BMC Oral Health

https://doi.org/10.1186/s12903-026-08931-1

Article in Press

Long-term oral and dental effects in childhood acute lymphoblastic leukemia survivors: a cross-sectional study comparing early and late post-treatment periods

Received: 2 January 2026

Accepted: 8 June 2026

Published online: 16 June 2026

Cite this article as: Güney S.E., Kızıldağ S., Kılınç G. *et al.* Long-term oral and dental effects in childhood acute lymphoblastic leukemia survivors: a cross-sectional study comparing early and late post-treatment periods. *BMC Oral Health* (2026). https://doi.org/10.1186/s12903-026-08931-1

Saime Esin Güney, Servet Kızıldağ, Gülser Kılınç, Hale Ören & Gülçin Bulut

We are providing an unedited version of this manuscript to give early access to its findings. Before final publication, the manuscript will undergo further editing. Please note there may be errors present which affect the content, and all legal disclaimers apply.

If this paper is publishing under a Transparent Peer Review model then Peer Review reports will publish with the final article.

ARTICLE IN PRESS

© The Author(s) 2026. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

ARTICLE IN PRESS

Long-term oral and dental effects in childhood acute lymphoblastic leukemia survivors: a cross-sectional study comparing early and late post-treatment periods

Saime Esin Güney[1]*, Servet Kızıldağ[2], Gülser Kılınç[1], Hale Ören[3], Gülçin Bulut[1]

[1]Department of Pediatric Dentistry, Faculty of Dentistry, Dokuz Eylül University, İzmir, Turkey

[2]Department of Medical Laboratory Techniques, Vocational School of Health Services, Dokuz Eylül University, İzmir, Turkey

[3]Department of Pediatric Hematology, Faculty of Medicine, Dokuz Eylül University, İzmir, Turkey

*Corresponding author: saimeesin.guney@deu.edu.tr

Abstract

Background: Childhood cancer survivors face significant long-term oral health challenges following antineoplastic treatment. The primary aim of this study was to examine the effect of time elapsed since completion of antineoplastic treatment on oral health parameters — caries experience, salivary function, and dental developmental anomalies — in childhood ALL survivors. Secondary objectives included comparing oral health parameters between survivors and healthy sibling controls and identifying independent predictors of caries outcomes.

Methods: This cross-sectional study included 38 ALL survivors (aged 5–18 years) and 20 healthy sibling controls. Dental caries was assessed using the International Caries Detection and Assessment System (ICDAS II) and DMFT/dft indices. Salivary flow rate (SFR) and pH were measured using standardized protocols. Dental developmental anomalies were assessed by combined clinical and panoramic radiographic examination. Comparisons were performed using the Mann-Whitney U test, the Kruskal-Wallis test, and the chi-square test, with multivariable linear regression used to identify independent predictors of caries outcomes.

Results: Early survivors demonstrated significantly higher mean ICDAS scores (median 1.38 vs 0.60; $p = 0.007$) and elevated DMFT/dft indices (median 12.0 vs 7.0; $p = 0.002$), together with significantly lower SFR (median 0.28 vs 0.40 mL/min; $p = 0.017$), compared with late survivors. Dental developmental anomalies were significantly more prevalent in survivors (84.2%) than controls (10%; $p < 0.001$); microdontia was most common (37.7%), followed by root malformation (24.5%) and taurodontism (15.1%). Multivariable regression identified age and time since treatment completion as independent predictors of ICDAS scores (adjusted $R^2 = 0.285$, $p = 0.014$), while time since treatment completion independently predicted DMFT/dft scores ($B = -4.522$, $p = 0.003$).

ARTICLE IN PRESS

Conclusions: Dental developmental anomalies were highly prevalent among childhood ALL survivors and, being a direct consequence of treatment, were independent of the time elapsed since its completion. In contrast, salivary flow rate and caries experience were poorer among survivors examined within 24–36 months of treatment completion than among those examined later, indicating gradual recovery of salivary function over time. Closer preventive dental monitoring during the first years after treatment, supported by sustained oncology–dental collaboration, is therefore recommended.

Keywords: Acute lymphoblastic leukemia, Childhood cancer survivors, Dental anomalies, Oral health, ICDAS, Salivary function.

Background

Advances in pediatric oncology have substantially improved survival rates for childhood cancers, with five-year survival now exceeding 80% in developed countries [1, 2]. Acute lymphoblastic leukemia (ALL) represents the most common pediatric malignancy, accounting for approximately 25% of all childhood cancers, with survival rates approaching 90% following contemporary treatment protocols [3]. However, this therapeutic success has revealed a substantial burden of treatment-related late effects that significantly impact survivors' quality of life [4, 5].

Oral and dental complications constitute a significant yet underrecognized category of late effects in childhood cancer survivors (CCS) [6, 7]. Systematic reviews and meta-analyses have reported dental developmental anomaly prevalence rates ranging from 46% to 62% in this population [8, 9]. These anomalies, including microdontia, dental agenesis, root malformations, and enamel hypoplasia, result from cytotoxic disruption of odontogenic processes during critical developmental windows [10, 11]. Children exposed to antineoplastic therapy before the age of 5 years are at particularly high risk, as this period coincides with the active mineralization of the permanent dentition [12, 13].

Chemotherapy (CT) and radiotherapy (RT) affect dental development through complex and multifactorial mechanisms. Antineoplastic agents exert both cytostatic and cytotoxic effects on malignant cells and rapidly proliferating odontogenic tissues during critical stages of tooth development [14, 15]. Antineoplastic agents such as vincristine, vinblastine, doxorubicin, and cyclophosphamide have been shown to disrupt normal dental development, with clinical evidence documenting taurodontism, delayed tooth eruption, and root development abnormalities in survivors treated with these regimens [8]. Radiotherapy-related dental sequelae appear to be dose-dependent, with increasing radiation doses associated with a higher prevalence of root shortening, blunted roots, and premature apical closure [16]. Although the minimum RT dose required to induce dental developmental changes remains unclear, doses as low as 10 Gy have been reported to cause permanent

ARTICLE IN PRESS

damage to immature ameloblasts, while doses around 30 Gy may arrest dental development entirely [16].

Beyond developmental anomalies, survivors frequently experience salivary gland dysfunction. Salivary gland dysfunction has been reported in a proportion of childhood cancer survivors at long-term follow-up, though its persistence and clinical significance may vary depending on treatment protocol and time since treatment completion [17, 18]. Hyposalivation creates an oral environment conducive to caries development by reducing buffering capacity, diminishing clearance of fermentable carbohydrates, and altering the microbial ecology [18]. Because many survivors fail to recognize salivary dysfunction symptoms, objective salivary assessment is preferable to relying solely on symptom-based screening.

The temporal evolution of oral health parameters following treatment completion remains incompletely characterized. While acute oral toxicities during active therapy are well-documented, the trajectory of recovery—or persistence—of these effects during the survivorship period requires further elucidation [19, 20]. Understanding the critical time points at which oral health parameters stabilize can inform evidence-based surveillance protocols and guide the timing of preventive interventions.

Both the Children's Oncology Group and the European Academy of Paediatric Dentistry have issued guidelines recommending dental evaluation and structured follow-up for childhood cancer survivors [6, 21, 22]; nevertheless, implementation remains inconsistent, and recommendations on the timing and intensity of surveillance lack robust empirical support.

The primary aim of this study was to examine the effect of time elapsed since completion of antineoplastic treatment on oral health parameters — caries experience, salivary function, and dental developmental anomalies — in childhood ALL survivors. Secondary objectives were: (1) to compare these oral health parameters between survivors and healthy sibling controls; and (2) to identify independent predictors of caries outcomes in this population. For analysis, the post-treatment interval was operationalized by stratifying survivors into early (24–36 months) and late (37–60 months) groups using the sample median, as detailed in the Methods.

Methods

Study design and setting

This cross-sectional observational study was conducted between November 2024 and April 2025 at ***** University Hospital, *****. Participants were recruited from the Pediatric Hematology outpatient follow-up clinic and referred to the Pediatric Dentistry Department for a comprehensive oral examination. The study protocol was approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee (approval number: 2024/04-18) and conducted in accordance with the Declaration of Helsinki. Written

ARTICLE IN PRESS

informed consent was obtained from parents or legal guardians, and assent was obtained from participants aged 7 years and older.

Participants

The case group consisted of 38 children (17 males, 21 females; aged 5–18 years) with histologically confirmed ALL who had completed chemotherapy 24–60 months prior to enrollment. Patients were treated with the AIEOP-BFM ALL 2000 protocol [23]. Inclusion criteria comprised: (1) histologically confirmed ALL diagnosis; (2) completion of chemotherapy 24–60 months before study enrollment; (3) age between 5 and 18 years; and (4) documented complete remission status. Exclusion criteria included: (1) active malignancy or disease recurrence; (2) ongoing chemotherapy; (3) history of hematopoietic stem cell transplantation; (4) presence of systemic disease unrelated to cancer history; and (5) current orthodontic appliance use.

Disease- and treatment-related data were abstracted from hospital medical records in collaboration with the Pediatric Hematology Department and included ALL immunophenotype, treatment protocol, age at diagnosis, date of treatment completion, and cranial radiotherapy status and dose; these are summarized in Table 1. Each participant's general medical history was reviewed at enrollment; consistent with the eligibility criteria, no participant had a systemic disease unrelated to the oncological diagnosis.

Although eligibility was defined by current age (5–18 years) for pragmatic recruitment reasons, the clinically relevant exposure window is the age at antineoplastic treatment. In the present study sample, the median age at diagnosis was 3.5 years (IQR 2–5); the oldest participant was diagnosed at 11 years of age, and no participant received antineoplastic treatment thereafter. As the permanent dentition completes maturation by approximately 16 years of age [24], all participants were necessarily exposed to treatment well within the active window of odontogenesis and dental maturation, during which the developing dentition remains susceptible to treatment-induced disturbance. Consequently, the hypothetical scenario of a patient treated after completion of dental maturation did not arise in this study sample.

For subgroup analysis, survivors were stratified by time since treatment completion into early survivors (24–36 months post-treatment; n = 18) and late survivors (37–60 months post-treatment; n = 20). This cutoff was based on the median time since treatment completion in the study sample (median = 36 months) and should be considered exploratory.

The control group comprised 20 healthy siblings (8 males, 12 females) of the cancer survivors, matched for age range (5–18 years). Control inclusion criteria required: (1) no history of malignancy or chronic systemic disease; (2) no regular medication use; (3) American Society of Anesthesiologists (ASA) physical status classification I; and (4) no current orthodontic treatment.

ARTICLE IN PRESS

Clinical examination

All clinical examinations were performed by a single calibrated examiner (S.E.G.) to ensure consistency. The examination protocol was conducted over two visits, for two main reasons. First, participants were referred from the Pediatric Hematology clinic on the day of their oncology appointment; the initial visit was used to obtain written informed consent and to record each participant's dental and medical history. Second, because standardized unstimulated salivary collection must be performed within a fixed morning window (09:00–10:00) to control for circadian variation in salivary output, a separate morning appointment was scheduled for salivary assessment. Oral hygiene instruction using the modified Bass technique was provided during the first visit; the interval between visits was short and insufficient to produce clinically meaningful changes in the measured oral health parameters.

One month prior to data collection, the single examiner who performed all clinical assessments participated in structured training and calibration exercises conducted with 20 children under the supervision of an experienced examiner who served as the "gold standard." The intra-examiner agreement for the primary examiner was determined to be $\kappa = 0.87$, reflecting substantial agreement.

Given the sibling-controlled study design, in which participants from the same family attended examinations concurrently, assessor blinding to group allocation was not feasible. This represents an acknowledged limitation of the study.

Dental caries assessment

Dental caries was assessed using the International Caries Detection and Assessment System II (ICDAS II), which enables detection of both early non-cavitated and cavitated lesions, offering greater sensitivity than traditional DMFT indices alone [25]. ICDAS II criteria score lesions from 0 (sound surface) to 6 (extensive, distinct cavity with visible dentin). Examinations were conducted under standardized lighting conditions with teeth dried using compressed air. Mean ICDAS scores were calculated as the sum of all surface scores divided by the number of examined surfaces. The maximum ICDAS score was recorded to capture the most severe lesion. Additionally, the DMFT index (decayed, missing due to caries, and filled permanent teeth) and the dft index (decayed and filled primary teeth) were calculated according to World Health Organization criteria [26].

Oral hygiene assessment

Oral hygiene status was evaluated using the Simplified Oral Hygiene Index (OHI-S), comprising debris and calculus components assessed on index tooth surfaces [27]. A structured dental history and oral hygiene habit questionnaire were not administered; oral hygiene was instead assessed objectively through the OHI-S.

ARTICLE IN PRESS

Salivary analysis

Unstimulated whole saliva was collected between 09:00 and 10:00 hours to control for circadian variation. Participants rinsed their mouths with deionized water and remained seated in an upright position for 5 minutes before collection. Saliva was collected passively into pre-weighed graduated tubes over a 10-minute period using the draining method. Salivary flow rate (SFR) was calculated as volume (mL) divided by collection time (minutes). Salivary pH was measured within 30 minutes of collection using a calibrated bench-top pH meter (Hanna Instruments HI 221, Woonsocket, RI, USA). The pH meter was calibrated daily using standard buffer solutions (pH 4.01 and 7.01).

Dental developmental anomaly assessment

Dental developmental anomaly assessment was performed through a dual approach combining both clinical examination and panoramic radiographic evaluation. Clinical assessment was performed under standardized lighting conditions with compressed air drying, enabling direct visualization of enamel surface defects, discoloration, and structural abnormalities. Digital panoramic radiographs were obtained for all participants and evaluated for dental developmental anomalies by two independent examiners (S.E.G. and G.K.). The use of two independent radiographic examiners was intentional: while clinical examination was performed by a single examiner to minimize variability, dental developmental anomalies on panoramic radiographs require meticulous interpretation and can be subtle in presentation; two independent assessors were therefore employed to reduce the risk of missed findings. Anomalies assessed included: microdontia, dental agenesis, taurodontism, root malformation, concrescence, and enamel hypoplasia. Inter-examiner reliability for dental anomaly assessment was evaluated using Cohen's kappa coefficient, demonstrating substantial agreement ($\kappa = 0.82$). Intra-examiner reliability was calculated separately for each assessor: $\kappa = 0.90$ for the first examiner and $\kappa = 0.86$ for the second examiner, both indicating substantial to excellent agreement. Representative panoramic radiographs illustrating the spectrum of dental developmental anomalies observed in survivors are presented in Figures 1 and 2.

Statistical Analysis

All analyses were performed using IBM SPSS Statistics (v.26.0). The distribution characteristics of continuous variables were assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests, while homogeneity of variance was evaluated with Levene's test. Since most variables did not meet the assumption of normality, nonparametric methods were preferred for comparative analyses. Descriptive statistics were presented as medians (interquartile ranges) for continuous variables and as frequencies (percentages) for categorical variables. For group comparisons, the Mann–Whitney U test was used for two-group analyses, and the Kruskal–Wallis test

ARTICLE IN PRESS

for three-group analyses; post-hoc pairwise comparisons were adjusted using the Bonferroni correction. Categorical variables were analyzed using the Chi-square test. To evaluate differences related to time since treatment completion, subgroup analyses were conducted between early survivors (24–36 months) and late survivors (37–60 months).

Multivariable linear regression analyses were performed to identify independent predictors of oral health outcomes. Mean ICDAS score and DMFT/dft scores were included as dependent variables, while age (entered as a continuous variable, in years), sex, salivary flow rate, salivary pH, presence of dental developmental anomalies, time since treatment completion (early vs late), and history of radiotherapy were evaluated as independent variables. Regression assumptions (normality of residuals, linearity, and multicollinearity) were examined, and collinearity diagnostics (VIF) were within acceptable limits. Additionally, stepwise regression models were constructed to identify the most meaningful predictors. A p-value < 0.05 was considered statistically significant for all analyses.

Results

Participant characteristics

A total of 58 participants were enrolled, comprising 38 ALL survivors and 20 healthy sibling controls. The case group consisted of 17 males (44.7%) and 21 females (55.3%), with a median age of 9.0 years (interquartile range, IQR: 7.0–11.0). The control group included 8 males (40%) and 12 females (60%), with a median age of 10.5 years (IQR: 8.25–13.75). No significant differences were observed between groups for age ($p = 0.098$) or sex distribution ($p = 0.729$). Among survivors, 6 (15.8%) had received cranial radiotherapy as part of their treatment protocol.

Clinical and treatment characteristics of the ALL survivor group are summarized in Table 1. The median age at diagnosis was 3.5 years (IQR: 2–5), with the youngest participant diagnosed at 11 months and the oldest at 11 years of age. Notably, 76.3% of participants (n = 29) received antineoplastic treatment at or before the age of 5 years — the period identified in the literature as conferring the highest risk of odontogenic disruption [12, 13] — while the remaining 23.7% (n = 9) were diagnosed at age 6 years or older.

Table 1. Clinical and treatment characteristics of the childhood ALL survivor group

Characteristic	ALL Survivor Group (n = 38)
Sex, Female/Male	21/17
Current age, median (IQR), years	9.0 (7.0–11.0)

ARTICLE IN PRESS

Characteristic	ALL Survivor Group (n = 38)
Age at diagnosis, median (IQR), years	3.5 (2–5)
ALL subtype, B-cell ALL, n (%)	26 (68.4%)
ALL subtype, T-cell ALL, n (%)	12 (31.6%)
Treatment protocol	AIEOP-BFM ALL 2000
Radiotherapy, n (%)	6 (15.8%)
Radiotherapy dose, median (IQR), Gy	12 (12–18)
Age at diagnosis ≤5 years, n (%)	29 (76.3%)
Age at diagnosis ≥6 years, n (%)	9 (23.7%)

Data presented as median (IQR) or n (%). IQR: interquartile range.

Comparison between survivors and controls

Table 2 presents the comparison of oral health parameters between the case and control groups. No statistically significant differences were observed between survivors and controls for mean ICDAS score (median 0.89 vs 1.27; p = 0.245), maximum ICDAS score (5.0 vs 5.0; p = 0.831), DMFT/dft index (9.0 vs 11.5; p = 0.137), OHI-S score (1.49 vs 1.40; p = 0.381), salivary flow rate (0.38 vs 0.50 mL/min; p = 0.241), or salivary pH (7.46 vs 7.35; p = 0.162).

Table 2. Comparison of oral health parameters between ALL survivors and healthy sibling controls

Parameter	Control Group (n = 20)	Case Group (n = 38)	p-value
Age (years)	10.5 (8.25–13.75)	9.0 (7.0–11.0)	0.098[a]
Sex, male n (%)	8 (40%)	17 (44.7%)	0.729[b]
ICDAS mean score	1.27 (0.75–1.82)	0.89 (0.45–1.62)	0.245[a]
ICDAS maximum score	5.0 (4.0–5.75)	5.0 (3.0–6.0)	0.831[a]
DMFT + dft index	11.5 (7.5–13.75)	9.0 (6.0–13.25)	0.137[a]
OHI-S score	1.40 (0.87–1.50)	1.49 (1.00–1.99)	0.381[a]

ARTICLE IN PRESS

Parameter	Control Group (n = 20)	Case Group (n = 38)	p-value
SFR (mL/min)	0.50 (0.23–0.71)	0.38 (0.20–0.50)	0.241[a]
Salivary pH	7.35 (7.18–7.53)	7.46 (7.27–7.73)	0.162[a]

Data presented as median (IQR) or n (%). SFR: salivary flow rate; OHI-S: Simplified Oral Hygiene Index; ICDAS: International Caries Detection and Assessment System. [a]Mann-Whitney U test; [b]Chi-square test.

Subgroup analysis by time since treatment completion

Stratified analysis comparing controls, early survivors, and late survivors revealed significant differences across groups (Table 3). Mean ICDAS scores were significantly higher in early survivors than in late survivors (median 1.38 vs 0.60; p = 0.007), and DMFT/dft indices were likewise significantly higher in early than late survivors (median 12.0 vs 7.0; p = 0.002). OHI-S scores did not differ significantly across the control, early-, and late-survivor groups (median 1.40 vs 1.49 vs 1.49; p = 0.600). Early survivors also demonstrated significantly lower SFR than late survivors and controls (median 0.28 vs 0.40 vs 0.50 mL/min; p = 0.017). No significant differences were observed for maximum ICDAS score or salivary pH across groups.

Table 3. Comparison of oral health parameters across control, early survivor, and late survivor groups

Parameter	Control (n = 20)	Early (n = 18)	Late (n = 20)	p-value
Age (years)	10.5 (8.25–13.75)	8.5 (6.75–11.0)	10.0 (8.0–11.0)	0.121[a]
Sex, male n (%)	8 (40%)	7 (38.9%)	10 (50%)	0.742[b]
ICDAS mean score	1.27 (0.75–1.82)	1.38 (0.59–2.50)	0.60 (0.34–1.17)	0.007[a]*
ICDAS maximum score	5.0 (4.0–5.75)	5.0 (5.0–6.0)	4.0 (3.0–5.75)	0.076[a]
DMFT + dft index	11.5 (7.5–13.75)	12.0 (8.5–14.25)	7.0 (4.25–9.0)	0.002[a]*
OHI-S score	1.40 (0.87–1.50)	1.49 (1.06–2.12)	1.49 (0.85–1.97)	0.600[a]

ARTICLE IN PRESS

Parameter	Control (n = 20)	Early (n = 18)	Late (n = 20)	p-value
SFR (mL/min)	0.50 (0.23–0.71)	0.28 (0.20–0.40)	0.40 (0.31–0.60)	0.017[a]*
Salivary pH	7.35 (7.18–7.53)	7.21 (6.92–7.69)	7.29 (7.17–7.39)	0.347[a]

*Data presented as median (IQR) or n (%). Early: 24–36 months post-treatment; Late: 37–60 months post-treatment. SFR: salivary flow rate; OHI-S: Simplified Oral Hygiene Index; ICDAS: International Caries Detection and Assessment System. [a]Kruskal-Wallis test; [b]Chi-square test. *p < 0.05.*

Dental developmental anomalies

Dental developmental anomalies were identified in 32 of 38 survivors (84.2%) compared with 2 of 20 controls (10%), representing a statistically significant difference (p < 0.001; Table 4). Among the 53 individual anomalies documented in the survivor group, microdontia was most prevalent (n = 20; 37.7%), followed by root malformation (n = 13; 24.5%), taurodontism (n = 8; 15.1%), hypoplasia (n = 5; 9.4%), agenesis (n = 4; 7.5%), and concrescence (n = 3; 5.7%). Multiple anomaly types were observed in 14 of the 32 survivors with anomalies (43.8%). In the control group, one case of concrescence and one case of supernumerary tooth were identified.

Table 4. Prevalence and distribution of dental developmental anomalies in ALL survivors and controls

Prevalence	Control Group (n = 20)	Case Group (n = 38)	p-value
Anomaly present, n (%)	2 (10%)	32 (84.2%)	<0.001[a]*
Anomaly absent, n (%)	18 (90%)	6 (15.8%)	
Distribution of anomaly types	**Total anomalies (n = 2)**	**Total anomalies (n = 53)**	
Microdontia	0	20 (37.7%)	
Root malformation	0	13 (24.5%)	
Taurodontism	0	8 (15.1%)	
Enamel hypoplasia	0	5 (9.4%)	
Dental agenesis	0	4 (7.5%)	
Concrescence	1 (50%)	3 (5.7%)	

ARTICLE IN PRESS

Prevalence	Control Group (n = 20)	Case Group (n = 38)	p-value
Supernumerary teeth	1 (50%)	0 (0%)	

*[a]Chi-square test. *p < 0.05. Note: Some patients exhibited multiple types of anomalies.*

Radiotherapy subgroup analysis

Among survivors, comparison between those who received radiotherapy (n = 6) and those who did not (n = 32) revealed no significant differences in SFR (median 0.20 vs 0.40 mL/min; p = 0.147), salivary pH (median 7.23 vs 7.31; p = 0.172), mean ICDAS score (median 0.73 vs 0.89; p = 0.279), maximum ICDAS score (median 5.0 vs 5.0; p = 0.445), or DMFT/dft index (median 8.50 vs 9.00; p = 0.519). Patients who received radiotherapy were significantly older than those who did not (median 11.0 vs 8.5 years; p = 0.021). However, these findings should be interpreted with caution, as the limited number of irradiated participants (n = 6) likely resulted in insufficient statistical power to detect potential differences, and a Type II error cannot be excluded.

Multivariable regression analysis

Multivariable linear regression analysis for mean ICDAS score identified age and time since treatment completion (early versus late) as independent predictors (Table 5). The full model was statistically significant (F = 3.107; p = 0.014) and explained 28.5% of the variance in ICDAS scores (adjusted R^2 = 0.285). Increasing age was associated with decreasing ICDAS scores (B = −0.124; 95% CI: −0.221 to −0.027; p = 0.014). A longer time since treatment completion (late group) was independently associated with lower ICDAS scores than the early group (B = −0.607; 95% CI: −1.200 to −0.015; p = 0.045).

Table 5. Multivariable linear regression analysis for ICDAS mean score

Variable	B	95% CI	p-value
Age	−0.124	−0.221 to −0.027	0.014*
Time since treatment completion (late vs early)	−0.607	−1.200 to −0.015	0.045*
Salivary flow rate	−0.021	−0.154 to 0.112	0.746
Salivary pH	−0.571	−1.326 to 0.184	0.133
Sex	0.136	−0.399 to 0.672	0.607

ARTICLE IN PRESS

Variable	B	95% CI	p-value
Radiotherapy history	−0.279	−1.072 to 0.514	0.478
Dental anomaly presence	0.072	−0.659 to 0.802	0.843

*Model summary: Adjusted R^2 = 0.285, F = 3.107, p = 0.014. CI: confidence interval. *p < 0.05.*

For the DMFT/dft index, stepwise regression identified time since treatment completion as the sole independent predictor (Table 6). The model was statistically significant (F = 10.096; p = 0.003) and explained 19.7% of the variance (adjusted R^2 = 0.197). A longer time since treatment completion (late group) was associated with significantly lower DMFT/dft scores than the early group (B = −4.522; 95% CI: −8.160 to −0.756; p = 0.003).

Table 6. Stepwise linear regression analysis for DMFT/dft score

Variable	B	95% CI	p-value
Time since treatment completion (late vs early)	−4.522	−8.160 to −0.756	0.003*

*Model summary: Adjusted R^2 = 0.197, F = 10.096, p = 0.003. Stepwise selection method employed. CI: confidence interval. *p < 0.05.*

ARTICLE IN PRESS

Discussion

This study provides a comprehensive characterization of oral health status in ALL survivors during the 24–60 month post-treatment period, revealing a substantial prevalence of dental developmental anomalies and identifying notable differences in oral health parameters between early- and late-survivor subgroups, with several parameters showing statistically significant variation according to time since treatment completion.

The dental anomaly prevalence of 84.2% in our study sample substantially exceeds the 46–62% range reported in previous systematic reviews and meta-analyses [8, 9]. This elevated rate may reflect several factors, including the comprehensive radiographic assessment methodology employed, the relatively young age at treatment initiation in our study population, and the specific chemotherapeutic regimens utilized. Notably, the median age at diagnosis in our study sample was 3.5 years (IQR: 2–5), with 76.3% of participants (n = 29) having received antineoplastic treatment at or before the age of 5 years — precisely the period identified as conferring the highest risk of odontogenic disruption due to coincidence with the active mineralization phase of the permanent dentition [12, 13]. The age range at diagnosis extended from 11 months to 11 years, and no participant was treated after the age of 11 years, confirming that all participants were

ARTICLE IN PRESS

exposed to antineoplastic agents during a recognized window of dental vulnerability [24]. These characteristics of our study sample likely account, at least in part, for the high prevalence of dental developmental anomalies observed. Microdontia emerged as the predominant anomaly (37.7%), consistent with findings from Boutin et al. [28], Kaste et al. [29], and Kılınç et al. [30], who similarly identified crown size abnormalities as the most frequent chemotherapy-induced dental developmental disturbance. The pathophysiological basis involves cytotoxic interference with the function of ameloblasts and odontoblasts during the critical mineralization window [10, 11].

Importantly, the primary hypothesis of this study concerns the effect of time elapsed since treatment completion on salivary function and caries experience — outcomes that follow a post-treatment recovery trajectory — rather than the prevalence of developmental anomalies, which is determined by age at treatment. As all participants were treated well within the window of dental development and maturation, the concern that some survivors might have been treated outside this window does not apply to the present sample and does not affect the interpretation of either outcome.

Notably, our survivors demonstrated salivary parameters and caries indices comparable to those of healthy controls when analyzed as a single group. This finding contrasts with some previous reports suggesting persistent salivary dysfunction in cancer survivors [18, 31] but aligns with studies suggesting potential differences in salivary function according to time since treatment completion [32]. However, the subgroup analysis revealed a more nuanced picture: early survivors (24–36 months post-treatment) exhibited significantly lower salivary flow rates than late survivors and controls, suggesting ongoing salivary gland recovery during this period. The lower salivary flow rates observed in early survivors likely reflect incomplete recovery of salivary gland function following antineoplastic treatment. Chemotherapeutic agents exert cytotoxic effects on rapidly proliferating salivary gland acinar cells, leading to a transient, and sometimes prolonged, reduction in secretory capacity. The observation that late survivors showed salivary flow rates comparable to those of controls suggests that salivary gland function recovers gradually over time, a process that appears to extend beyond the first 24–36 months following treatment completion.

These survivorship-period findings are best interpreted in the context of the dynamic salivary changes that occur during active antineoplastic therapy. Studies evaluating children during chemotherapy for ALL have documented acute suppression of salivary function: a significant decline in unstimulated salivary flow rate has been reported by the end of the induction phase, with salivary flow, pH, and buffering capacity each positively correlated with absolute neutrophil counts, indicating a concurrent compromise of local oral defense [33]. Reduced salivary flow rate and pH during treatment have likewise been described in leukemic children relative to healthy siblings [34].

ARTICLE IN PRESS

Importantly, these effects appear largely transient: although children treated for ALL exhibit lower mean salivary flow than matched controls, the salivary gland alterations occurring during treatment do not appear to impair flow permanently [35]. Our data extend these observations into the survivorship period, demonstrating that salivary flow rates among early survivors remained below those of late survivors and controls, whereas late survivors achieved values comparable to controls. Taken together, these findings are consistent with a trajectory of acute intra-treatment salivary suppression followed by gradual post-treatment recovery that may continue beyond the first 24–36 months after treatment completion.

The significantly elevated caries indices in early survivors compared with late survivors represent a key clinical finding. Both ICDAS mean scores and DMFT/dft indices demonstrated this temporal pattern, and multivariable regression confirmed that time since treatment completion was an independent predictor of caries outcomes, even after adjustment for age, sex, salivary parameters, radiotherapy history, and dental anomalies. Importantly, oral hygiene status (OHI-S) did not differ significantly between survivors and controls or across the early-, late-survivor, and control groups, indicating that the elevated caries indices among early survivors are unlikely to be attributable to differences in oral hygiene and more plausibly reflect salivary dysfunction and treatment-related factors. These results corroborate findings from the Dutch Childhood Cancer Survivor Study (DCCSS LATER 2), which documented more favorable oral health profiles among survivors evaluated at longer intervals following treatment completion [36]. The temporal improvement in oral health parameters observed between early and late survivors is biologically plausible: as salivary gland acinar cells undergo progressive functional recovery, restored salivary flow enhances oral clearance, buffering capacity, and antimicrobial defense, thereby reducing caries susceptibility over time. Longitudinal studies are warranted to confirm this recovery trajectory and to establish evidence-based timing recommendations for preventive dental care in childhood ALL survivors.

The observation of differences between survivors evaluated before and after 36 months post-treatment raises the hypothesis that this period may be associated with changes in oral health vulnerability, rather than defining a definitive biological threshold. It is important to clarify that dental developmental anomalies represent a direct, largely time-independent consequence of antineoplastic treatment, with their prevalence more strongly associated with age at treatment initiation than with time elapsed since treatment completion. By contrast, salivary gland function and its downstream effects on caries susceptibility appear to follow a time-dependent recovery trajectory. Current Children’s Oncology Group guidelines recommend a dental evaluation at baseline and every 6 months thereafter [6], but do not provide specific guidance on stratifying surveillance intensity. Our data suggest that salivary gland function may remain compromised during the early post-treatment period, with gradual recovery

ARTICLE IN PRESS

observed over time. Intensified preventive dental care — including salivary assessment, fluoride application, and dietary counseling [37] — is therefore recommended during the first 24–36 months following treatment completion, while standard risk-based protocols may be appropriate thereafter.

The presence of dental anomalies did not emerge as an independent predictor of caries outcomes in multivariable analysis, a finding that may reflect the dominant influence of salivary dysfunction and time since treatment completion on caries risk in this population.

Radiotherapy status did not emerge as a significant determinant of oral health outcomes in our analysis. While no statistically significant association was observed between radiotherapy and oral health outcomes in this study, the limited number of irradiated participants (n = 6) likely resulted in insufficient statistical power to detect potential differences, and a definitive conclusion regarding the absence of a biological effect cannot be drawn. These findings should be interpreted in light of important distinctions between craniospinal and head-and-neck radiotherapy. Craniospinal irradiation targets the neuraxis rather than orofacial structures, resulting in substantially lower incidental doses to the salivary glands and dentition compared with therapeutic head-and-neck radiotherapy. Direct comparisons with studies evaluating populations treated with head-and-neck irradiation are therefore not appropriate. Within the context of prophylactic craniospinal protocols, our data suggest that low-dose cranial irradiation (12–18 Gy) may exert subtler oral effects that are not detectable in studies with small irradiated subgroups, underscoring the need for larger studies with detailed dosimetric analyses targeting orofacial structures specifically [42, 43].

Strengths and Limitations

This study has several notable strengths. The sibling-controlled design represents a key methodological strength, providing rigorous control for multiple sources of confounding that are particularly relevant in oral health research. First, dental developmental anomalies are known to have a heritable component, and genetic susceptibility to odontogenic abnormalities may vary between unrelated individuals; the use of biological siblings as controls effectively neutralizes this potential confounding factor [12, 13]. Second, siblings share the same household environment, socioeconomic background, dietary habits, oral hygiene practices, and access to dental care — factors that are known determinants of caries experience and oral health behavior. This design therefore enables a more precise estimation of the treatment-specific contribution to observed oral health differences than would be possible with unrelated controls. A further methodological strength is the application of the ICDAS II system, which enables detection of early non-cavitated lesions and provides a more sensitive evaluation of caries burden than traditional DMFT/dft indices alone [25, 38, 39, 40, 41]. The dual assessment approach — combining ICDAS II, DMFT/dft indices, objective salivary measurements, and panoramic radiographic evaluation — provides a

ARTICLE IN PRESS

comprehensive characterization of oral health that is more sensitive than earlier studies that relied predominantly on traditional caries indices [35].

Several limitations should be acknowledged. The cross-sectional design precludes establishing causal relationships and does not capture longitudinal changes within individual patients. The relatively small sample size, although adequate for primary comparisons, limited statistical power for subgroup analyses, particularly the radiotherapy comparison. The selection of sibling controls, while providing excellent matching for genetic and environmental factors, may not accurately represent the general population. The use of current age rather than age at diagnosis as an inclusion criterion is acknowledged as a limitation, although the age-at-diagnosis distribution in this sample confirms that all participants were treated within the window of dental development. Behavioral and dietary determinants of caries — such as toothbrushing frequency, fluoride use, dietary habits, and prior dental attendance — were not recorded through a structured history; oral hygiene was instead evaluated objectively using the OHI-S, and the absence of self-reported behavioral data is acknowledged as a limitation. Furthermore, assessor blinding was not possible due to the sibling-controlled design, as participants from the same family attended clinical examinations together, which may have introduced observation bias. Finally, the single-center design may limit generalizability to populations receiving different treatment protocols.

Future research directions should include prospective longitudinal studies tracking oral health trajectories from treatment completion through extended survivorship, validation of the 36-month threshold in larger multicenter cohorts, and investigation of targeted preventive interventions during the high-risk early survivor period.

ARTICLE IN PRESS

Conclusion

This study demonstrates a substantial prevalence of dental developmental anomalies among childhood acute lymphoblastic leukemia survivors and identifies meaningful differences in oral health parameters according to time since treatment completion. Survivors evaluated within the first 24–36 months after treatment exhibited lower salivary flow rates and higher caries indices than those assessed later, suggesting a tendency toward more favorable oral health outcomes with increasing time since treatment. These findings indicate that salivary gland function may remain compromised during the early post-treatment period, with gradual recovery over time; therefore, intensified preventive dental care is recommended during the first 24–36 months following treatment completion. Time since treatment completion emerged as an independent predictor of caries outcomes, underscoring its potential to inform risk-adapted follow-up approaches in survivorship care. Overall, the results underscore the importance of close and

ARTICLE IN PRESS

sustained collaboration between pediatric oncology and dental care teams to support long-term oral health in this growing survivor population.

Figure legends

Figure 1. Panoramic radiograph of a childhood acute lymphoblastic leukemia survivor showing microdontia of multiple permanent teeth, dental agenesis of the mandibular second permanent premolars, and root malformations of the mandibular incisors.

Figure 2. Panoramic radiograph of a childhood acute lymphoblastic leukemia survivor showing generalized root malformations and dental agenesis of the bilateral mandibular second permanent molars.

List of Abbreviations

ALL: Acute lymphoblastic leukemia; CCS: Childhood cancer survivors; CT: Chemotherapy; dft: Decayed and filled primary teeth index; DMFT: Decayed, missing due to caries, and filled permanent teeth index; ICDAS II: International Caries Detection and Assessment System II; OHI-S: Simplified Oral Hygiene Index; RT: Radiotherapy; SFR: Salivary flow rate.

Declarations

Ethics approval and consent to participate

This study was approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee (approval number: 2024/04-18). Written informed consent was obtained from parents or legal guardians of all participants, and assent was obtained from children aged 7 years and older. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable. This manuscript does not contain an individual person’s data in any form.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors’ contributions

ARTICLE IN PRESS

SEG conceived and designed the study, conducted all clinical examinations, collected the data, and served as the primary contributor to manuscript preparation. SK performed the salivary sample analyses and contributed to data interpretation. GK played a central role in conceptualizing the study, contributed to the study design, conducted radiographic evaluations, and assisted in manuscript preparation. HÖ contributed to the study design, facilitated patient recruitment through the pediatric hematology clinic, and contributed to clinical data acquisition. GB oversaw the study process and contributed to manuscript preparation and critical revision. All authors reviewed and approved the final manuscript.

Acknowledgements

The authors thank the patients and their families for participating in this study, as well as the staff of the Pediatric Hematology Department for their assistance with patient recruitment.

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17-48.
2. Howlader N, Noone AM, Krapcho M, et al., editors. SEER Cancer Statistics Review, 1975-2018. Bethesda, MD: National Cancer Institute; 2021.
3. Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. N Engl J Med. 2015;373(16):1541-52.
4. Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355(15):1572-82.
5. Armstrong GT, Kawashima T, Leisenring W, et al. Aging and risk of severe, disabling, life-threatening, and fatal events in the childhood cancer survivor study. J Clin Oncol. 2014;32(12):1218-27.
6. Children's Oncology Group. Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers, Version 6.0. Monrovia, CA: Children's Oncology Group; October 2023. Available at: www.survivorshipguidelines.org
7. Al-Ansari S, Stolze J, Bresters D, et al. Late complications in long-term childhood cancer survivors: what the oral health professional needs to know. Dent J. 2024;12(1):17.
8. Pombo Lopes J, Rodrigues I, Machado V, Botelho J, Bandeira Lopes L. Chemotherapy and radiotherapy long-term adverse effects on oral health of childhood cancer survivors: a systematic review and meta-analysis. Cancers. 2023;16(1):110.
9. Mishra R, Kapur A, Mathur VP, Sardana D. Late oral adverse effects of chemotherapy for hematological malignancies in children: a systematic review and meta-analysis of case-control studies. Oral Oncol. 2024;159:107103.

ARTICLE IN PRESS

10. Minicucci EM, Lopes LF, Crocci AJ. Dental abnormalities in children after chemotherapy treatment for acute lymphoid leukemia. Leuk Res. 2003;27(1):45-50.

11. Dahllöf G, Rozell B, Forsberg CM, Borgström B. Histologic changes in dental morphology induced by high dose chemotherapy and total body irradiation. Oral Surg Oral Med Oral Pathol. 1994;77(1):56-60.

12. Hölttä P, Alaluusua S, Saarinen-Pihkala UM, Peltola J, Hovi L. Agenesis and microdontia of permanent teeth as late adverse effects after stem cell transplantation in young children. Cancer. 2005;103(1):181-90.

13. Immonen E, Nikkilä A, Peltomäki T, Aine L, Lohi O. Late adverse effects of childhood acute lymphoblastic leukemia treatment on developing dentition. Pediatr Blood Cancer. 2021;68(9):e29200.

14. Pedersen LB, Clausen N, Schrøder H, Schmidt M, Poulsen S. Microdontia and hypodontia of premolars and permanent molars in childhood cancer survivors after chemotherapy. Int J Paediatr Dent. 2012;22:239-243.

15. Lopez BC, Esteve CG, Perez MGS. Dental treatment considerations in the chemotherapy patient. J Clin Exp Dent. 2010;3:31-42.

16. Busenhart DM, Erb J, Zmoos S, et al. Late effects of chemo and radiation treatment on dental structures of childhood cancer survivors: a systematic review and meta-analysis. Eur Arch Paediatr Dent. 2019;20(5):353-368.

17. Stolze J, Teepen JC, Raber-Durlacher JE, et al. Prevalence and risk factors for hyposalivation and xerostomia in childhood cancer survivors following different treatment modalities--a Dutch Childhood Cancer Survivor Study Late Effects 2 Clinical Study (DCCSS LATER 2). Cancers. 2022;14(14):3379.

18. Vistoso Monreal A, Polonsky G, Shiboski C, Sankar V, Villa A. Salivary gland dysfunction secondary to cancer treatment. Front Oral Health. 2022;3:907778.

19. Avşar A, Elli M, Darka O, Pinarli G. Long-term effects of chemotherapy on caries formation, dental development, and salivary factors in childhood cancer survivors. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;104(6):781-9.

20. Nemeth O, Hermann P, Kivovics P, Garami M. Long-term effects of chemotherapy on dental status of children cancer survivors. Pediatr Hematol Oncol. 2013;30(4):374-85.

21. Seremidi K, Gizani S, Anderson M, Dahllöf G, Barr-Agholme M, Parekh S, Tsilingaridis G; European Academy of Paediatric Dentistry (EAPD). Best clinical practise guidance for oral health care management of long-term childhood cancer survivors (CCS): an EAPD policy document. Eur Arch Paediatr Dent. 2025;26(4):753-757.

ARTICLE IN PRESS

ARTICLE IN PRESS

22. Seremidi K, Gizani S, Dahllöf G, et al. Dental management of long-term childhood cancer survivors: a systematic review. Eur Arch Paediatr Dent. 2024.

23. Flohr T, Schrauder A, Cazzaniga G, Panzer-Grümayer R, van der Velden V, Fischer S, et al.; International BFM Study Group (I-BFM-SG). Minimal residual disease-directed risk stratification using real-time quantitative PCR analysis of immunoglobulin and T-cell receptor gene rearrangements in the international multicenter trial AIEOP-BFM ALL 2000 for childhood acute lymphoblastic leukemia. Leukemia. 2008;22:771-82.

24. AlQahtani SJ, Hector MP, Liversidge HM. Brief communication: The London atlas of human tooth development and eruption. Am J Phys Anthropol. 2010;142(3):481-90.

25. Ismail AI, Sohn W, Tellez M, et al. The International Caries Detection and Assessment System (ICDAS): an integrated system for measuring dental caries. Community Dent Oral Epidemiol. 2007;35(3):170-8.

26. World Health Organization. Oral Health Surveys: Basic Methods. 5th ed. Geneva: WHO; 2013.

27. Greene JC, Vermillion JR. The simplified oral hygiene index. J Am Dent Assoc. 1964;68:7-13.

28. Boutin C, Huynh N, Rompré P, Laverdiere C, Asselin ME. Prevalence, severity, and description of dental anomalies in children treated for acute lymphoblastic leukemia. Pediatr Dent. 2023;45(6):419-26.

29. Kaste SC, Hopkins KP, Jones D, Crom D, Greenwald CA, Santana VM. Dental abnormalities in children treated for acute lymphoblastic leukemia. Leukemia. 1997;11(6):792-6.

30. Kılınç G, Bulut G, Ertuğrul F, Ören H, Demirağ B, Demiral A, et al. Long-term Dental Anomalies after Pediatric Cancer Treatment in Children. Turk J Haematol. 2019;36(3):155-61.

31. Nemeth O, Kivovics M, Pinke I, Marton K, Kivovics P, Garami M. Late effects of multiagent chemotherapy on salivary secretion in children cancer survivors. J Am Coll Nutr. 2014;33(3):186-91.

32. Patni T, Lee CT, Li Y, et al. Factors for poor oral health in long-term childhood cancer survivors. BMC Oral Health. 2023;23(1):79.

33. Mishra R, Kapur A, Goyal A, Gauba K, Trehan A. Salivary parameters and their correlation with neutrophil counts in children with acute lymphoblastic leukemia. Eur Arch Paediatr Dent. 2021;23(2):281-287.

34. Hegde AM, Joshi S, Rai K, Shetty S. Evaluation of oral hygiene status, salivary characteristics and dental caries experience in acute lymphoblastic leukemic (ALL) children. J Clin Pediatr Dent. 2011;35(3):319-23.

ARTICLE IN PRESS

ARTICLE IN PRESS

35. Maciel JC, de Castro CG, Brunetto AL, Di Leone LP, da Silveira HE. Oral health and dental anomalies in patients treated for leukemia in childhood and adolescence. Pediatr Blood Cancer. 2009;53(3):361-5.

36. Stolze J, Vlaanderen KCE, Holtbach FCED, et al. Long-term effects of childhood cancer treatment on dentition and oral health: a dentist survey study from the DCCSS LATER 2 study. Cancers. 2021;13(21):5264.

37. Nessa J, Jahan I, Asha M, Afrin S, Zakir A, Shikder H, et al. Prevention of oral manifestations in acute lymphoblastic leukemic children (ALL) by meticulous mouth preparation including fluoride application. J Community Med Public Health Rep. 2022;3(7). doi:10.38207/jcmphr/2022/sep03070298

38. Mehdipour A, Masoumi M, Fateh R, Aghaali M, Mohammadidana F, Saleh A, Rasouli A, Kabiri F. Comparative study of the profile of supragingival dental plaque and tooth decay in patients with lupus erythematosus and rheumatoid arthritis. BMC Oral Health. 2025. doi:10.1186/s12903-025-05762-4.

39. Pryimak KV, Zoriy IA, Bidenko NV, Borysenko AV, Batig VM, Hlushchenko TA, Batih IV, Sheremet MI. Assessment of dental caries in children with organic lesions of the nervous system using ICDAS II criteria. J Med Life. 2021. doi:10.25122/jml-2020-0155.

40. Cerón-Bastidas XA, Suarez A, Guauque-Olarte S. Differences in Caries Status and Risk Factors among Privileged and Unprivileged Children in Colombia. Acta Stomatol Croat. 2018;52(4):330-9.

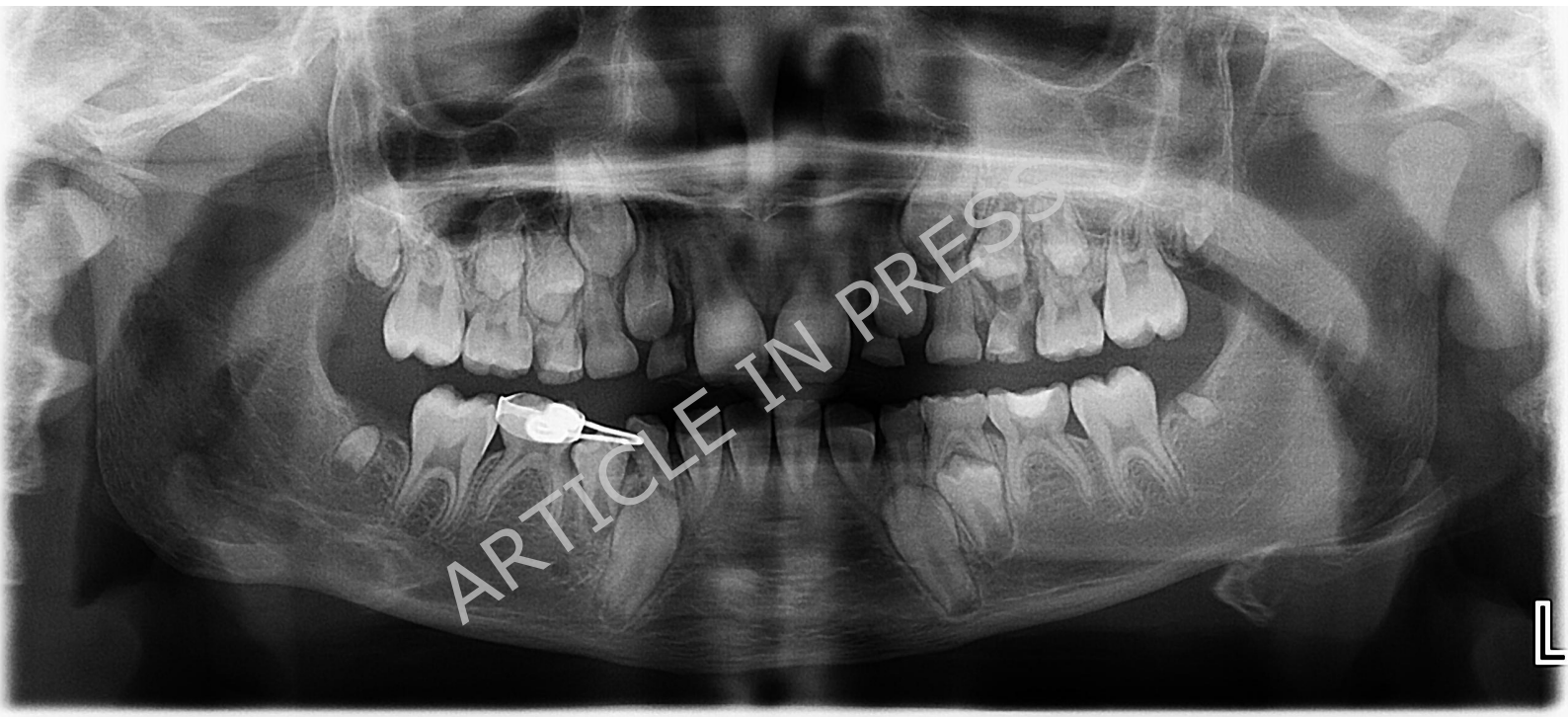
41. Amorim RG, Figueiredo MJ, Leal SC, Mulder J, Frencken JE. Caries experience in a child population in a deprived area of Brazil, using ICDAS II. Clin Oral Investig. 2012;16(2):513-20.

42. Milgrom SA, van Luijk P, Pino R, et al. Salivary and dental complications in childhood cancer survivors treated with radiation therapy to the head and neck: a PENTEC comprehensive review. Int J Radiat Oncol Biol Phys. 2024;119(4):1103-16.

43. Wilberg P, Kanellopoulos A, Ruud E, Hjermstad MJ, Fosså SD, Herlofson BB. Dental abnormalities after chemotherapy in long-term survivors of childhood acute lymphoblastic leukemia 7-40 years after diagnosis. Support Care Cancer. 2016;24(4):1497-504.

ARTICLE IN PRESS

ARTICLE IN PRESS



ARTICLE IN PRESS

