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Original Article

## Oral Manifestations and Salivary pH Changes in Children undergoing Antineoplastic Therapy

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### Abstract

**Objective:** To identify the oral manifestations and salivary pH before and after chemotherapy in pediatric patients. **Material and Methods:** The sample consisted of 46 children. It was included children from 2 to 12 years, diagnosed with Acute Lymphoblastic Leukemia (ALL) and they would be subjected to chemotherapy. The first evaluation was performed before chemotherapy and consisted of anamnesis, oral clinical examination and saliva collection to measure the pH. The second evaluation was performed among 10 to 15 days after the start of chemotherapy treatment and consisted of new saliva collection and clinical examination. **Results:** The results showed that the gender most affected by childhood cancer was male. The predominant age group were children aged 8-12 years. The most frequent oral manifestations were mucositis (35%), xerostomia (26%), toothache and dysphagia (22%). There was also a significant reduction in salivary pH after chemotherapy,  $p < 0.0001$ , indicating that the average pre and post chemotherapy are different ( $\Delta = 10.6$ ) with statistical significance at the 5% level. **Conclusion:** Patients with ALL can present any lesion in the oral cavity during or after the start of chemotherapy and undergo changes in the amount of salivary pH. The dentist needs and know the oral manifestations and intervene in the oral health of patients with ALL, contributing and assisting in their treatment.

**Keywords:** Cancer Patients; Chemotherapy; Oral Manifestations.

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## Introduction

Acute Lymphoblastic Leukemia (ALL) results in excessive and uncontrolled production of blasts of lymphoid type, hindering the normal production of red cells, white cells and platelets. The survival chances increased with the advances in the types of antineoplastic treatment [1].

Treatment for these patients consists essentially of chemotherapy and radiotherapy. In addition to these therapeutic bone marrow transplantation (BMT) has been progressively used for treating resistant neoplasms and/or recurrence. The chemotherapeutic agents and radiotherapy have a large dental interest due to their ability to induce oral manifestations [2].

The lesions in the oral cavity include the most frequent complications of cancer chemotherapy, due to the high sensitivity of tissues and oral structures to the toxic effects of chemotherapy [3].

The oral manifestations commonly evidenced in leukemic patients are paleness of the mucosa, gingival hyperplasia, spontaneous gingival bleeding, petechiae, mucositis, opportunistic infections and lymphadenopathy. These manifestations may delay treatment, aggravate the pathological picture and lead the patient to death. Such manifestations are more observed in acute leukemia, and in patients undergoing chemotherapy treatment [4].

Gingivitis is a change found in cancer patients, but is usually pre-existing and subsequently compounded by systemic framework, in other words, by immunosuppression and decrease in cleaning efficiency. Care is fundamental, because fungal, viral and bacterial infections can significantly worsen the clinical picture of this patient already weakened and takes it to death [5].

The therapeutic anticancer resources used for the cure of disease, repercussions in various organs and how there is no possibility of mouth to be separate from other parts of the body, the orofacial structures are also affected by the applied therapy as soon as the tissues of this region suffer effects of both direct stomatotoxicity as indirect [6].

Oral infections caused by cancer and/or its treatment are not well documented. The oral health is often not recorded in the patient's record. It has been claimed that doctors and nurses show less attention to the mouth than to other body parts. Oral problems can be underreported by patients and inadequately addressed by doctors, especially for patients with advanced cancer. Any cancer and/or its treatment are able to induce inflammation and damage to oral tissue. Pain and discomfort are common and can decrease the intake of fluids and nutrients, which in severe cases can lead to dehydration and malnutrition [7].

The dentist surgeon must have knowledge of the oral manifestations caused by leukemia and the anticancer treatment to improve the oral health of the patient. Given the above, our goal is to identify the oral manifestations and salivary pH before and after chemotherapy in children with acute lymphocytic leukemia of a reference center for the treatment of cancer in Belém, Brazil.

## Material and Methods

This study evaluated the oral manifestations in pediatric leukemic patients through accurate clinical examination of the structural components of the oral cavity. The same has been duly approved by the National Committee on Ethics and Research (CONEP), the Southern Cross University, obtained a favorable opinion in accordance with protocol number CE/UCS-005/2014. Parents or guardians have been informed about the survey and expressed their agreement by signing the free and informed consent form (ICF).

This survey was conducted on the premises of the Ophir Loyola Hospital in the city of Belém, Pará, Brazil. For this descriptive clinical study total sample consisted of 46 patients of both genders, treated among April to September 2014, distributed in an age group 2-12 years old. The study included patients with conclusive diagnosis of Acute Lymphoblastic Leukemia (ALL) undergoing antineoplastic therapy. Children in the terminal phase of the disease and children with other systemic diseases or syndromes were excluded of the study.

Anamnesis and clinical examination were performed in order to collect information regarding dental and medical condition of the child was conducted. The medical records had personal data relating to the child (name, age, gender, address, contact telephone), data from the disease (cancer treatment) and dental assessment (oral and salivary collection manifestations).

The clinical condition of the oral cavity was evaluated by visual inspection, prior prophylaxis made one hour before the examination by the heads of children, to investigate the presence of Stomatological changes. For the execution of this phase was used clinical flat mirror number 5 and wooden spatula. Since this research was conducted at the hospital, often in the patient's own bed, we used the artificial lighting a lantern wrapped with plastic bag for biosecurity criteria.

To reduce the variability of inter diagnosis and increase the reliability of the data collected, there was a training and calibration prior to the start of the examinations. The objectives of this step according to the World Health Organization are: to ensure uniformity of interpretation, understanding and application of the criteria of various diseases and conditions to be observed and recorded; ensure that each of the examiners can analyze in a consistent pattern [8]. The calibration process has been planned for two examiners. The inter diagnostic concordance was 0.78 being considered a good agreement [9].

The investigator started clinical examination by analyzing the external oral surface, followed by intraoral analysis for analysis of dental elements, covering from 55 to 65 and 75 to 85 in deciduous teeth and from 17 to 27 and 37 to 47 in denture mixed [10]. All data were recorded in the medical record. At this stage the evaluators followed all bio-security standards, such as washing hands before and after clinical examination, use of Personal Protective Equipment - PPE (gloves, mask, cap and coat), sterilization of instruments and proper disposal of waste materials. The diagnosis of mucositis was established using the scale defined by the WHO.

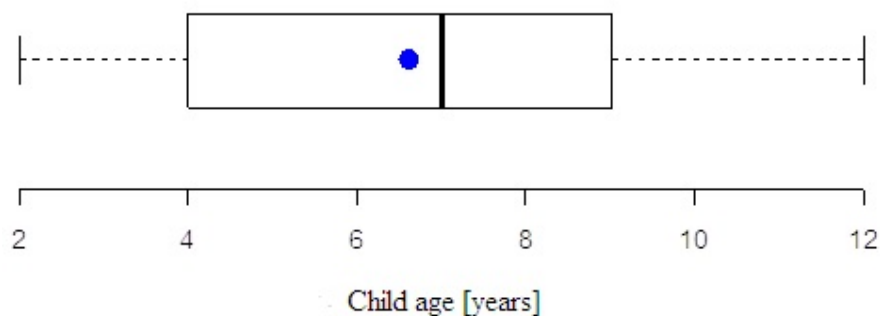
For data analysis we used descriptive statistics and inferential statistical techniques. The descriptive statistical techniques involved obtaining absolute and percentage distributions and obtaining the average statistics, standard deviation and coefficient of variation. In the inferential

analysis, statistical significance was set at  $p$  levels  $<0.05$  was considered doubtful and track the level realized in the range  $0.05 \leq p < 0.10$ . Data were analyzed using the statistical software R for Windows, version 3.1.0 and its Hmisc package version 3.14-4, epitools version 0.7-7, 1.2-4 colorspace version car version 2.0-21, and descr version 1.0.2.

## Results

The gender most affected by childhood cancer was the masculine against 34 children of 12 females. There is a proportion of male children higher than 50%.

In the distribution of patients according to age, it was observed that the prevailing prevalence were children aged 8-12 years with 46%, followed by the age group 2-4 years with 35% and then the age of 5-7 years to 19%. Was obtained as average of 6.6 with a standard deviation of 3.0. When applied Boxplot of ages, it was granted a median of seven years and interquartile range of four to nine years (Figure 1).



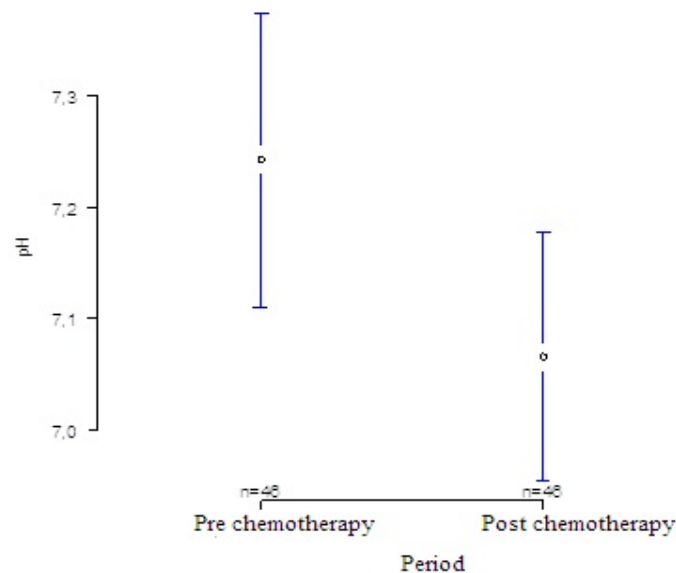
**Figure 1. Boxplot of the ages of the children in the sample.**

When we analyzed the pre oral manifestations and post-chemotherapy, we found that the highest prevalence stomatological changes were observed in mucositis with 35%, followed by xerostomia with 26%, dysphagia, and odontoalgia with 22%. If we analyze the oral manifestations prior to starting chemotherapy, we see that only mucositis, xerostomia and gingival bleeding were present and in small proportion (Table 1).

**Table 1. Oral manifestations before and after chemotherapy.**

Oral manifestations	Pre Chemotherapy	Post Chemotherapy	Diference
Mucositis	2%	37%	0,35%
Xerostomia	2%	28%	0,26%
Candidiasis	0%	2%	0,02%
Changing the Palate	0%	15%	0,15%
Gingival bleeding	2%	15%	0,13%
Lip herpes	0%	9%	0,09%
Odontoalgia	0%	22%	0,22%
Dysphagia	0%	22%	0,22%
Others	13%	17%	0,04%

In the analysis of the initial salivary pH, we found the maximum value of 8.49, the mean of 7.24 and minimum of 6.34, since salivary final pH has presented a maximum value of 7.80, the mean of 7.06 and minimum of 5.98 (Figure 2).



**Figure 2. Measurement of pH before and after chemotherapy treatment.**

## Discussion

The gender most affected by childhood cancer was the masculine with 74% of cases, females corresponded to only 26%. The gender most affected by childhood cancer was the male with 74% of cases, while women accounted for only 26%. These data are very similar to recent studies [2,11]. The data also are consistent with the prevalence observed in research conducted in Belém do Pará [10], where found a percentage of 59.37% for male and 40.63% for female. The incidence of studies in Brazil confirms that the highest prevalence of childhood cancer affects males in most tumors [10].

In the distribution of patients according to the age group, it was observed that the highest prevalence of children was in the age group of 8 to 12 years (46%). Corroborating with this research, a recent study [2] obtained higher percentages (37.6%) of children in the age group of 8 to 12 years, however, the mean age of the same was higher than this research, it obtained a value of 10.69. Authors obtained a sample of 32.5% of children aged 0-5 years 32.5% among 6-10 years and 35% over 10 years, in other words, the higher incidence of cancer also prevailed in the higher age group [11].

In chemotherapy in the induction phase are administered high doses of anticancer agents, in order to promote rapid death of leukemic cells. It is in this phase that occurs the greatest number of side effects, such as oral lesions, however, is a therapy that has relatively fast response to cancer treatment, around four to six weeks after administration. The consolidation or intensification period is designed to destroy residual leukemic cells that may remain in significant numbers after the induction phase is a short but very intense in concentration or combination of drugs used. In the

maintenance phase is expected to complete remission of the disease, which is evidenced by bone marrow aspiration tests (myelography), revealing 5% of immature cells and no clinical evidence of leukemia [12].

Through the observed findings, it is clear that the oral manifestations emerged after chemotherapy. The antineoplastic post-treatment oral affections are compounded when the individual has come from a poor oral health. This condition may be due to several causes, where the lack of information and access to health services are very relevant when surveyed in the literature [13].

Antineoplastic chemotherapy is performed in 70% of patients diagnosed with leukemia [14]. Of these, about 40% to 100% have oral complications due to chemotherapy. In a previous study, twenty participants (83.3%) reported having presented at least one oral manifestation resulting from chemotherapy, while four (16.7%) never noticed changes in the oral cavity [15].

The major side effects of anticancer therapy are mucositis, xerostomia, and the temporary immunosuppression, allowing dental or opportunistic infections. It is also observed gingival bleeding and thrombocytopenia resulting from disturbances in the formation of tooth buds, when chemotherapy is administered in odontogenesis stage [11].

For these authors the most frequent oral lesions were mucositis [16,12], candidiasis [17,6], periodontitis [18] and gingivitis [17]. The most frequent sites of involvement of oral manifestations were oral mucosa and labial mucosa [19].

Oral mucositis is an inflammation of the mucosa, and often painful, which occurs during five to seven days after anticancer therapy which depends on the degree of tissue loss and aggression of pathogens. This change in the mucosa can progress to cell desquamation resulting in symptomatic ulcer, hindering the speech power and alimentation [20]. For most researchers, is mucositis caused by chemotherapy and occurs due to a dynamic process resulting in the destruction of basal cells and its prevalence is among 40% and 76% of 29 patients undergoing chemotherapy [21].

In cases where severe mucositis occurs in approximately 50% of patients, it becomes necessary to change and/or often temporarily interrupting treatment plans. This fact requires a high cost due to the increased length of stay and use of other drugs. It also decreases the quality of life, increasing morbidity and mortality [22].

Although it was not possible to assess the salivary flow, due to the difficulty of collecting the saliva of children of 2-4 years, it was reported for them and for those responsible for the sensation of dry mouth (xerostomia). Xerostomia brings results in a hypofunction of the salivary glands, which leads to change in the child's diet, which in turn alters the microflora, producing increased *Streptococcus mutans*, and this change, coupled with poor oral hygiene observed, favors the emergence of injuries caries [11].

The establishment of a protocol of care oral hygiene of children hospitalized with cancer is of paramount importance, as well as the monitoring of a dental surgeon, since they are vulnerable during this period [11]. The presence of the professional and the establishment of a protocol could

soften the oral lesions due to cancer treatment and thereby improve the QoL of these hospitalized patients.

Through the lack of a dental treatment protocol in the institution, it was possible to detect who had children in unsatisfactory oral conditions (source of infection) and they would already start the anticancer treatment; Fit to this researcher pass on this information to the health care team responsible (doctors and nurses) for proper referral to the dental industry. Some of these patients have stemmed with a very poor general health, necessitating start the anticancer treatment urgently and other cases, for unknown reasons, have not been forwarded to the HOL of the dental industry.

The data on salivary pH of healthy children home are not easily found, there are few published studies on the subject so far. Conducting a thorough search, we could find only 2 researches; one evaluated [21] children aged between 5 and 12 years and obtained pH 7.8 and rest of the other children 5-11 years and obtained rest of pH 7:27.

Although the reference values for healthy patients are considered, it is observed in the literature [24] that cancer patients suffer of reduced salivary pH values compared to healthy patients. In this study it was observed that the chemotherapy caused a significant decrease in salivary pH.

## Conclusion

The main oral changes resulting from chemotherapy in cancer patients are: mucositis, xerostomia, candidiasis, change in taste, bleeding gums, cold sores, dysphagia and toothache. As to salivary pH, there was a significant reduction of the same, according t test for Student samples before and after chemotherapy.

It is extremely important the integration of dentists with the oncology team in patient care at every stage of the disease, it will act in the prevention, treatment and monitoring of oral diseases; act also on patient education and motivation for proper oral hygiene, in order to minimize the deleterious effects of chemotherapy, thereby improving the child's quality of life.

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