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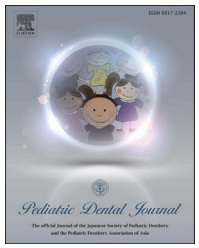

Research Paper

Comparison of oral health characteristics in pediatric cancer and cancer free patients: A multicenter study

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ABSTRACT

Introduction: Comparing oral health of cancer to non-cancer children proves that cancer and its treatment can cause oral complications.
Design: Two groups of children, 50 treated for cancer, and 51 cancer-free, at two different centers, signed informed consent forms. Both the examination of teeth, oral functions and soft tissue with a questionnaire including the patients' demographic characteristics, medical history, dietary and oral hygiene, and changes due to the oncologic treatment allowed gathering data.
Results: The two groups had no demographic nor socio-economic differences. Dietary habits were not significantly different. Daily brushing was more frequent in cancer-free (96.1%) versus sick (76%) children. Oral hygiene was poor (34%) or very poor (24%) in cancer patients and average for non-cancer subjects (68.6%). Cancer patients had more caries, without significant differences between groups. Gingiva was healthy in 96.1% of non-cancer and 76% of cancer patients ($p = 0.044$). In cancer patients, intra-oral soft tissue lesions were aphtous ulcers (52.9%), candidiasis (23.5%), and herpes (17.6%). Xerostomia was significantly different ($p = 0.001$) between cancer (32%) and non-cancer subjects (3.9%). Chemotherapy alone is an independent predictor of poor oral health (HR 17.7, 95% CI [5.2 −60.9], $p < 0.001$).
Conclusion: Cancer patients had poor oral health compared to non-cancer children, with insufficient knowledge concerning the relationship between oral and general health. Education programs, screenings and treatment at cancer centers may help reduce risks of complications.

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1. Introduction

Malignancies represent the second most common cause of childhood mortality [1]. Cancer occurs from atypical cells proliferating uncontrollably [2], reproducing faster than normal cells, leading to a cell excess affecting the normal functioning of body organs. The most frequent childhood cancers are leukemia, central nervous system tumors and lymphoma [1]. Whether applied solely or in combination, treatment modalities comprise chemotherapy, radiation therapy and bone marrow transplant [3], with reported survival rates exceeding 80% five years after initial diagnosis. The most common side effect of chemotherapy is bone marrow suppression leading to leukopenia 10 days after initiation of treatment, thrombocytopenia 10–14 days later, and less frequently anemia. Most side effects disappear at the end of treatment.

Up to 90% of children treated for cancer encounter short, intermediate and long-term oral health complications, related to the disease itself or its treatment [4,5]. Ranging from mucositis and infections to craniofacial and developmental anomalies [6,7], oral health complications are often underestimated, and may induce in some instances septicemia and other life-threatening conditions. Factors influencing the severity of cancer-associated oral health problems include patient's age and immune status, treatment type and dosage [8,9], and oral hygiene practices.

The most frequently reported oral health problems following chemotherapy are mucositis, fungal infections or candidiasis, gingival bleeding, herpetic lesions, aphthous ulcers, and xerostomia. The latter, mostly associated with radiation therapy, may lead to rampant caries developing in the absence of saliva's protective remineralizing effect. Radiation therapy may induce hypovascularization, osteoradionecrosis, mucositis, trismus, caries, and dental and maxillofacial developmental abnormalities (hypodontia, microdontia and abnormally shaped roots).

Oncologic treatment may also change patients' dietary behavior, often making them switch to a softer, more cariogenic, high sugar-content diet, especially during periods of treatment-induced impaired immunity. This may lead to new carious lesions, which, associated with poor oral hygiene, may quickly become deep, painful, and possibly result in oral cavity infections [10].

Infections may prompt cancer patients to seek emergency dental care while undergoing oncologic treatment [6,10], a period during which such care, albeit necessary, is often difficult to provide [10], due to potential side effects of the oncologic treatment (low platelets counts and compromised immunity), and reduced patient cooperation following debilitated general health and/or high anxiety levels stemming from repeated contact with the medical or hospital environment.

It could be postulated that appropriate preventive measures would help reduce the oral disease burden for patients undergoing oncologic treatment. Gaps seem to exist in conveying this notion along the chain of events surrounding the management of childhood cancers. Improved knowledge of the relationship between cancer, its treatment and oral health is a necessary step towards improving the oral and general health of pediatric cancer patients. Therefore, the main purpose of the present study is to investigate such a relationship in a group of young cancer patients in comparison to non-cancer patients in a multicenter setting.

2. Materials and methods

A cross sectional multi-centric study comparing the oral health of a group of pediatric cancer patients and a group of cancer-free controls was conducted in two separate medical and dental centers in Lebanon. Ethical approval for the study was obtained from both centers (IRB ID: BIO-2018-0325) (CEHDF1163).

50 pediatric patients aged 2–18 years undergoing oncologic treatment at a children's cancer center (group A) and 51 cancer-free, similarly aged children (Group B) at a dental treatment center were recruited. In group A, the most common type of cancer was leukemia (68%). Other types were Hodgkin's lymphoma, neuroblastoma, Wilms tumor, medulloblastoma, Ewing sarcoma, etc. All cancer patients received chemotherapy; nine were further exposed to radiation therapy. The age at which patients started their cancer treatment and the duration of the treatment were different among the children. In group B, pediatric patients presented at the dental center seeking pediatric dental consultation and therefore dental treatments if necessary. They were screened for comorbidities to include in the study as controls. Healthy patients with no comorbidities were eligible to be included in the study. Informed consent was provided by healthy controls who were willing to be enrolled in the study. Patients with congenital disorders or syndromic conditions requiring multidisciplinary care or surgical intervention were excluded. Each participating child's assent and their legal guardian's consent were sought and obtained before inclusion in the study.

Oral and dietary hygiene of all children were evaluated through a questionnaire administered to the care-taking parent by one investigator. Each subject's oral health was assessed by another investigator, and radiographic examination was performed when deemed necessary for diagnostic or treatment purposes.

2.1. *Questionnaire*

The questionnaire determined demographic characteristics, including socio-economic and educational information concerning participants and their parents. The patient's general medical history, including cancer type and its treatment protocol, was recorded. Another section elicited information concerning participants' diet and oral hygiene. Changes consequent to oncologic treatment were investigated in addition to harmful tics and oral habits (e.g. thumb sucking, onychophagia, …).

2.2. *Oral cavity examination*

Clinical evaluation encompassed assessment of teeth and oral functions (swallowing, dental occlusion at rest) via visual examination, soft tissue palpation and use of a sterile dental mirror to examine the teeth, under artificial bright light, with the child seated in a private room in the parent's presence.

Teeth present in the oral cavity and normal oral cavity structures and functions were recorded in a dental chart. Teeth' and oral structures' lesions or function abnormalities present at examination time, plus any lesion that had already occurred and been treated previously, were reported. In the present study, dental surfaces were considered without distinguishing between temporary and permanent teeth, therefore lesions, extractions and restorations were not reported as dmf or DMF index but as numbers of decayed, missing and filled surfaces.

Oral health status was recorded using the simplified Oral Health Index (OHI) which takes as a reference teeth number 16/55, 11/51, 26/65, 36/75, 31/71, 46/85. For each tooth the number 0 stands for no deposit, 1 for non visible plaque, and 2 for visible plaque. If the sum is between 15 and 18 the patient has very poor hygiene, between 10 and 15 it is poor oral hygiene, and between 5 and 10 it is good oral hygiene.

Diagnostic information was also collected from routine dental radiographs obtained as necessitated by each individual patient's diagnostic and treatment needs (intra-oral: periapical or bite-wing, or extra-oral: panoramic, or any other type of radiographs), none being taken solely for the study's purposes. Photographs were taken when necessary to document oral cavity lesions and their evolution.

2.3. *Statistical analysis*

After data collection, the statistical software SPSS for Windows (Version 25.0, Chicago, IL, USA) was used for the results' analysis with a statistical significance threshold of $p < 0.05$. Poor oral health was defined as the presence of a current or past oral lesion. A bivariate analysis was performed to identify the factors associated with poor oral health. Multivariate analysis was used to determine independent predictors of poor oral health. Normality of continuous variables' distribution was evaluated by the Kolmogorov-Smirnoff test. Analysis of variance and the Student tests were used for comparing quantitative variables; Chi-square and Fisher's Exact tests were used for comparing qualitative variables.

3. Results

3.1. *Socio-demographic characteristics*

A total of 101 participants (54 boys, 47 girls) with a mean age of 7.89 ± 3.60 years (range: 2–18 years) were included in the study. Group A's (50 cancer patients) mean age was 8.58 ± 4.35, and group B's (51 non-cancer patients) was 7.22 ± 2.55.

Sociodemographic characteristics were not significantly different between groups ($p > 0.05$) (Table 1). 40.6% of mothers had University degrees and 27.7% of fathers.

3.2. *Dietary habits*

Daily number of meals, snacks and soft drinks were not significantly different between groups ($p > 0.05$). There was a statistically significant difference ($p = 0.001$) in non-cariogenic snacks consumption, reported by 11.8% of non-cancer and 46.0% of cancer children (Table 2).

3.3. *Oral hygiene*

Daily toothbrushing was reported by 96.1% of non-cancer and 76% of sick subjects ($p = 0.004$). Dental floss was used by 7.8% of cancer-free subjects and only one cancer patient (2.0%),

Table 1 – Sociodemographic characteristics of The total group, groups A and B.

		Group A Cancer (N = 50)	Group B Non-Cancer (N = 51)	Total	-p-value
	Age	8.58 ± 4.35	7.22 ± 2.55	7.89 ± 3.60	0.059
Gender	Boy	26 (52.0%)	28 (54.9%)	54 (53.5%)	0.770
	Girl	24 (48.0%)	23 (45.1%)	47 (46.5%)	
Age of father	<25 years old	0 (0.0%)	1 (2.0%)	1 (1.0%)	0.061
	26–35 years old	14 (28.0%)	5 (9.8%)	19 (18.8%)	
	36–45 years old	17 (34.0%)	25 (49.0%)	42 (41.6%)	
	>45 years old	17(34.0%)	20(39.2%)	37 (36.6%)	
	No answer	2 (4.0%)	0 (0.0%)	2 (2.0%)	
Age of mother	<25 years old	3 (6.0%)	3 (5.9%)	6 (5.9%)	0.081
	26–35 years old	22 (44.0%)	11 (21.6%)	33 (32.7%)	
	36–45 years old	18 (36%)	30 (58.8%)	48 (47.5%)	
	>45 years old	7 (14%)	7 (13.7%)	14 (13.9%)	
Educational level of father	Father absent	2 (4.0%)	1 (2.0%)	3 (3.0%)	0.147
	Before the baccalaureat	26 (52.0%)	15 (29.4%)	41 (40.6%)	
	Baccalaureat	9 (18.0%)	13 (25.5%)	22 (21.8%)	
	University studies	10 (20.0%)	18 (35.3%)	28 (27.7%)	
	Post university studies	3 6.0%)	4 (7.8%)	7 (6.9%)	
Educational level of mother	Mother absent	1 2.0%)	0 (0.0%)	1 (1.0%)	0.710
	Cannot read nor write	2 (4.0%)	0 (0.0%)	2 (2.0%)	
	Before the baccalaureat	18 (36.0%)	16 (31.4%)	34 (33.7%)	
	Baccalaureat	7 (14.0%)	9 (17.6%)	16 (15.8%)	
	University studies	19 (38.0%)	22 (43.1%)	41 (40.6%)	
	Post university studies	3 (6.0%)	4 (7.8%)	7 (6.9%)	
	Number of siblings	3.02 ± 1.39	3.25 ± 0.98	3.14 ± 1.20	0.328
	Brotherhood position	2.32 ± 1.52	1.86 ± 1.06	2.09 ± 1.32	0.082

Table 2 – Comparison of dietary habits between groups A and B.

		Group A Cancer (N = 50)	Group B Non-Cancer (N = 51)	Total	p
All meals		2.86 ± 0.46	2.90 ± 0.54		0.665
Number of meals per day	1 meal	1 (2.0%)	1 (2.0%)	2 (2.0%)	0.697
	2 meal	6 (12.2%)	7 (13.7%)	13 (13.0%)	
	3 meal	41 (83.7%)	39 (76.5%)	80 (80.0%)	
	4 meal	1 (2.0%)	4 (7.8%)	5 (5.0%)	
All snacks		2.02 ± 0.92	2.24 ± 0.76		0.202
Number of snacks per day	1 snacks	20 (40.0%)	10 (19.6%)	30 (29.7%)	0.031
	2 snacks	9 (18.0%)	19 (37.3%)	28 (27.7%)	
	3 snacks	21 (42.0%)	22 (43.1%)	43 (42.6%)	
All meals and snacks		4.86 ± 1.05	5.14 ± 0.78		0.277
Number of meals and snacks per day	2	1 (2.0%)	0 (0.0%)	1 (1.0%)	0.055
	3	3 (6.0%)	0 (0.0%)	3 (3.0%)	
	4	16 (32.0%)	11 (21.6%)	27 (26.7%)	
	5	12 (24.0%)	23 (45.1%)	35 (34.7%)	
	6	18 (36.0%)	16 (31.4%)	34 (33.7%)	
	7	0 (0.0%)	1 (2.0%)	1 (1.0%)	
Type of snacks	Cariogenic	27 (54%)	45 (88.2%)	72 (71.3%)	0.001
	Non cariogenic	3 (6.0%)	0 (.0%)	3 (3.0%)	
	Both	20 (40%)	6 (11.8%)	26 (25.7%)	
Soft drinks	No	25 (50%)	26 (51.0%)	51 (50.5%)	0.922
	Yes	25 (50%)	25 (49.0%)	50 (49.5%)	
All soft drink		0.56 ± 0.61	0.69 ± 0.91		0.126
Number of soft drinks per day	0	25 (50.0%)	26 (51.0%)	51 (50.5%)	0.139
	1	22 (44.0%)	20 (39.2%)	42 (41.6%)	
	2	3 (6.0%)	0 (.0%)	3 (3.0%)	
	3	0 (0.0%)	5 (9.8%)	5 (5.0%)	

without significant difference between groups (p = 0.362). Fluoride supplements, taken by 33.3% of non-cancer and 18% of cancer patients, showed no significant difference between groups (p = 0.078).

3.4. *Oral health status*

The largest percentage of cancer patients had very poor (24%) or poor oral hygiene (34%), while 68.6% of cancer-free subjects had average hygiene (Table 3). Although caries level was higher in group A (8.92 ± 11.44) versus (6.84 ± 9.44 for group B), the difference was not significant (p = 0.322). However, numbers were significantly higher in group B for missing surfaces (4.12 ± 7.26 versus 1.92 ± 4.85 for group A) (p = 0.001) and restored surfaces (9.22 ± 1.04 versus 1.70 ± 5.20 for group A) (p = 0.001). There were no abnormalities in teeth development in both groups.

3.5. *Mucosal health*

Examination showed healthy gingiva in 96.1% non-cancer and 76% of cancer patients, a significant difference (p = 0.044). There were soft tissue lesions in 3.9% of cancer-free and 34% of cancer patients (p < 0.001).

Soft tissue pathologies found in non-cancer subjects were dental abscesses (1 subject) and candidiasis (1 subject), whereas in cancer patients they were due to aphthous ulcers (52.9%), candidiasis (23.5%), and herpes (17.6%). More cancer (32%) than cancer-free subjects (3.9%) had dry mouth (p = 0.001). Halitosis was not significantly associated with any group of participants; 21.6% of non-cancer and 14% of cancer subjects (p = 0.320) complained about it (Table 4). Among patients with cancer, poor oral health did not increase the risk of herpes (3.4% vs. 9.5%, p = 0.565), aphthous ulcers (20.7% vs. 19%, p = 1.000), or candidiasis (6.9% vs. 4.8%, p = 1.000).

3.6. *Tics and oral habits*

There was no significant difference between groups regarding tics and habits harmful to the oral cavity (p = 0.978); the most common in the present sample were thumb sucking (8) and onychophagia (16) (Table 5). In the chemotherapy-only group, 33 patients had no lesions with a treatment's duration of 19.15 ± 15.61 months, and 17 had lesions with a treatment's duration of 13.59 ± 12.61 months. In the chemotherapy-associated-to-radiotherapy group, 7 patients had no lesions with a treatment's duration of 7.72 ± 13.12 months, and two patients had lesions with a treatment's duration of 2.50 ± 2.81 months.

3.7. *Duration of treatment*

Duration of chemotherapy alone (p = 0.210) and when combined with radiotherapy (p = 0.609) was not significantly associated with intra-oral lesions' presence. On bivariate analysis comparing patients with poor oral health to those with good oral health, factors associated with poor oral health were treatment with chemotherapy (87.9% of patients treated with chemotherapy had poor oral health, compared to 30.9% in those who did not receive chemotherapy, p < 0.001), a history of cancer (87.9% of patients with cancer had poor oral health, compared to 30.9% of cancer-free patients, p < 0.001), as well as consuming a smaller number of daily meals (mean number of meals 3.7 (SD = 0.6) in patients with poor oral

Table 3 – Comparison of oral hygiene practices between groups A and B.

		Group A Cancer (N = 50)	Group B Non-Cancer (N = 51)	Total	p
Toothbrushing	No	12 (24%)	2 (3.9%)	14 (13.9%)	0.004
	Yes	38 (76%)	49 (96.1%)	87 (86.1%)	
Toothbrushing frequency	1	17 (44.7%)	24 (51.1%)	41 (48.2%)	0.002
	2	13 (34.2%)	23 (48.9%)	36 (42.4%)	
	3	8 (21%)	0 (0.0%)	8 (9.4%)	
Dental floss	No	49 (98%)	47 (92.2%)	96 (95%)	0.362
	Yes	1 (2.0%)	4 (7.8%)	5 (5.0%)	
Fluoride supplement	No	41 (82%)	34 (66.7%)	75 (74.3%)	0.078
	Yes	9 (18%)	17 (33.3%)	26 (25.7%)	
Oral Hygiene Index	Average Hygiene	21 (42%)	35 (68.6%)	56 (55.4%)	0.022
	Poor Hygiene	17 (34%)	11 (21.6%)	28 (27.7%)	
	Very poor hygiene	12 (24%)	5 (9.8%)	17 (16.8%)	
Number of carious lesions		8.92 ± 11.44	6.84 ± 9.44		0.322

Table 4 – Comparison of mucosal health between groups A and B.

		Group A Cancer (N = 50)	Group B Non-Cancer (N = 51)	Total	P
Healthy gingiva	No	12 (24%)	2 (3.9%)	14 (13.9%)	0.044
	Yes	38 (76%)	49 (96.1%)	87 (86.1%)	
Soft tissue Lesion	No	33 (66%)	49 (96.1%)	82 (81.2%)	<0.001
	Yes	17 (34%)	2 (3.9%)	19 (18.8%)	
Type of lesion	Abscess	0 (0.0%)	1 (50.0%)	1 (5.3%)	<0.001
	Aphthous lesion and candidiasis	1 (5.9%)	0 (0.0%)	1 (5.3%)	
	Aphthous lesion	8 (47.1%)	0 (0.0%)	8 (42.1%)	
	Candidiasis	3 (17.6%)	1 (50.0%)	4 (21.1%)	
	Herpes	3 (17.6%)	0 (0.0%)	3 (15.8%)	
	Other	2 (11.8%)	0 (0.0%)	2 (10.5%)	
Dry mouth	No	34 (68%)	49 (96.1%)	83 (82.2%)	0.001
	Yes	16 (32%)	2 (3.9%)	18 (17.8%)	
Halitosis	No	43 (86%)	40 (78.4%)	83 (82.2%)	0.320
	Yes	7 (14%)	11 (21.6%)	18 (17.8%)	
Number of carious lesions		8.92 ± 11.44	6.84 ± 9.44		0.322

Table 5 – Tics and oral habits of groups A and B.

	Group A Cancer (N = 50)	Group B Non-Cancer (N = 51)	Total
None	25	21	46
	50.0%	41.2%	45.5%
Thumb sucking	2	1	3
	4.0%	2.0%	3.0%
Thumb sucking, baby bottle	3	1	4
	6.0%	2.0%	4.0%
Thumb sucking, onychophagia	1	0	1
	2.0%	0.0%	1.0%
Baby bottle	9	10	19
	18.0%	19.6%	18.8%
Baby bottle, pacifier	1	5	6
	2.0%	9.8%	5.9%
Baby bottle, onychophagia	1	0	1
	2.0%	0.0%	1.0%
Breastfeeding	2	3	5
	4.0%	5.9%	5.0%
Onychophagia	5	9	14
	10.0%	17.6%	13.9%
Food pocketing and breastfeeding	1	0	1
	2.0%	0.0%	1.0%
Bruxism	0	1	1
	0.0%	2.0%	1.0%

health compared to a mean of 4 meals (SD = 0.6) in patients with good oral health, p = 0.05).

3.8. *Bivariate analysis*

On multivariate analysis, treatment with chemotherapy was the only independent predictor of poor oral health (HR 17.7, 95% CI [5.2–60.9], p < 0.001). Notably, a history of cancer was also significantly associated with poor oral health, but all cancer patients received chemotherapy, which makes the two variables correlated, and for this reason history of cancer was removed from the logistic regression model to prevent multicollinearity (Tables 6 and 7).

4. Discussion

The present study is a multi-centric study, the first concerning oral health conducted in collaboration between two major universities in Lebanon.

The most common cancer among participating cancer patients was leukemia. This finding, consistent with other studies [11,12], allowed a better data comparison, since

patients with similar diseases will most likely undergo similar treatment protocols.

Tics and habits have not been mentioned in any other study of this kind; the goal in obtaining this information was to find a possible correlation between cancer and the development of new tics in sick children, and observe their impact on oral health. However, results showed no significant difference between cancer-free and sick patients in this regard.

Oncological treatments usually cause nausea, compelling parents to compensate for feeding disturbances with the child's favorite snacks. By compounding the numbers of meals and snacks, findings were that a majority (45.1%) of cancer-free children eat five times daily, while most sick children (36%) eat six times daily. An explanation may be that sick children eat more frequently but in small quantities due to treatment-generated lack of appetite. After each food intake, the oral cavity's pH level may drop dramatically before returning progressively to normal. Dental enamel consists of densely packed mineral crystals, mainly hydroxyapatite (HA), subject to being leaked into the oral cavity when the latter's pH drops below 5.5, considered the critical threshold for enamel demineralization. When salivary pH progressively returns to normal, saliva's mineral components help enamel remineralize, before cavitation leading to dental caries can occur. Caries is therefore avoided by a balance in the oral cavity between repeating cycles of enamel demineralization and remineralization. Yet, an increased frequency of consumption (snacks or meals) would prevent acidified salivary pH from returning to above critical demineralization levels between two occurrences of food intake, increasing the risk of developing caries, therefore the cancer group may be more likely to develop cavities. Surprisingly, a significantly larger proportion of sick patients consumed non-cariogenic snacks (46%) compared to a minority (11.8%) of non-cancer patients ($p = 0.001$). Our findings are similar to Gupta et al.'s (2016) [13], possibly indicating that parents of sick children may be more attentive to the latter's general health by ensuring healthier food consumption.

A significant difference was found between cancer-free and sick patients regarding oral hygiene habits, with 96.1%

Table 7 – Independent predictors of poor oral health on multivariate analysis.

Poor oral health				
Predictors	Hazard ratio	95% CI		p-value
		Lower	Upper	
Cancer history	17.7	5.2	60.9	**<0.001**
Number of meals per day	0.352	0.1	1.1	0.062

Table 6 – Baseline demographics and clinical characteristics of patients presenting with good oral health and patients with poor oral health.

	Good oral health (N = 68)	Poor oral health (N = 33)	p-value	
History of cancer - no. (%)	21 (30.9)	29 (87.9)	**<0.001**	
Female gender - no. (%)	30 (44.1)	17 (51.5)	0.485	
Age - y. (sd)	7.9 (3.4)	7.9 (4.1)	0.972	
Education level of the father - no. (%)	Cannot read nor write	0 (0)	0 (0)	0.991
	Did not receive the baccalaureat	27 (39.7)	14 (42.4)	
	Baccalaureate	15 (22.1)	7 (21.2)	
	University studies	19 (27.9)	9 (27.3)	
	Post-graduate studies	4 (5.9)	2 (6.1)	
Education level of the mother - no. (%)	Cannot read nor write	1 (1.5)	1 (3)	0.831
	Did not receive the baccalaureat	22 (32.4)	12 (36.4)	
	Baccalaureate	10 (14.7)	6 (18.2)	
	University studies	28 (41.2)	13 (39.4)	
	Post-graduate studies	6 (8.8)	1 (3)	
Number of siblings - no. (sd)	3.3 (1.1)	2.9 (1.3)	0.130	
Brotherhood position - no. (%)	First	28 (41.2)	17 (51.5)	0.352
	Second	19 (27.9)	7 (21.2)	
	Third	12 (17.6)	4 (12.1)	
	Fourth	6 (8.8)	1 (3.0)	
	Fifth	2 (2.9)	3 (9.1)	
	Sixth	1 (1.5)	0 (0)	
	Seventh	0 (0.0)	1 (3.0)	
Under chemotherapy - no. (%)	21 (30.9)	29 (87.9)	**<0.001**	
Under radiotherapy - no. (%)	5 (7.4)	4 (12.1)	0.430	
Tics and oral habits - no. (%)	38 (55.9)	17 (51.5)	0.679	
Soft drinks - no. (%)	35 (51.5)	15 (45.5)	0.571	
Tooth brushing - no. (%)	61 (89.7)	26 (78.8)	0.136	
Flossing - no. (%)	4 (5.9)	1 (3)	0.535	
Fluoridated supplements - no. (%)	17 (25)	9 (27.3)	0.806	
Fluoridated toothpaste - no. (%)	57 (83.8)	27 (81.8)	0.801	
Number of meals per day - no. (sd)	4.0 (0.6)	3.7 (0.6)	**0.050**	
Number of snacks per day - no. (sd)	2.2 (0.8)	2.0 (1.0)	0.448	

of non-cancer and 76% of sick patients reportedly brushing their teeth, a difference explained by several factors. One reason may be medical staff at the cancer treatment center requesting temporary suspension of brushing [1] in cancer patients; there is no evidence in the literature to support such a request for preventing gum bleeding and bacteremia from toothbrushing. Additionally, discomfort during brushing due to mucosal lesions may also explain poor oral hygiene compliance. Half of those brushing their teeth (44.7% of group A and 51.1.% of group B) did so once a day with no difference between groups, showing insufficient brushing frequency in all children, in agreement with another study [13] where 40% cancer-free children brushed their teeth once a day compared to 57% sick children. Dental floss was used by 5% of all participants in the present study, a very low number possibly due to lack of education on flossing's role in maintaining oral health. Fluoride supplements were administered to 25.7% of all children with no difference between groups, while in Gupta et al.'s. study (2016) no children had taken fluoride supplements [13]. During oral examination, no probes were used to avoid bleeding; some studies have done the same [2] while others used a blunt periodontal probe [1,3].

Oral hygiene was classified according to the simplified Oral Hygiene Index (OHI) classification, adopted in other studies [2,3,12]. The plaque index was significantly different between groups, similar to findings from other studies [2,3,12,13]. This difference correlates with toothbrushing frequency, found significantly higher in cancer-free subjects, whose majority (68.6%) had average hygiene compared to only 42% of sick subjects; conversely more sick children had poor (34% versus 21.6% non-cancer) and very poor hygiene (24% versus 9.8% non-cancer). The caries, restorations and missing teeth in the present study were reported by numbers of decayed, restored and missing surfaces without taking into consideration whether the tooth was temporary or permanent, a method used by some studies [3], while others have distinguished between dmf and DMF [1,2]. In the present study, despite the higher number of decayed surfaces in sick subjects, the difference remained insignificant. The higher prevalence of dental caries in the cancer group may be explained by children and their parents being overwhelmed by cancer issues thereby neglecting dental health. Other reasons may include changes in diet and oral hygiene habits following discomfort caused by soft tissue lesions. However, the non-significant difference may be due to cancer-free patients also having a history of neglected oral hygiene and having started to apply instructions given to them only after their dental center visit. In addition, cancer-free children in the present study consumed more cariogenic foods, hence possibly the high caries rate. These results are consistent with those of other studies [1,14,15]. However, numbers of missing and restored surfaces were significantly higher in non-cancer subjects, which can be due to cancer patients having their general health problems as a priority and not visiting the dentist as often as non-cancer patients.

The present study sought through a questionnaire to find out if patients had previously presented mucosal lesions, which other studies have done [1,12,16]. Access to patients' dental records would have provided more accurate information on soft tissue lesions, but this was not feasible given the disparity of dentists who cared for our sample of cancer patients (private clinics or dispensaries). The high rate of gingivitis in the cancer group (24%) can be explained by the alteration of the immune response during treatment with patients becoming more susceptible to infections, and by the poor hygiene observed. Only 3.9% of non-cancer subjects had previously had an oral cavity soft tissue lesion against 34% of sick subjects, a result consistent with those of other studies [1,12,16]. The majority of these lesions were reported as aphthous ulcers (52.9%), probably because patients did not know the lesion's real nature. Other lesions found were attributable to candidiasis and herpes.

The most common symptom was dry mouth (32% cancer and 3.9% cancer-free children), also similar to other studies [12,16,17]. Oral dryness or xerostomia is a consequence of salivary gland dysfunction, a common complication of anticancer treatments. Hyposalivation predisposes the mouth to infections and a risk of developing cavities and contributes to the development of Candida albicans. The appearance of these lesions can be altered by the patient's level of immunosuppression; accordingly, a laboratory analysis is necessary for precise diagnosis. A program to control oral microbial flora, maintenance of good oral hygiene and palliative treatment when needed should all be applied to reduce mucosal lesions' morbidity.

The bivariate analysis showed that chemotherapy alone is an independent predictor of poor oral health which agrees with the findings of other studies [18, 19, 20, 21]. In fact, chemotherapy may cause changes in the oral mucosa and the salivary glands. This can disrupt the healthy balance of bacteria leading to poor oral health.

If the patient is under cancer treatment, elective dental care should not be performed. In case of a dental emergency, the dental treatment plan should be discussed with the attending physician who will give recommendations regarding any antibiotics or analgesics prescriptions or platelet transfusions. There are hematological factors to consider before managing these patient: Absolute Neutrophils Counts (ANC), Platelet Count (PLT) and other coagulation tests.

Since cancer patients in the present study consulted different dentists with practices located outside the cancer center, getting their dental records was not always possible. A study comparing two groups of children with cancer, one having obtained necessary dental care before oncological treatment initiation, and the other not having had this opportunity could provide additional information regarding dental care's impact on these children's general health and quality of life. The main limitations of this study are the cross-sectional design and the heterogeneity of the cancer group in terms of diagnosis and treatment. Although this limits the clinical relevance of the findings, the present study provides an important foundation for future prospective studies investigating the impact of cancer on oral health in pediatric populations.

5. Conclusion

In conclusion, the oral health of pediatric cancer subjects was found to be significantly different from that of cancer-free

children. The majority of cancer patients did not practice proper oral hygiene, presented a high number of carious lesions and experienced soft tissue lesions, possibly due to the child, parents, and health care team not being fully aware of the possible side effects and long-term sequelae of cancer treatments in the oral cavity and how to prevent or manage them. These findings lead to advocating that all cancer patients undergo an oral examination before cancer therapy's onset, with oral prophylaxis and prompt treatments prior to oncologic treatment, to minimize complications and optimize oral health. Dental care should include advice on dietary and oral hygiene practices, topical fluoride applications and preventive treatments when possible. Periodic dental examinations should also be performed regularly during oncologic treatment thereby helping to improve pediatric cancer patients' quality of life during and health outcomes after cancer treatment.

Conflict of interest

The authors declare no conflict of interest.

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