Oral Health Among Children With Haematological Malignancies In Syria

MHD Bahaa Aldin Alhaffar  
Damascus University

Khattab Mustafa  
Damascus University

Samira Alsabbagh  
Damascus University

Ola Alhaffar  
Damascus University

Ameer Kakaje (ameer.kakaje@hotmail.com)  
Damascus University  https://orcid.org/0000-0002-3949-6109

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Abstract

Background: Since 2011, Syria has been facing a conflict that impacted all aspects of life. Haematological malignancies are mainly treated with chemotherapy which can further harm oral health. This study evaluates oral health of children with haematological malignancies and on chemotherapy in Syria.

Methods: This is a cross-sectional study of (40) patients from the major paediatric hospital in Damascus. Decayed, Missing, Filled Teeth (DMFT) and Oral Assessment Guide (OAG) indices were used to evaluate oral health. Data about cancer was collected from medical records.

Results: Patients aged between 3-14 years. Three types of paediatric cancer were included; acute lymphoblastic leukaemia (ALL) 52.2%, Hodgkin’s Lymphoma (HL) 27.5%, and Burkitt Lymphoma (BL) 20%. Average DMFT was (6.7 ± 3.2) and average OAG index was (10.8 ± 1.7). DMFT was significantly correlated with OAG (r=0.021). In patients undergoing chemotherapy, better DMFT and OAG indices were reported in males who had cancer for shorter periods, had higher frequency of toothbrushing, or/and were helped while toothbrushing. However, age and cancer type did not significantly affect DMFT and OAG.

Conclusion: Children undergoing chemotherapy in Syria had worse oral health and pain compared to other children from the same age in similar studies. More attention should be given to these patients in order to improve their overall health and their quality of life especially during the ongoing conflict.

Introduction:
The Syrian crisis significantly impacted all aspects of life since it started in 2011 (1). The health sector was severely damaged. Estimations demonstrated that around 13 million people need medical care in Syria. In 2016, the World Health Organization (WHO) received only one-third of the necessary funding to support humanitarian response activities (1, 2). Moreover, over 80% of Syrians were under the poverty line and over 90% suffered from a direct or indirect effect of the war (3). Over half the children were severely affected by the war (4).

In Syria, cancer is the third cause of death. Several studies investigated the common types of cancer and gave a general perspective about the epidemiology of cancers (5). Chemotherapy prevents the abnormal growth of these cells; unfortunately, it affects healthy cells as well (6). Mucositis, xerostomia (7), infections, salivary glands dysfunction, and dysgeusia are among the common side effects of chemotherapy (8). Overall, 70% of cancers are treated with chemotherapy around the world, 40% of which showed oral manifestations. This number increases to (90%) for children under 12 years of age (9). It is well documented that oral health has a direct effect on systematic health. One research from Syria reported that the average number of Decayed, Missing, Filled Teeth index (DMFT) was 3.36 among Syrian children which is higher than what is recommended by the WHO (2). Acute lymphoblastic leukaemia (ALL) and lymphoma are among the most common malignancies in children and they are mainly treated by chemotherapy.

In recent decades, cancer and its care have become a global concern due to its financial, social, and health implications (10). The WHO predicted that the number of cancer patients will increase by 2030, and that developing countries will be affected the most (11). Fortunately, due to the combination of chemotherapy and
dosage intensification, there has been a significant rise in survival rates among children (12). As oral manifestations can be quite common and reduce the quality of life, it is crucial to document the effects of cancer and chemotherapy on oral health among children. This study is the first in war-torn Syria to estimate the effects of ALL, lymphoma, and chemotherapy on oral health.

**Methods:**

This is a cross-sectional study which investigated the oral health among children with either ALL or lymphoma. Data were collected from February 2019 to April 2019.

**Sample:**

The study sample consisted of 40 patients. Data was collected between January and March of 2019 from the Department of Haematology, Children University Hospital in Damascus University, which is one of only two major paediatric hospitals in Syria to treat cancer patients (13).

Children who suffered from ALL, or lymphoma were included in the study regardless of the therapy. However, children who were in a bad general condition were not enrolled.

Malignancies were diagnosed by bone marrow aspiration, lymph nodes, bone marrow biopsy, or/and flowcytometry.

Informed consents were obtained from parents/guardians before the examination. Ethical approval was obtained from the Ministry of Higher Education and the Paediatric Hospital in Damascus.

**Questionnaires:**

A validated questionnaire consisting of three sections was used for data collection:

**First section:** Personal information: (gender, age, governate, admission number).

**Second section:** Cancer-related information: (type of cancer, date of diagnosis, treatment protocol).

**Third section:** Oral health information: (The number of decayed, missing, and filled teeth -DMFT index-, frequency of tooth brushing, family contribution in oral hygiene, and Oral Assessment Guide OAG (14).

DMFT is the recommended method by the WHO for primary and permanent teeth and is crucial for epidemiological studies to assess health status in a community (15, 16). OAG is a useful tool that can be used to assess the condition of oral cavity (14, 17).

**Examination Tools**

Dental mirrors, blunt probes, tweezers, boxes for used instruments, boxes for sterilized instruments, face masks, gloves, flashlights, hand sanitizers, and surface sanitizers.

**Procedures**
A visit was made to the hospital every other week for a period of 10 weeks. One of the data collectors arrives before each visit to determine who to enroll in the study according to the inclusion/exclusion criteria. Afterwards, another data collector arrives to collect the personal and cancer-related information and to examine the oral health status after obtaining ethical approval from the children’s parents. Data collectors were MSc students who were trained to deal with vulnerable children.

**Statistical Analysis**

The data was analysed using SPSS V.22 (Statistical Package for the Social Sciences, IBM software, Chicago).

**Results:**

The sample consisted of 40 patients. Their ages ranged from 3-14 years old. 75% of the sample were males and 25% were females. Children were from 6 different governates across Syria and the highest percentage (27.5%) was from Rif Dimashq governate.

Three main types of paediatric cancer were observed which are ALL 52.2%, Hodgkin’s Lymphoma (HL) 27.5%, and Burkitt Lymphoma 20%. All enrolled children were receiving either chemical treatment 82.5% or surgical treatment 17.5%. Of the patients in the sample, 50% were diagnosed within the past 6 months, 30% have been receiving treatment for one year, 12.5% for two years, and 7.5% for more than two years (Table 1).
Table 1
– demographic variables of the sample

| Variables                  | Number | Percentage | Average DMFT | Average OAG index |
|----------------------------|--------|------------|--------------|-------------------|
| **Age in years**           |        |            |              |                   |
| 3 – 5.5                    | 7      | 17.5%      | 1.8          | 8.5               |
| 6 – 8.5                    | 12     | 30%        | 6.08         | 9.6               |
| 9 – 11.5                   | 12     | 30%        | 5.6          | 9.2               |
| 12 -14                     | 9      | 22.5%      | 4.6          | 11.2              |
| **Gender**                 |        |            |              |                   |
| Males                      | 30     | 75%        | 5.7          | 10.6              |
| females                    | 10     | 25%        | 3.8          | 9                 |
| **Governate**              |        |            |              |                   |
| Damascus                   | 9      | 22.5%      | 4.3          | 9.5               |
| Rif Dimashq                | 11     | 27.5%      | 6.3          | 11.3              |
| Hama                       | 8      | 20%        | 4.7          | 9                 |
| Homs                       | 4      | 10%        | 5            | 10.5              |
| Daraa                      | 3      | 7.5%       | 4.8          | 11.5              |
| As-Suwayda                 | 5      | 12.5%      | 4            | 9.5               |
| **Cancer**                 |        |            |              |                   |
| ALL                        | 21     | 52.5%      | 4.14         | 9.3               |
| HL                         | 11     | 27.5%      | 5.3          | 9.6               |
| BL                         | 8      | 20%        | 4.8          | 11.4              |
| **First diagnosed**        |        |            |              |                   |
| 6 months or less           | 20     | 50%        | 4.15         | 9.25              |
| 6 months to 1 year         | 12     | 30%        | 4            | 9.6               |
| 1 - 2 years                | 5      | 12.5%      | 5.5          | 11                |
| More than 2 years          | 3      | 7.5%       | 6.3          | 11.8              |
| **Treatment protocol**     |        |            |              |                   |
| Chemotherapy               | 33     | 82.5%      | 5.6          | 11.3              |
| No chemotherapy            | 7      | 17.5%      | 4.8          | 9.5               |
| **Number of daily toothbrushing** |        |            |              |                   |
| 0                          | 20     | 50.0%      | 7.5          | 11.8              |
| 1                          | 14     | 35.0%      | 5.2          | 9.9               |
| 2                          | 5      | 12.5%      | 4            | 9.8               |
| 3                          | 1      | 2.5%       | 4            | 9.5               |
Oral health has been evaluated using two indices (DMFT, OAG). The average DMFT for the sample was $(6.7 \pm 3.2)$ and ranged between 0 and 14. The average OAG score was $10.8 \pm 1.7$ and ranged between 8 and 16 (Table 1).

The data showed that 50% of the patients in the sample did not brush their teeth on a daily basis. Of the patients that brushed their teeth, 35% did it only once per day, 12.5% did it twice per day and 2.5% brushed their teeth 3 times daily. Over 82% of the children did not receive assistance from their families regarding oral hygiene while the rest did receive help (Table 1). A remarkable positive correlation was found between DMFT and OAG indices using Pearson's correlation test $p=0.019$ (Table 2).

A significantly higher DMFT and OAG indices were found in females compared to males using independent sample T-test, and the $p$ values were 0.039 and 0.041, respectively. However, age and the type of cancer were not associated with these indices when using the analysis of variance (ANOVA) test (Table 3). Additionally, higher DMFT and OAG indices were found in patients who had cancer for longer periods of time and who were treated by chemotherapy. However, more frequent toothbrushing was significantly associated with lower indices. Finally, family assisting with oral hygiene was also significantly associated with lower indices (Table 3).
| Variables          | N  | Mean DMFT | Mean OAG | Statistical test | P-value | Result            |
|-------------------|----|-----------|----------|------------------|---------|-------------------|
| **Gender**        |    |           |          |                  |         |                   |
| female            | 10 | 5.7       | 10.6     | Independent sample T-test | 0.039   | Significant difference |
| male              | 30 | 3.8       | 9        |                  | 0.041   |                   |
| **Age**           |    |           |          |                  |         |                   |
| 3 – 5.5           | 7  | 1.8       | 8.5      | ANOVA           | 0.085   | No Significant difference |
| 6 – 8.5           | 12 | 6.08      | 9.6      |                  | 0.065   |                   |
| 9 – 11.5          | 12 | 5.6       | 9.2      |                  | 0.021   |                   |
| 12 -14            | 9  | 4.6       | 11.2     |                  |         |                   |
| **Cancer**        |    |           |          |                  |         |                   |
| ALL               | 21 | 4.14      | 9.3      | ANOVA           | 0.377   | No Significant difference |
| HL                | 11 | 5.3       | 9.6      |                  | 0.748   |                   |
| BL                | 8  | 4.8       | 11.4     |                  |         |                   |
| **First diagnosed** |   |           |          |                  |         |                   |
| 6 months or less  | 20 | 4.15      | 9.25     | ANOVA           | 0.036   | Significant difference |
| 6 months to 1 year| 12 | 4         | 9.6      |                  | 0.016   |                   |
| 1 - 2 years       | 5  | 5.5       | 11       |                  |         |                   |
| More than 2 years | 3  | 6.3       | 11.8     |                  |         |                   |
| **Treatment**     |    |           |          |                  |         |                   |
| Chemotherapy      | 33 | 5.6       | 11.3     | Independent sample T-test | 0.032   | Significant difference |
| No chemotherapy   | 7  | 4.8       | 9.5      |                  | 0.018   |                   |
| **Number of daily toothbrushing** | | | | | | |
| 0                 | 20 | 7.5       | 11.8     | ANOVA           | 0.001   | Significant difference |
| 1                 | 14 | 5.2       | 9.9      |                  | 0.045   |                   |
| 2                 | 5  | 4         | 9.8      |                  |         |                   |
| 3+                | 1  | 4         | 9.5      |                  |         |                   |
| **Family assist** |    |           |          |                  |         |                   |
| no                | 33 | 6.6       | 9.8      | Independent sample T-test | 0.030   | Significant difference |
| yes               | 7  | 4.8       | 9.2      |                  | 0.049   |                   |

**Discussion:**

This study found that children with haematological malignancies and undergoing chemotherapy suffer from more oral manifestations than children who did not conduct chemotherapy by using DMFT and OAG indices. Moreover, DMFT and OAG were significantly correlated (r=0.021). While oral health among males was better,
age and cancer type were not associated with DMFT and OAG indices despite age and cancer type being universally different depending on the gender. Children who were newly diagnosed with malignancies, family assistance in toothbrushing and frequency of toothbrushing per day were associated with better oral health.

The ongoing war in Syria has led to deterioration of the treatment of cancer patients due to lack of specialized physicians and the limited access to screening and management options. It is reported that the limited availability of radiation therapy, magnetic resonance imaging (MRI), genetic testing, and many other important examination procedures has subsequently caused inability of some physicians in Syria to provide the needed treatment (18, 19). Moreover, 50% of hospitals in Syria were overcrowded due to shortages in medical staff, medications, and equipment. There was also an urgent need for infant incubators, imaging machineries, and ambulances. A large number of primary health care centres had no sanitation systems and only (44%) of these centres had nebulizers. Most of the available resources were redirected into more critical and emergent cases, neglecting other aspects of health. Subsequently, the previous factors had its negative effect on children cancer patients as they are the most vulnerable and require special care (20). War affects people directly or indirectly as it is associated with an increased risk of several medical conditions such allergic rhinitis (21) and laryngopharyngeal reflux (22) both of which were observed as a distress of the war in Syria.

Dental carries were seen in 70% of normal children in Syria, with 48% appearing in the early childhood (23). Another study found that 61% of children at the age of 5 had caries (24). It was demonstrated by multiple studies that children with cancer, especially ALL, suffered after receiving chemotherapy from multiple oral manifestations where 92% suffered from gingivitis and 82% from caries. Mucositis, periodontitis, cheilitis, recurrent herpes, primary herpetic gingivostomatitis, mucosal petechiae, ecchymoses, and aphthous ulcers were among other manifestations found in these patients (25). DMFT scores were found to be higher in patients who received therapy for cancer even after five years of therapy cessation (26). It was found that prophylactic professional oral health care (POHC) in patients treated with chemotherapy can be an effective procedure, especially for oral mucositis (27). This was also found in children with ALL who received chemotherapy as oral care protocol where it resulted in good health status outcomes (28). Similar to our study, lower DMFT was associated with a higher frequency of tooth brushing among children (29) and it was found that oral hygiene can be effective in reducing oral complications in cancer patients (17). This indicates that simple procedures such as tooth brushing can be conducted to avoid the occurrence of oral complications.

Studies from Syria found that the mean score of DMFT was 2.4 at the age of 3 years which increased to 5.6 at the age of 5 years (23) and the mean DMFT was 3.27 at the age of 5 years (24). Additionally, in Iran, the DMFT mean score for children for ages between 5 and 6 was 5.05 (30), which was higher than what was found in our sample among the same age group. In Jordan, the mean score of DMFT was 3.3 for healthy 6-year old children and 1.1 for 12 year old’s (31). In Saudi Arabia, the mean DMFT was 1.72 for 6-year-old children and 2.66 for 12-year old children (32). In Syria, the mean DMFT was 3.36 for 12-year-old children (33). These scores by comparison were all lower than the results in our sample among the same age group. In Egypt, one study found that children with a mean age of 7.2 years had higher DMFT in males (38)
compared with females (28). While another study in Syria found a slightly higher DMFT in females at the age of 12 years (33). However, our study found that females had higher DMFT than males.

One study found that 26.7% of children who were treated with chemotherapy with a mean age of 8.4 years had an OAG score of 12 (34). When compared to those studies, our study showed higher results of the OAG index which ranged between 8-16 with an average of 10.8.

Limitations:

We do acknowledge that our study had limitations that might have biased the results. Sample size was small due to limited resources. No proper sample size or study power calculations were feasible as we could not enrol more participants. Moreover, we could not isolate the effect of chemotherapy or the malignancy itself on oral health. We also could not identify which chemotherapy regime caused these complications. Furthermore, due to the continuous interruption of the patients' treatment because of the war, we could not accurately determine which regiments the patients had been fully taken or which dosages in total were taken. Finally, we could not perform follow-ups due to limited resources and difficulties for researchers to find the children in future visits.

Conclusions:

Children suffering from paediatric cancer have worse overall oral health and more oral-related pain compared to healthy children of the same age. In particular, chemotherapy significantly worsens children's oral health. More attention should be given to paediatric cancer patients in Syria to improve their overall health and to improve the oral health related quality of life, especially during the Syrian crisis. Simple practises such as toothbrushing can significantly improve oral health.

Abbreviations:

BL: Burkitt Lymphoma.

DMFT: Decayed, Missing, Filled teeth.

GI: Gingival Index.

HL: Hodgkin's Lymphoma

PI: Plaque Index.

POHC: Prophylactic Professional Oral Health Care.

WHO: World Health Organization.

Declarations:

Ethics approval and consent to participate:
Approved on 20/12/2018, Ethical Committee Damascus university (Damascus University, Damascus, Syria; +963 113341864; manager@hcsr.gov.sy),

**Consent for publication:**

Not applicable

**Availability of data and materials:**

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

**Competing interests:**

The authors declare that they have no competing interests.

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**Authors' contributions:**

**MBA:** Conceptualization; Software; Methodology; Formal analysis; Investigation; Supervision; original draft: review & editing; Data curation.

**KM:** Conceptualization; original draft: Supervision; Writing - review & editing

Project administration; Resources; Investigation; Methodology.

**SA:** Supervision; Investigation; original draft: Writing.

**OH:** Investigation; methodology; original draft: Writing- review & editing

**AK:** resources; reviewed the manuscript; methodology; original draft: Writing- review & editing

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**Author's information:**

Authors were former/current students at this faculty of the time of the research and therefore understand the population well.

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