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# Dental caries among childhood cancer survivors

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**Abstract**

One of many possible complications of cancer therapy in children is enamel demineralization and such changes in the ion content of dental hard tissues may increase susceptibility to caries. The study aims to assess the prevalence of dental caries among childhood cancer survivors.

A cross-sectional study was conducted on 225 children aged between 4 and 18 years, including 75 cancer patients and 150 sex- and age-matched controls. The cancer survivors were recruited from single pediatric oncology center. The control group was formed from students of randomly selected kindergartens and schools. Dental investigation was held between July 2013 and January 2016, approximately 5 years after the cessation of anticancer treatment (range: 6–155 months). The occurrence of dental caries was assessed with DMF/dmf index (showing the mean number of decayed, missing and filled permanent/deciduous teeth). Univariate statistical approach was performed and $P$-values $< .05$ were considered as statistically significant.

The frequency of dental caries was comparable in both groups (85.4% vs 84%). However, the DMF index was higher in cancer patients than in controls: the median and interquartile ranges were 2 (0–4) vs 0 (0–2); $P < .01$. This correlates with duration of anticancer therapy ($r = 0.26$; $P < .05$). Moreover, children who had radiotherapy of the head and neck regions had significantly higher DMF scores than the ones who did not: 4.5 (1–6) vs 2 (0–4); $P < .05$. Socioeconomic and education status within family also has a significant impact on DMF scores in the cancer group. In conclusion, cancer patients, particularly those with a poor social background, should receive professional dental care as their caries process is more active than that of healthy peers.

**Abbreviations:** ALL = acute lymphoblastic leukemia, ANLL = acute non-lymphoblastic leukemia, B-NHL = B-cell non-Hodgkin's lymphoma, D (d) = decayed tooth, dmf = average number of decayed, missing and filled deciduous teeth, DMF = average number of decayed, missing and filled permanent teeth, F (f) = filled tooth, Gy = Grays, HL = Hodgkin's lymphoma, M (m) = missing tooth, PI = Plaque Index, PNET = primitive neuroectodermal tumor, RMS = Rhabdomyosarcoma.

**Keywords:** cancer survivors, children, dental caries, dental examination

## 1. Introduction

About 8 million children aged under 18 live in Poland, 1100 to 1200 of whom develop malignancies annually.[1] Progress in contemporary medicine has led to an increased survival rate among cancer patients, but up to 40% suffer from late complications of oncologic treatment, including heart failure, neurotoxicity, nephrotoxicity, growth impairment, hormonal disorders, and secondary cancers.[2]

Children and adolescents are of particular risk of developing long-term complications; particularly those associated with teeth, as cancer treatment occurs during the most active stage of organ development. As the formation of primary teeth starts in utero and continues over the next 3 to 4 years, primary tooth germs are rarely damaged during cancer therapy. However, permanent teeth undergo hard tissue formation early in life, with the first molar teeth hardening soon after birth, and finishes at the age of 14 to 16 years with the root completion of second molars, or even 18 to 25 years for third molars.[3]

As presecretory odontoblasts undergo rapid division during odontogenesis in children, they are particularly vulnerable to the negative effects of alkylating agents or radiation.[4] The sequential events of dentin calcification are followed by the formation and growth of enamel crystals which obtain calcium and phosphorus ions from calcified collagen fibrils.[5] If the process is disturbed, the mineralization of the enamel may be impaired, which clinically appears as opacities or increased susceptibility to caries. Moreover, the development of the tooth may also be disturbed by anticancer treatment, resulting in a shortage of roots, microdontia, or even oligodontia.[6,7]

Children are three times more likely than adults to develop oral complications such as mucositis, xerostomia, bleeding, and infections during cancer treatment.[8] Cancer patients may require diet modifications or parenteral nutrition during long-term therapy. Periods of acute pain of the oral mucosa may also lead to negligence in everyday oral hygiene habits. Although special attention is devoted to alleviating pain within the oral cavity using anesthetic rinses and gels, the patients, their parents,

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and medical staff often demonstrate unsatisfactory awareness of the potential dangers of caries development.

The selection of contemporary papers describing prevalence of dental caries in childhood cancer survivors is scarce, and most available studies have been performed before 2000. Therefore, the aim of the study was to provide a more recent assessment of the incidence of dental caries in cancer survivors and to identify the variables that can influence their dental state.

## 2. Material and methods

### 2.1. Study groups description

The children included to the study had been treated for cancer in the Department of Pediatrics, Oncology, Hematology and Diabetology, Medical University of Lodz. They were recruited through an ongoing program for the assessment of late adverse effects of anticancer treatment in survivors of childhood cancers.

Of the 109 cancer survivors included in the program, 75 received a dental examination as part of the study: 31 patients (28.4%) did not respond to the call and 3 children refused to participate. Dental examination was performed approximately 5 years (range: 6–155 months) after the cessation of anticancer treatment, with the youngest patient being 47 months old (4 years) and the oldest 215 months (18 years). The patients were dentally examined in the Department of Pediatrics and Orthodontics of the Institute of Dentistry, Medical University of Lodz between July 2013 and January 2016.

The control group was formed from students of randomly selected classes from local kindergartens, primary schools, and high schools. An initial group of 296 healthy children aged between 4 and 18 years were dentally examined during a time period corresponding to the recruitment of the cancer survivors group. After completion of recruitment, the patients were matched in a 1:2 ratio with healthy controls using the propensity score procedure described in Section 2.2. In total, 225 children (75 with cancer and 150 control patients) were entered into the study.

Ethical approval for the study (IRB No. RNN/37/13/KE) was provided by the Bioethics Committee of the Medical University of Lodz on February 19, 2013. Written informed consent for dental examination was obtained from both parents or guardians and patients above the age of 16.

In both groups, the incidence of caries was estimated according to the dmf index in deciduous teeth or DMF index in permanent teeth (number of decayed + missing + filled teeth). In cancer survivors, oral hygiene was also assessed according to Plaque Index (PI) by Silness-Löe.[9] The PI was graded as follows: 0 – no plaque, 1 – plaque visible after usage of dye, 2 – plaque can be seen with the naked eye, 3 – abundance of plaque.

In the cancer group, several variables connected with the risk of caries were studied with a questionnaire. The variables were chosen based on an earlier paper[10] and included the following: socioeconomic background, duration of breast and bottle feeding, number of meals per day, frequency of eating sweets, age at the start of brushing teeth, frequency of brushing teeth, age at first dental visit, frequency of dental visits, and usage of additional preventive aids in everyday oral care. The influences of type of chemotherapy and radiotherapy used, length of therapy, and type of neoplasm on caries incidence were also investigated.

### 2.2. Statistical analysis

Normally distributed variables were summarized as means with standard deviations, while non-normally distributed or ordinal variables were presented as medians and 25 to 75 percentile ranges. Normality was evaluated using the Shapiro–Wilk test. Outcome variables (DMF and the respective subcategories), due to their ordinal nature, were compared using non-parametric tests: the Mann–Whitney $U$ test was used for two group comparisons, Spearman's rank correlation test for correlation assessment, or Kruskal–Wallis test for multiple group comparisons (followed by Dunn-Bonferroni post hoc testing in case of significance). Propensity score matching was performed using a K-nearest neighbors procedure ($K=3$) with propensity scores calculated on the basis of patient age and sex. $P$-values lower than .05 were considered as statistically significant.

## 3. Results

### 3.1. Diseases and time of treatment

Most cancer patients (68%) suffered from acute lymphoblastic leukemia (ALL), Wilms tumor or neuroblastoma. Other patients had acute non-lymphoblastic leukemia (ANLL), B-cell non-Hodgkin's lymphoma (B-NHL), Hodgkin's lymphoma (HL), Rhabdomyosarcoma (RMS), primitive neuroectodermal tumor (PNET), germinal or brain tumors, ovarian tumor, or hepatoblastoma (Table 1). The youngest child was 1 month at the onset of disease while the oldest was 196 months (16 years). On average, anticancer therapy lasted 18.2 months (range: 1–47 months).

### 3.2. Number of teeth affected by dental caries in the study groups

Among the cancer survivors, seven children had deciduous dentition, 43 had mixed dentition, and the remaining 25 children had only permanent teeth. Eleven (14.6%) cancer survivors and 24 (16%) control children were free from caries. The cancer survivor group had significantly more deciduous teeth with active caries (d) ($P<.05$) and more teeth extracted because of caries (m) ($P<.01$) than the children from the control group. On the other hand, they had fewer deciduous teeth filled (f) than controls ($P<.001$). In older children, the difference in caries incidence was even more pronounced. The total DMF score was higher among cancer survivors ($P<.01$) and they also had more teeth filled (F) than the healthy controls ($P<.05$). The numbers of missing teeth (M) were low and similar in both groups. The details are presented in Table 2.

**Table 1**

**Distribution of cancer type among patients.**

| Disease | Girls | Boys | Total |
|---|---|---|---|
| Acute lymphoblastic leukemia (ALL) | 8 | 23 | 31 (41.33%) |
| Wilms tumor | 6 | 5 | 11 (14.66%) |
| Neuroblastoma | 3 | 6 | 9 (12%) |
| Rhabdosarcoma (RMS) | 1 | 5 | 6 (8%) |
| Brain tumor | 3 | 2 | 5 (6.66%) |
| Hepatoblastoma | 0 | 3 | 3 (4%) |
| Acute non-lymphoblastic leukemia (ANLL) | 1 | 2 | 3 (4%) |
| Non-Hodgkin's lymphoma (B-NHL) | 0 | 2 | 2 (2.66%) |
| Hodgkin's lymphoma (HL) | 0 | 2 | 2 (2.66%) |
| Primitive neuroectodermal tumor (PNET) | 0 | 1 | 1 (1.33%) |
| Germinal tumour | 0 | 1 | 1 (1.33%) |
| Tumor ovari | 1 | 0 | 1 (1.33%) |
| Total | 23 | 52 | 75 (100%) |

**Table 2**

**Prevalence of caries express with decayed (d), missing (m), and filled (f) deciduous teeth and decayed (D), missing (M), and filled (F) permanent teeth.**

| Variable | Cancer | | Controls | | *P*-value |
|---|---|---|---|---|---|
| | Mean ± SD* | Median (25–75%) | Mean ± SD* | Median (25–75%) | |
| d | 3.7 ± 3.83 | 3 (1–6) | 2.28 ± 2.59 | 1 (0–4) | **0.0319** |
| m | 0.46 ± 0.27 | 0 (0–0) | 0.03 ± 0.27 | 0 (0–0) | **0.0023** |
| f | 0.86 ± 1.34 | 0 (0–2) | 1.81 ± 1.92 | 1 (0–3) | **0.0009** |
| dmf | 5.02 ± 4.1 | 4 (1–8) | 4.14 ± 2.94 | 4 (2–6) | 0.3722 |
| D | 1.36 ± 2.52 | 0 (0–2) | 0.94 ± 1.97 | 0 (0–1) | 0.0588 |
| M | 0.05 ± 0.34 | 0 (0–0) | 0.02 ± 0.2 | 0 (0–0) | 0.7388 |
| F | 1.17 ± 1.79 | 0 (0–2) | 0.63 ± 1.23 | 0 (0–1) | **0.0433** |
| DMF | 2.60 ± 3.14 | 2 (0–4) | 1.59 ± 2.79 | 0 (0–2) | **0.0053** |

SD = standard deviation.
* Data not included in statistical analysis.

### 3.3. The association between type of cancer, type of anticancer treatment, and dental status

No significant associations were noted between the type of diagnosed cancer and activity of caries (data not shown). Ten patients in the group underwent additional radiotherapy of the head and neck region (dosing 12–54 Gy). Four of them had ALL, three had RMS, two had brain tumors, and one had ANLL. These patients had significantly higher scores of deciduous teeth filled (f) and higher scores of DMF and D in permanent teeth ($P < .05$) (Table 3). The activity of caries positively correlated with the duration of anticancer treatment, evidenced by correlations with F scores ($r = 0.30$; $P < .05$) and DMF score ($r = 0.26$; $P < .05$) (Table 4 and Figs. 1 and 2).

**Table 3**

**Influence of radiotherapy on prevalence of caries.**

| Variable | No RTX | With RTX | *P*-value |
|---|---|---|---|
| d | 3 (0.5–6.5) | 2.5 (1–4) | 0.762965 |
| m | 0 (0–0) | 0 (0–0) | 0.747707 |
| f | 0 (0–1) | 2 (1–3) | **0.012871** |
| dmf | 4 (1–8) | 5 (4–6) | 0.499063 |
| D | 0 (0–2) | 2 (0–3) | **0.043573** |
| M | 0 (0–0) | 0 (0–0) | 0.574069 |
| F | 0 (0–2) | 1.5 (0–2) | 0.230553 |
| DMF | 2 (0–4) | 4.5 (1–6) | **0.048725** |

RTX = radiotherapy of head and neck region.

**Table 4**

**Correlation between caries scores and duration of anticancer treatment. The value of number refers to the type of dentition (deciduous or permanent).**

| Variable | Number | Spearman's rank correlation coefficient | *P*-value |
|---|---|---|---|
| d | 50 | −0.211031 | 0.141264 |
| m | 50 | 0.238176 | 0.095788 |
| f | 50 | 0.106054 | 0.463547 |
| dmf | 50 | −0.060700 | 0.675401 |
| D | 68 | 0.155800 | 0.204545 |
| M | 68 | 0.086755 | 0.481767 |
| **F** | **68** | **0.301600** | **0.012439** |
| **DMF** | **68** | **0.266063** | **0.028305** |

### 3.4. Oral hygiene and its influence on number of affected teeth

Cancer survivors were divided into two groups depending on PI score: children with visible dental plaque ($PI > 1$) and those without or little plaque ($PI < 1$). Forty (53.3%) cancer patients had visible dental plaque and they had more deciduous teeth with active caries (d) and more teeth extracted because of caries (m); $P < .05$. The total number of permanent teeth affected by caries (DMF) was also higher ($P < .05$) among the patients with dental plaque. The details are shown in Table 5.

### 3.5. The socioeconomic and education status of family members in relation to dental caries activity in children

A few social factors were found to have a statistically significant influence on the intensity of caries of permanent teeth in cancer patients. Twelve children whose father had a higher education level had lower scores of DMF (0 (0–0)), than those whose father had a secondary (2 (0–4)) or elementary education (3.5 (0–6)) ($P < .05$); (24 and 12 children respectively). Twenty-one children whose mother had a higher education had lower DMF scores (2 (0–3.5)) than those whose mother had a secondary (3 (0–4)) or primary education (3 (0–5)), $P < .01$; (18 and 9 children respectively). Thirty-four children whose previous dental checkup occurred within 6 months of the date of our dental examination had lower DMF scores (0 (0–3)) than 14 of those whose visit had been earlier (3.5 (2–6)), $P < .01$. The age at the first dental visit was also found to have a statistically significant influence on caries activity at later ages. Thirty children whose first dental visit had been when they were younger than 2 years had lower DMF scores (0 (0–2)) than 12 children whose first visit had been at a later age (2 (0–4)), $P < .01$. Twenty-five children whose teeth were regularly brushed before the age of 2 years had better permanent teeth than 20 children who started brushing later: 0 (0–3) vs 3 (0–5); $P < .05$.

Cancer survivors who brushed their teeth "more often than once a day" had lower DMF scores than those who brushed their teeth "once or seldom", but the relationship was not significant. No significant associations were also noted between the declared frequency of brushing teeth and PI values. The frequency of eating sweets ("never" vs "few times a week" vs "everyday") was not reflected in caries indices.

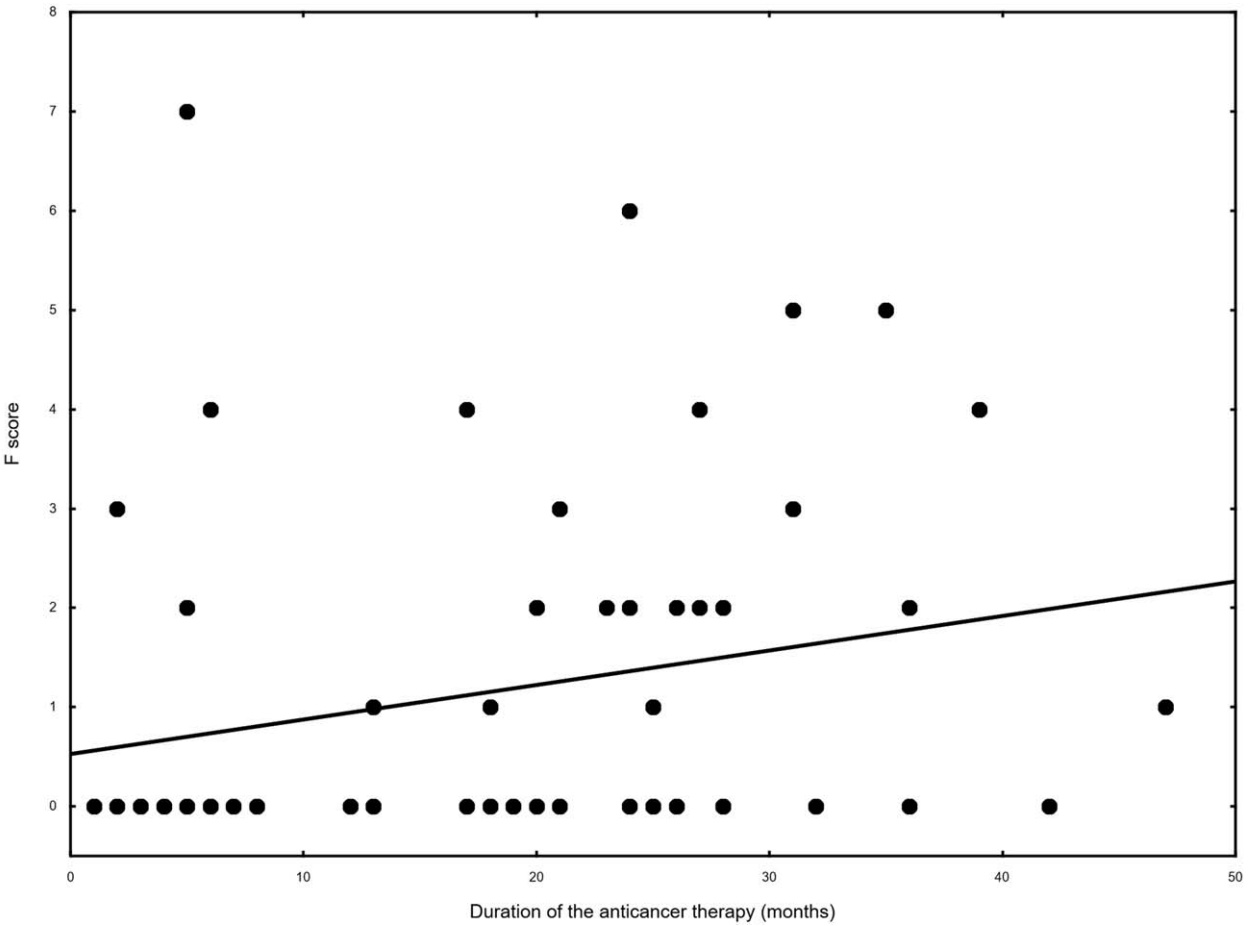


**Figure 1.** Correlation between the duration of the anticancer therapy (in months) and the number of permanent teeth filled, defined as F scores, among the pediatric cancer survivors. The activity of caries positively correlated with the duration of anticancer treatment, evidenced by correlations with F scores ($r = 0.30$; $P < .05$).

## 4. Discussion

In the present study, similar frequencies of caries were observed in the cancer and control groups (85.4% vs 84%), and the overall mean dmf score in deciduous teeth did not differ significantly between the groups. However, the cancer survivors had significantly more deciduous teeth with active caries lesions, more teeth were extracted because of caries and fewer teeth were restored. Few studies have examined the state of deciduous dentition of cancer survivors, as most papers focus on permanent dentition. However, two independent studies report that the patients after neuroblastoma had higher caries scores in primary dentition than controls.[11,12]

Our present findings indicate the mean DMF value of permanent teeth to be significantly higher among the cancer survivors than the healthy children. This is in accordance with most papers demonstrating a correlation between cancer therapy and increased incidence of caries[6,13,14]; however, other papers indicate no such correlation.[15] In study by Duggal et al,[16] 46 long-term cancer survivors were found to have similar total DMF scores to their siblings but they had significantly more untreated permanent teeth.

The limitation of our study is that being a cross-sectional analysis, no information exists regarding dental status before anticancer treatment and it is not possible to provide direct evidence that dental caries progressed as a result of anticancer therapy.

The cancer survivors included in caries prevention programs based mostly on supplementation of fluoridated gel or chlorhexidine rinsing usually have the same scores of caries as their healthy age-mates.[15] In addition, it has been found that 86.7% children who were free of caries at the moment of diagnosis and undergoing proper caries prophylaxis, presented dentition free from caries even 3 years after cancer therapy.[17]

The biggest contemporary study held on a group of 1273 Danish cancer survivors found that the age of children at the moment of treatment (5–6 years) and the presence of additional radiotherapy were most important caries risk factors at later ages.[18] The influence of radiotherapy on saliva gland function and subsequent decreased saliva flow, and their influence on increased risk of caries, have been widely discussed and documented.[4] In children, the radiation used in cancer therapy may additionally interfere with mitotic activity of rapidly dividing preodontoblasts, resulting in normal dentine being replaced by so-called "osteodentin". This altered dentine has insufficient concentrations of phosphorylated phosphoproteins, which leads to impaired nucleation of enamel crystals and enamel following mineralization.[5,19]

Earlier studies on the impact of radiotherapy on dental development stated that a dose as low as 4 Gy can cause adverse effects in dentition. Moreover, a direct association has been documented between cranial radiation with a dose of 24 Gy and increased incidence of dental caries.[20,21] In the investigated

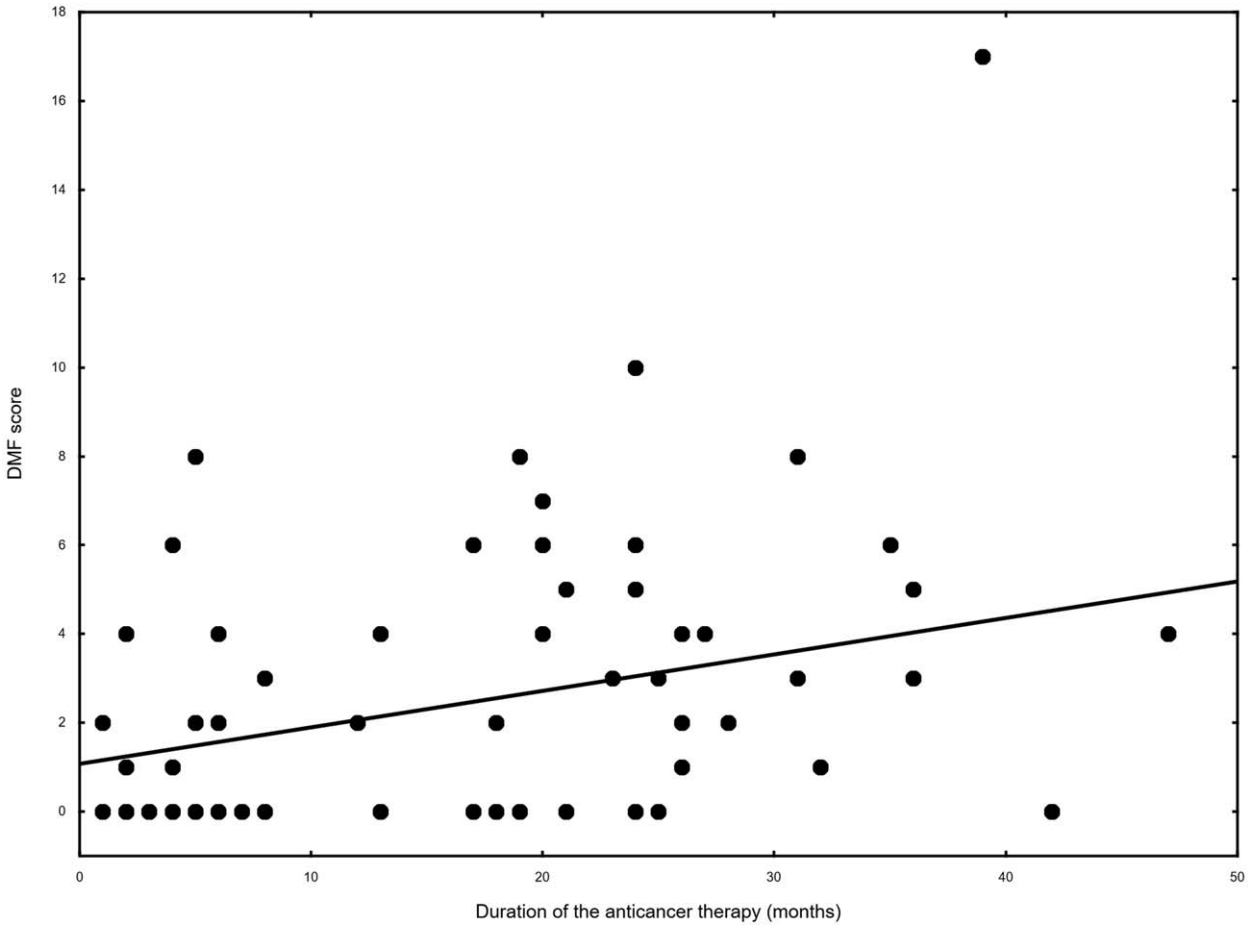


**Figure 2.** Correlation between the duration of the anticancer therapy (in months) and the number of decayed, missing, or filled permanent teeth, defined as DMF scores, among the pediatric cancer survivors. The activity of caries positively correlated with the duration of anticancer treatment, evidenced by correlations with DMF score ($r = 0.26$; $P < .05$).

group, 10 patients who underwent radiotherapy of the head and neck (12–54 Gy) presented higher scores of D and DMF than those who did not. An earlier study performed on 62 long-term survivors also demonstrated positive correlations between caries incidence and, separately, head and neck radiotherapy, the number of fluoride gel treatments and the number of months of chemotherapy.[15]

Our present findings also indicate that the duration of treatment had an influence on the incidence of caries, expressed by higher DMF and F scores. However, the greater number of treated decayed teeth might indicate that more attention was paid to the dental state of patients remaining under the supervision of the oncologist for longer.

The present study also examined the influence of other variables not directly connected with cancer treatment on the incidence of caries in cancer survivors. Children who had visible dental plaque had significantly higher caries scores than those who did not. It is extremely important to maintain good

**Table 5**

**Correlation between dental plaque expressed with Plaque Index (PI) and prevalence of caries. The value of number refers to the type of dentition (deciduous or permanent).**

| Variable | PI < 1 | | PI > 1 | | *P*-value |
|---|---|---|---|---|---|
| | Number | Median (25%-75%) | Number | Median (25–75%) | |
| d | 25 | 2 (0–5) | 25 | 7 (3–9) | **0.0366** |
| m | 25 | 0 (0–0) | 25 | 0 (0–2) | **0.0294** |
| f | 25 | 0 (0–2) | 25 | 0 (0–1) | 0.7358 |
| dmf | 25 | 4 (1–7) | 25 | 9 (4–10) | 0.0914 |
| D | 32 | 0 (0–2) | 36 | 2 (0–3) | 0.0735 |
| M | 32 | 0 (0–0) | 36 | 0 (0–0) | 0.4842 |
| F | 32 | 0 (0–2) | 36 | 1 (0–4) | 0.2120 |
| DMF | 32 | 1.5 (0–4) | 36 | 4.5 (1–6) | **0.0252** |

oral hygiene in patients during and after cancer treatment, not only because of the higher risk of caries. A Swedish longitudinal study found that poor oral hygiene correlated with visible dental plaque, as well as with increased cancer mortality.[22] However, no correlation was observed between the frequency of brushing teeth and dental plaque index. This might be in part due to the fact that respondents might have given inaccurate answers, which they may have seen as more desirable, resulting in a better impression of the quality of their hygienic habits. This problem associated with the reliability of answers in questionnaires has been a matter of many other studies.[23]

Our findings confirm that the education level of parents influences the state of dentition of their children. The level of education is associated with better awareness of health needs and better social and economic status of family. This might influence the frequency of dental visits by the child, the term of the first dental visit and an appreciation by the parent of the need for introducing proper dental hygienic habits, such as brushing the teeth, as soon as the first tooth appears in the child's mouth. Although the study did not evaluate the frequency of dental caries among first degree relatives, which should be acknowledged as a limitation, it does examine the social and economic status of the participants; such findings are often used in literature to determine the hygiene habits within the family.[24]

To summarize, pediatric cancer survivors are more likely to develop dental caries, with factors associated with professional dental care appearing to have the greatest influence on the incidence of dental caries in children a few years after cancer therapy. This demonstrated the need for strict cooperation between oncologists and dentists in the prevention of distant dental complications stemming from cancer treatment in child patients.

## 5. Conclusion

Pediatric patients with cancer have an increased risk of advanced dental caries that might be prevented by extensive dental care education.

## Author contributions

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