck radiation.

### **Oral Manifestations**

A pediatric cancer patient's quality of life is severely impacted by their diagnosis, and their oral hygiene regimen has to be customized based on their disease's stage (10).

The kind of cancer, the features of the treatment received, the age at diagnosis, the kind of chemotherapy, the dosage, and the location of the radiation treatment all affect the potential complications that might arise in the mouth. Oral complications can be increased by factors such as pre-existing caries, gingivitis, and poor hygiene (11,12).

Special short- and long-term complications may occur in childhood cancers, including specific and non-specific oral tissue symptoms. Specific symptoms are seen in mucosa, salivary gland, muscle and bone tissues, taste sensation/dysfunction, teeth and gums. Oral mucositis (OM) and related pain, neurotoxicity, mucosal fibrosis, gingival hypertrophy, osteoradionecrosis, medication-related osteonecrosis, soft tissue necrosis, trismus, secondary tumors, post-transplant lymphoproliferative disorders, dental anomalies and craniofacial changes, dental caries, dry mouth (e.g., salivary gland dysfunction, xerostomia), and dental caries are among the complications (2,8,10,12,13).

While bleeding in the mouth is considered an early symptom in some types of cancer (Acute lymphocytic leukemia (ALL)), it can be more serious with the direct effect of chemotherapy and radiotherapy (14). These drugs cause thrombocytopenia, anemia, and granulocytopenia, increasing the probability of bleeding and susceptibility to infections (15).

**Oral mucositis (OM)** Generally, mucositis occurs between 3- 5 months of cancer treatment. It is seen between days after radiotherapy and before chemotherapy. Clinically, the buccal mucosa may initially take on a whitish colour, but subsequently this condition progresses to erythema and a few days later results in a patchy appearance, also containing fibrinous exudate. If high doses of radiation are administered over a short period of time, ulceration of the covering fibrinous membrane begins earlier (16).

**Opportunistic infections:** Candidiasis and herpes simplex virusinfections are the most common opportunistic infections. As a result of cancer therapies that cause dryness in the mouth, candida species that are normally inactive in the oral soft tissues become active and develop tiny, sticky lesions on the oral mucosa, tongue, and palate.

Members of the herpesviridae family, such as varicella zoster and herpes simplex, can potentially infect people by causing dry mouth. Herpes simplex manifests as ulcerated sores on the palate, gums, corners of the mouth, and lips. Varicella zoster can cause severe morbidity not just from blister lesions on the lips but also from effects on the lungs, central nervous system, and liver (16,17).

**Dental caries:** Neither illness nor therapy directly causes tooth decay. Diseases or treatments do not directly cause tooth decay. Tooth decay develops due to decreased saliva production and flow due to treatments reducing salivary gland function, children's tendency to eat soft and cariogenic foods, changes in oral flora, and unable to maintain oral hygiene due to gingivitis (18). Saliva becomes more acidic due to damage to the salivary glands caused by radiation, which also increases the presence of highly cariogenic oral microbiota including *Lactobacillus* and *Streptococcus mutans* (19).

**Dry mouth:** Hyposalivation (decreased salivation) and/or xerostomia (feeling of dry mouth due to decreased salivation) develop due to salivary gland dysfunction, especially after radiotherapy or chemotherapy (20). The second most frequent adverse effect of chemotherapy is xerostomia. Additionally, it has been demonstrated that there is a clear correlation between radiation dosage and salivary gland decrease. As saliva preserves dental health by shielding the teeth and oral mucosa, malfunction of salivary gland is a significant and sometimes disregarded late consequence that can have a detrimental influence on general health (21,22). Saliva's increased viscosity and slowed flow make it difficult to chew, swallow, and talk. It also stops taste buds from working, which weakens one's perception of taste (23,24).

**Mucosal fibrosis:** Oral submucous fibrosis (OSMF) is a chronic insidious disease that occurs mainly in the oral cavity and is associated with vesicle formation. Pallor, burning feeling, and ulceration of the oral mucosa are the initial signs, followed by recurring stomatitis, xerostomia, and, on rare occasions, leukoplakia, as well as difficulties swallowing or phonating. Fibrosis and hardness develop in the buccal mucosa and tongue, leading to trismus and dysphagia (25).

**Gingival hypertrophy:** Gingival enlargement and ulcerations cause thickening and pseudopocket formation in the gingiva due to treatment-related neutropenia or infiltration due to the increase in blast leukocytes (26). Inflamed gum tissues are the main entry route for bacteria and bacterial products, causing sepsis (27).

**Osteoradionecrosis:** One of radiation therapy's most dangerous consequences is osteoradionecrosis (ORN). It is more prevalent in the mandible than in the maxilla. It is characterized as trauma-induced or spontaneous mucosal degradation leading to a succession of radiations, hypovascular, hypocellular, hypoxic tissue development, and a non-healing wound (28).

**Medication-related osteonecrosis:** In cases when there is no history of radiation therapy or metastatic disease, it appears as exposed bone in the craniofacial area for over eight weeks. The most significant protective factor against MRONJ may be the biological and physiological conditions involved in bone production and growth, as well as the proper dental and oral environments (29).

**Trismus:** It is a complication characterized as the inability to completely open the mouth and has the potential to cause major morbidity and death (30). According to reports, 5% to 38% of individuals with head and neck cancer suffer trismus following radiation. Radiotherapy treatment can induce muscular fibrosis, loss of bone growth due to radionecrosis, and inadequate development, culminating in jaw dysfunction (31).

**Craniofacial and dental developmental anomalies:** Morphogenesis and calcification of teeth begins in the 5th week of IU life and continues for 14-15 years. During this period, with cancer treatment lasting 1-2 years, complications such as hypodontia, microdontia, regression in root development, hypoplasia, hypomineralization, and premature tooth eruption develop (32).

**Dental Protocols:** All patients receiving chemotherapy (immunosuppressive) treatment and/or patients who will receive head and neck radiation should be referred to a pedodontist for condition assessment and precautions planning before starting treatment (33,34)

The following parameters may be used to guide decisions regarding need for antibiotic prophylaxis (8,35-39).

Patients having cancer therapy are at risk of thrombocytopenia. The following factors can be used to identify the requirement for pre- and post-operative interventions. (8, 38, 39).

Pediatric dentists should evaluate the patient's oral health after determining their general health condition. They keep track of dental hygiene practices, dietary patterns, trauma history, and fluoride exposure through fluoridated water/salt or fluoride supplements (pills, gel, or varnish). Extra-oral and intra-oral examination is performed and necessary x-rays are taken. According to examination results pediatric dentist decides preventive and restorative treatment plan. When possible, dental care should be finished before starting cancer therapy. Fernandez-Pujante et al reported a review after searching 114 scientific articles from the databases. They have used 29 articles to obtain the protocols for Pediatric Patients Receiving Immunosuppressive Therapy and/or Radiation Therapy.

The protocols determined the applications in 3 phases (10).

**Phase 1:** From the Diagnosis of Cancer to Initiation of Chemo/Radiotherapy.

**Phase 2:** From the Initiation of Chemotherapy or Radiotherapy until 30–45 Days Post-Therapy.

**Phase 3:** Begins after Cancer Treatment and May Last from 1–2 Years to the Whole Life.

AAPD also made a similar classification and listed recommendations (8).

In the initial phase, both the AAPD and Fernandez-Pujante et al. noted that the main priority should be determined and eradicate potential causes of infection and local irritants in the oral cavity in order to avoid delaying cancer therapy or causing additional issues. Another goal should be to educate patients and parents about the need of providing good dental care in order to avoid issues that might jeopardize the cancer treatment process. It should not be overlooked that communication with the appropriate medical team about the patient's oral health state, treatment plan, and timing is critical. To advise patients/parents about the potential short- and long-term negative effects of cancer therapy in the oral cavity and craniofacial complex (8,10).

In general, the preventive program should include teaching brushing methods, using dental floss, recommending mouthwashes, diet analysis and recommendations, topical fluoride applications, use of lip protectors, using preventive agents against fungal infections,

recommendations for preventing trismus, ensuring that protective measures are taken in radiotherapy to be applied in the head and neck region, and education (7, 9).

Dental procedures must be finished within 7-10 days before beginning chemotherapy or radiation therapy. If this is not possible or is delayed, non-acute teeth should have temporary restorations and therapies undertaken. When deciding on dental treatments, more radical decisions like extraction should be made for teeth that will pose a risk during cancer treatment. Appliances that may cause injury in the mouth should not be used. Impacted teeth and persistent primary teeth should be eliminated before starting treatment. It is recommended to extract teeth with a poor prognosis two weeks, or at least seven to ten days, prior to the start of cancer treatment (8,10).

In order to avoid the potential side effects of cancer therapy, patients should be instructed to consume a minimum of two liters of water daily. Lip protective agents should be applied to the lips regularly, chewing sugar-free gum should be recommended to stimulate saliva flow, artificial saliva or pharmacological stimulants should be prescribed, and regular dentist check-ups should be recommended (8,10).

The second phase focuses on where chemotherapy or radiotherapy has begun and lasts until 30-45 days after treatment. This phase should focus on maintaining good oral health throughout cancer treatment, treating any oral side effects or complications, and educating patients and parents about the value of maintaining good oral hygiene to reduce discomfort from oral issues both during and after cancer treatment (8,10).

In this phase, the dentist should contribute to the multidisciplinary treatment plan. It should be checked whether the patient maintains oral hygiene practices, and the presence of secondary acute injuries should be checked 1-2 weeks after the start of cancer treatment. To ensure the continuation of oral health, it should be checked whether all the preventive practices recommended in the first phase are continued, and if pediatric dentists are met with the patient at this stage, these suggestions and practices should be implemented (8,10).

At this stage, specific symptoms of the oral mucosa should be examined. In the presence of mucositis, it is recommended to patients to stay away from the acidic, spicy, hard, hot and irritating foods. Because mucositis causes pain in the patient, cryotherapy (ice chips), saline 0.9% rinses, topical anaesthetics, or mucous rinses containing anaesthetics such as benzocaine (aerosol, gel), lidocaine 2% (viscous, ointment, or aerosol), diphenhydramine, and dyclonine hydrochloride 0.5 or 1.0% solution-Dyclonine) should be recommended. In cases of severe mucositis, nonopioid and opioid analgesics, as well as low-power laser treatment, are preferred. To treat secondary infections, your dentist may prescribe allopurinol, leucovorin, or nystatin.

If particular musculoskeletal difficulties emerge that limit mouth opening, regular stretching of masticatory muscles, muscle relaxants, and analgesics should be advised. If local bleeding is detected in the gums, tamponade with sterile gauze, topical hemostatic agents should be recommended, and in case of systemic bleeding problems, surgical procedures and block local anesthesia should be avoided.

In this stage, if a patient requires dental care, only procedures for emergencies should be performed in-hospital following a collaborative evaluation with the cancer team to determine the best time to administer the treatment (during the intervals between cancer treatment cycles, when the patient's hemoglobin level is more constant, or by utilizing local or systemic hemostatic procedures and antibiotic prophylaxis) (8, 10, 39).

"Begins after cancer treatment and may last from 1-2 years to the whole life" is the definition of the third phase. The goal of this phase is to preserve ideal oral health following cancer treatment, manage oral problems or long-term oral side effects caused by cancer therapy, and improve patient/parent education on the need of lifelong excellent oral hygiene (8,10).

To maintain the preventive strategies, dentist should continue with patient/parent training and general oral maintenance and prevention measures. All topical fluoride applications, mouthwash recommendations, and use of bicarbonate solution should be continued. The patient should maintain regulated dietary habits and continue trismus preventive exercises. Non-invasive dental treatments should be applied in the first year, and orthodontic treatment should be started at least 2 years later. Maintaining correct hydration, applying lip lubricants should be continued.

### **CONCLUSION**

Using standard protocols that prioritize prevention from the early stages to prevent or minimize complications that cancer treatments may cause in the mouth can improve children's quality of life.

For this reason, the importance of teamwork in cancer treatments should be frequently emphasized among healthcare professionals, and the contribution of pedodontists who will be part of this team should be taken into account. In order to contribute to the quality of life of children who undergo a difficult treatment process, relevant specialist organizations need to work together to develop protocols that will be applied as standard in all pediatric oncology centers.

### **MAIN POINTS**

- Main point of review is to underline the importance of coordinated work of pediatric oncology and pedodontics at early stages of cancer treatment, in order to prevent further complications.
- Most common oral manifestations that can occur during cancer treatment
- To form standardized dental prevention protocol for pediatric patients to be followed

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<b>Table 1. Antibiotic prophylaxis according to absolute neutrophil counts</b>	
<b>ANC*</b>	<b>Antibiotic prophylaxis</b>
— > 2,000 per cubic millimeter /mm <sup>3</sup>	No requirement for antibiotic prophylaxis



1,000 to 2,000/mm <sup>3</sup>	Apply clinical judgment based on the patient's health and scheduled operations
< 1,000/mm <sup>3</sup>	Defer elective dental treatment. Before beginning treatment in a dental emergency, consult with the medical team on whether to use a course of antibiotics or just one dosage for preventive coverage
*ANC: Absolute neutrophil count	

**Table 2.** Suggestions as per platelet count

Platelet count	Suggestion
>75,000/mm <sup>3</sup>	Does not require any further assistance to carry out the dental procedure
40,000–75,000/mm <sup>3</sup>	Platelet transfusion is necessary before and 24 hours after dental treatment. If the therapy includes bleeding, haemostatic measures such as local haemostatic drugs, sutures, sterile gauze to compress the bleeding location, and/or microfibrillar collagen sponges will be necessary
— < 40,000/mm <sup>3</sup>	In the event of an emergency, dental treatment must be postponed. The medical team must also determine whether to treat the patient in a hospital with platelet transfusion, additional bleeding control medication, and bleeding control measures (sutures, sterile compression gauzes, microfibrillar collagen sponges, and local hemostatic agents like topical thrombin).
	Before beginning dental treatment, the dentist should speak with the hematologist about the necessity of a posttransfusion platelet count if platelet transfusions are used. It would be preferable to have extra transfusions on hand in case of severe and protracted intraoperative or postoperative bleeding