

# Oral and Dental Health in Pediatric Oncology Patients

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## Abstract

This study aimed to underline the importance of recognizing that pediatric cancer patients should be referred to pediatric dentists to establish preventive and restorative treatment plans before starting cancer therapy, as they are highly susceptible to oral health issues. Oral complications are three times more common in pediatric oncology patients than in adults and constitute the primary non-hematologic side effects of cytotoxic chemotherapy and radiotherapy. Children undergoing immunosuppressive oncology treatments are at risk of acute and long-term oral and dental complications. Current guidelines recommend that children undergo an oral examination before commencing cancer therapy. 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 Pediatric Dentistry, these patients are considered high-risk patients and they should visit the dentist every 3 months. Fluoride is a preventive measure against dental caries, and the literature extensively documents the anticariogenic advantages of fluoride therapy. The primary objective of pediatric dentists is to educate pediatric patients and their families on the prevention of oral health problems.

**Keywords:** Cancer, children, healthcare

## INTRODUCTION

According to definitions, cancer is the leading cause of death in affluent countries and the second leading cause in developing countries.<sup>1</sup> Approximately 1 in 285 children under the age of 20 receive a cancer diagnosis, or 150 out of every million.<sup>2</sup> According to cancer incidence studies conducted in the Turkish Republic of North Cyprus (TRNC), the increase in the number of new cases highlights the need for some measures to be taken in this regard. Pervaiz et al.<sup>3</sup> reported in their article published in 2017 that there was an increase in the number of new cases between 2007 and 2012 compared with 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.<sup>4</sup> compared the incidence of cancer in patients with National Centre for Truth and Reconciliation (NCTR) with those in Northern and Southern European countries. Although the cancer cases in NCTR are in a similar line with those in European countries, they suggested that programs should be prepared to raise cancer awareness.

Sancar et al.<sup>5</sup> reported cancer incidence in individuals aged 15 years and older in their article published in 2017. The cancer types and incidences of the patients who applied to the 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 older.

The Ministry of Health of the TRNC reported a survey in 2019 in which the case distribution was based on age groups.<sup>5</sup> In the study, new cases diagnosed between 2012 and 2016 were evaluated. The ratio of cases in the 0-14 age group to total cases was 2.3%. The distribution of this age group according to the population was 36%.

Nevertheless, 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.<sup>6,7</sup>

According to the American Academy of Pediatric Dentistry (AAPD), pediatric dentists play an important role in the diagnosis, prevention,

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stabilization, and management of oral and dental conditions that can impair a child's quality of life before, during, and after immunosuppressive treatments and/or head and neck radiation.<sup>8</sup> Children receiving cancer therapy may have problems with their teeth and oral hygiene during and after treatment. Pediatric patients with cancer may have dental caries that are not treated, periodontal disease, and/or pathological lesions in the oral hard and soft tissues. In addition, patients may experience oral side effects from cancer treatments, show oral cancer symptoms, and experience long-term dental and orofacial problems following cancer therapy.<sup>9</sup> 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 must be customized based on their disease's stage.<sup>10</sup>

The type of cancer, features of the treatment received, age at diagnosis, type of chemotherapy, dosage, and 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.<sup>11,12</sup>

Special short- and long-term complications, including specific and non-specific oral tissue symptoms, may occur in childhood cancers. Specific symptoms are seen in the mucosa, salivary gland, muscle and bone tissue, taste sensation/dysfunction, teeth, and gums. Oral mucositis (OM) and related pain, neurotoxicity, mucosal fibrosis, gingival hypertrophy, osteoradionecrosis (ORN), 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.<sup>2,8,10,12,13</sup>

Although bleeding in the mouth is considered an early symptom in some types of cancer (such as acute lymphocytic leukemia, it can be more serious with the direct effect of chemotherapy and radiotherapy.<sup>14</sup> These drugs can cause thrombocytopenia, anemia, and granulocytopenia, increasing the probability of bleeding and susceptibility to infections.<sup>15</sup>

OM generally, mucositis occurs between 3 and 5 months after cancer treatment. It occurs between days after radiotherapy and before chemotherapy. Clinically, the buccal mucosa may initially take on a whitish color, but subsequently, this condition progresses to erythema and a few days later results in a patchy appearance that also contains fibrinous exudate. If high-dose radiation is administered over a short period, ulceration of the covering fibrinous membrane begins earlier.<sup>16</sup>

**Opportunistic infections:** Candidiasis and herpes simplex virus infections 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 only

from blister lesions on the lips but also from effects on the lungs, central nervous system, and liver.<sup>16,17</sup>

**Dental caries:** Neither illness nor therapy directly causes tooth decay. Diseases and treatments do not directly cause tooth decay. Tooth decay develops due to decreased saliva production and flow due to treatments that reduce salivary gland function, children's tendency to eat soft and cariogenic foods, changes in oral flora, and an inability to maintain oral hygiene due to gingivitis.<sup>18</sup> 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*.<sup>19</sup>

**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.<sup>20</sup> The second most common 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 the salivary gland is a significant and sometimes disregarded late consequence that can have a detrimental influence on general health.<sup>21,22</sup> Increased viscosity and slowed flow in saliva make it difficult to chew, swallow, and talk. It also stops taste buds from working, which weakens one's perception of taste.<sup>23,24</sup>

**Mucosal fibrosis:** Oral submucosal fibrosis is a chronic insidious disease that occurs mainly in the oral cavity and is associated with vesicle formation. Pallor, burning sensations, and ulceration of the oral mucosa are the initial signs of this condition, 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.<sup>25</sup>

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

**Osteoradionecrosis:** One of radiation therapy's most dangerous consequences is ORN. It is more common in the mandible than in the maxilla. It is characterized by trauma-induced or spontaneous mucosal degradation leading to a succession of radiation, hypovascular, hypocellular, and hypoxic tissue development, and a non-healing wound.<sup>28</sup>

**Medication-related osteonecrosis:** In patients without a history of radiation therapy or metastatic disease, it appears as exposed bone in the craniofacial area for >8 weeks. The most significant protective factors against MRONJ include the biological and physiological conditions involved in bone production and growth, as well as the proper dental and oral environment.<sup>29</sup>

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

**Craniofacial and dental developmental anomalies:** Morphogenesis and calcification of teeth begin in the 5<sup>th</sup> 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.<sup>32</sup>

**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 precaution planning before starting treatment.<sup>33,34</sup>

The following parameters can be used to guide decisions regarding the need for antibiotic prophylaxis (Table 1).<sup>8,35-39</sup>

Patients receiving cancer therapy are at risk of thrombocytopenia. The following factors can be used to identify the requirement for pre- and post-operative interventions (Table 2).<sup>8,38,39</sup>

Pediatric dentists should evaluate patients’ oral health after determining their general health. 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 examinations are performed, and necessary radiography is performed. According to examination results, pediatric dentists decide

preventive and restorative treatment plans. When possible, dental care should be completed before initiating cancer therapy.

Ferrández-Pujante et al.<sup>10</sup> reported a review after searching 114 scientific articles in the databases. They used 29 articles to obtain protocols for pediatric patients receiving immunosuppressive therapy and/or radiation therapy.

The protocols determined the applications in 3 phases.<sup>10</sup>

Phase 1: From the diagnosis of cancer initiate chemo/radiotherapy.

Phase 2: Initial 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.<sup>8</sup>

In the initial phase, both the AAPD and Ferrández-Pujante et al.<sup>10</sup> noted that the primary priority should be identifying and eradicating potential causes of infection and local irritants in the oral cavity to avoid delaying cancer therapy or causing additional issues. Another goal should be to educate patients and parents about the need for good dental care to avoid issues that might jeopardize the cancer treatment process. It should not be overlooked that communication with an appropriate medical team regarding the patient’s oral health status, treatment plan, and timing is critical. To inform patients/parents about the potential short- and long-term negative effects of cancer therapy in the oral cavity and craniofacial complex.<sup>8,10</sup>

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, use of 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.<sup>7,9</sup>

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

To avoid 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 checkups should be recommended.<sup>8,10</sup>

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, addressing any oral side effects or complications, and educating patients

Table 1. Antibiotic prophylaxis according to absolute neutrophil counts	
ANC*	Antibiotic prophylaxis
— >2,000 per cubic millimeter/mm <sup>3</sup>	No requirement for antibiotic prophylaxis
1,000-2,000/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 initiating treatment in a dental emergency, consult with the medical team about whether to administer a course of antibiotics or just one dose for preventive purposes.

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 involves bleeding, hemostatic measures such as local hemostatic drugs, sutures, sterile gauze to compress the bleeding location, and/or microfibrillar collagen sponges will be necessary.
— <40,000/mm <sup>3</sup>	Dental treatment must be postponed in the event of an emergency. 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 post-transfusion platelet count if platelet transfusions are used. It would be preferable to have extra transfusions in case of severe and protracted intraoperative or postoperative bleeding.

and parents about the value of maintaining good oral hygiene to reduce discomfort from oral issues both during and after cancer treatment.<sup>8,10</sup>

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 assessed whether all the preventive practices recommended in the first phase are continued, and if pediatric dentists meet with the patient at this stage, these suggestions and practices should be implemented.<sup>8,10</sup>

At this stage, the specific symptoms of the oral mucosa should be examined. In the presence of mucositis, it is recommended that pet owners stay away from acidic, spicy, hard, hot, and irritating foods. Because mucositis causes pain, cryotherapy (ice chips), saline 0.9% rinses, topical anesthetics, or mucous rinses containing anesthetics 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, non-opioid and opioid analgesics as well as low-power laser therapy 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 the masticatory muscles, muscle relaxants, and analgesics should be administered. If local bleeding is detected in the gums, tamponade with sterile gauze and topical hemostatic agents should be recommended. In case of systemic bleeding problems, surgical procedures and blockage of 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).<sup>8,10,39</sup>

"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 and parent education regarding the need for lifelong excellent oral hygiene.<sup>8,10</sup>

To maintain preventive strategies, dentists should continue with patient/parent training and general oral maintenance and prevention measures. The use of topical fluoride applications, mouthwash recommendations, and bicarbonate solution should be continued. The patient should maintain regulated dietary habits and continue trismus-preventing exercises.

Non-invasive dental treatments should be initiated in the first year, and orthodontic treatment should be started at least 2 years later. Maintaining proper hydration requires the application of lip lubricants.

## 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 treatment should be frequently emphasized among healthcare professionals, and the contribution of pedodontists who will be part of this team should be considered. 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 can 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.

## ETHICS

## DISCLOSURES

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