

# Evaluation of Oral Hygiene Status, Salivary Characteristics and Dental Caries Experience in Acute Lymphoblastic Leukemic (ALL) Children

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*Leukemia constitutes approximately 30% of all childhood cancers and Acute Lymphoblastic Leukemia (ALL) is the most common type of malignancy. Oral dryness, ulceration, increased dental decay seen is due to altered salivary flow rate and buffering capacity in these children. Oxidative stress may play an important role in the malignancies resulting in onset of inflammatory oral pathologies. Saliva constitutes first line of defense against free radical-mediated oxidative stress. The present study attempted to relate the oral health status, salivary flow rate, salivary pH, gingival health status, dental caries experience and total salivary antioxidant levels in ALL children. A total of 120 children aged 4-10 years (90 leukemic children, study group and 30 normal healthy siblings, control group) were divided into 4 groups of 30 each. Oral health status, gingival status and dental caries experience was recorded followed by un-stimulated saliva collection. Total antioxidant capacity of un-stimulated saliva was evaluated. The results depicted deterioration in oral health status, gingival status and increased dental caries experience in leukemic children. Salivary flow rate, salivary pH and total salivary antioxidant levels were lowered in leukemic children when compared with control group.*

**Keywords:** Salivary Flow Rate, Dental Caries, Total Antioxidant Capacity (TAC), Acute Lymphoblastic Leukemia.

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## INTRODUCTION

Leukemia is defined as a malignant disease that starts in blood forming tissue such as the bone marrow, and causes large number of blood cells to be produced and enter the blood stream.<sup>1</sup> Leukemia constitutes approximately 30% of all childhood cancers and Acute Lymphoblastic Leukemia (ALL) is the most common type of malignancy.<sup>2</sup>

Nearly 75% of childhood leukemias are of the ALL type 3. India has a population more than 1000 million, with more than 36% of its people under 15 years of age. In India, childhood leukemia constitutes 2.3% of the cancer patients. Each year 6000 children in India develop acute lymphoblastic leukemia.<sup>3,4</sup>

Treatment modalities accepted widely for ALL is Chemotherapy alone or chemotherapy with radiation. Chemotherapy may cause mucositis, infection, trismus or xerostomia, which further interrupts radiotherapy, inducing malnutrition or systemic infection. When chemotherapy and radiotherapy are combined, the aforementioned complications are additive if not synergistic. The pediatric patient who is beginning, currently receiving, or has received chemotherapy, a bone marrow transplant and / or radiation requires special consideration and altered oral/ dental treatment schemes due to systemic impact of any of these cancer treatments.<sup>4</sup>

Oxygen, an element indispensable for life, under certain situations, have severely deleterious effects on human body. Harmful effects of oxygen are due to formation of Reactive Oxygen Species (ROS) *i.e* free radicals, which are very unstable and highly reactive. To protect us against the oxidizing action of free radicals, every individual has an army of antioxidants of proteinic nature.<sup>5</sup>

Thus in any diseased state, free radicals produced are quite higher. Cancer is one such diseased state in which free

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radicals are increased significantly. Increased free radical leads to consumption of antioxidants thereby decreasing levels of antioxidants.<sup>5,6</sup> These changes in free radicals and antioxidant levels can also be seen in saliva of cancer patients.

Hence the present study was undertaken to observe the oral hygiene status, gingival health, salivary pH, salivary flow rate, and total salivary antioxidants levels in Acute Lymphoblastic Leukemia children.

**MATERIALS AND METHOD**

**Subjects**

A total of 120 children (90 leukemic children, study group and 30 normal healthy siblings, control group) between the age 4-10 yrs reported to the Department of Pediatric Oncology, Institute of Child Health (ICH), Chennai, Tamil Nadu, India, were included in the study after getting an approval from the ethical committee. The parental consent was obtained from each participant. The grouping was done as follows

Group 1: 30 ALL patients before starting chemotherapy, Group 2: 30 ALL patients up to 1-2 weeks of chemotherapy, Group 3: 30 ALL patients with more than 2 weeks of chemotherapy, Group 4 (Control group): 30 normal healthy siblings of the study population.

The patients included in the study group were diagnosed cases of Acute Lymphoblastic Leukemia (ALL), where chemotherapy was the treatment protocol. A Standard drug regimen protocol designed in collaboration with National Cancer Institute (USA) of MCP 841 for ALL children<sup>10</sup> being used at various centers in India and also in Institute of Child Health (ICH), Chennai, India was followed.

ALL children suffering from any other disease, children who were on radiotherapy or combination of chemotherapy and radiotherapy were excluded from the study.

**Clinical Procedure**

A standardized protocol was used for examining the patients in study group and control group. A pilot study was carried out by three examiners to remove the inter examiner variability. Single examiner was chosen for further oral examination and saliva collection. Single examiner examined the children in the study group and the control group. Oral examinations and saliva collection were performed at the Pediatric Oncology unit of Institute of Child Health (ICH), Chennai. The patients were made to sit on the bed, and examination was done in the day light using latex gloves, plain mouth mirror, probes, tweezers, container, cotton/gauze to remove any debris and dry the oral mucosa.

Oral health status was recorded using a modified WHO<sup>7</sup> format by the same examiner in all the groups. Caries assessment was done using ‘DMFT’ and ‘deft’ index. Oral hygiene assessment was done using ‘OHI-S’ index for mixed dentition and (‘OHIS-M’)<sup>8</sup> index for primary dentition. Gingival health assessment was done by Modified Gingival Index (MGI).<sup>9</sup>

Saliva collection was done in calibrated cylinder and flow rate was measured using standard formula. All the subjects were instructed to refrain from eating or drinking for a minimum of 2 hours before the saliva sample were collected. Before treatment un-stimulated saliva (1.0 - 1.5ml) was collected by allowing the patient sit in the coachman position, the patient was asked to passively drool into a funnel inserted into a graduated cylinder for 5 min.<sup>12</sup>

The un-stimulated salivary flow (USF) rate was calculated using the following formula<sup>12</sup>:

$$USF = \frac{\text{Total volume of collected saliva}}{\text{Time period for collection of saliva}}$$

The volume of saliva collected in the cylinder after 5 minutes was divided by 5 to determine the un-stimulated salivary flow rate.<sup>12</sup> Salivary pH was estimated using pH indicating paper. Color change seen in the pH paper was matched with the standard. The pH ranged between 7.5 to 6.5.<sup>12</sup> The collected saliva was stored in glass or plastic vials, then in the chiller at 4°C.

Total salivary antioxidant estimation was also done using a standard protocol. The reagent was prepared by combining sodium benzoate, acetic acid, and ethanol. The reagent was mixed with saliva and was incubated at 90°C for 90 min. The total antioxidant capacity of saliva was then evaluated using the spectrophotometric assay.<sup>11</sup>

The results were statistically evaluated using Student’s-t test and ANOVA with SPSS data processing software version 15.0.

**RESULTS**

The salivary flow was reduced in all the three groups with least mean value of 0.126ml/min seen in group 3, who were on long term chemotherapy which was statistically highly significant (ANOVA, p<0.001). (Table 1).

Salivary pH were decreased in all three groups with least mean value in leukemic children who were for more than

**Table 1.** Mean values of salivary flow rate, salivary pH and total salivary antioxidant levels in study group and control group

	Groups	Mean	SD	p-value (One way ANOVA)
Salivary flow rate (ml/min)	Group 1	0.42	0.20	<0.001(vhs)
	Group 2	0.35	0.16	
	Group 3	0.12	0.09	
	Group 4 (control)	0.85	0.31	
Salivary pH	Group 1	7.32	0.30	<0.001(vhs)
	Group 2	6.56	0.35	
	Group 3	5.85	0.30	
	Group 4 (control)	7.13	0.29	
Salivary antioxidants ((µmol/dl)	Group 1	0.95	0.23	<0.001(vhs)
	Group 2	0.75	0.18	
	Group 3	0.31	0.16	
	Group 4 (control)	0.45	0.31	

2 weeks of chemotherapy. Decreased salivary pH of group 1 and group 2 when compared with control group were not statistically significant. Whereas salivary pHs of leukemic children on long term chemotherapy (group 3) were significant when compared with other two study groups and control group. (ANOVA,  $p < 0.001$ ). (Table 1).

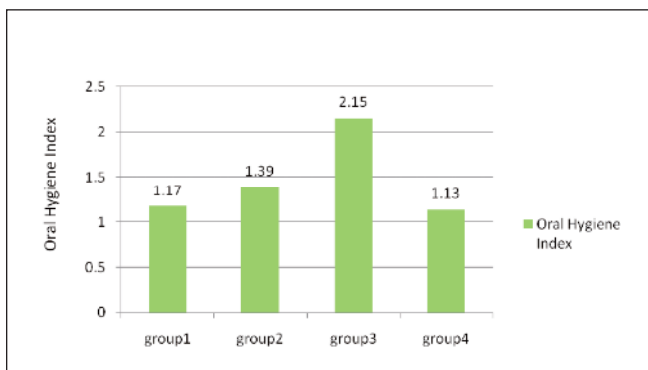
Total salivary antioxidant levels were increased in group 1 and group 2 leukemic children and decreased in group 3 leukemic children when compared with the control group. The increase in total salivary antioxidant levels in group 1 and group 2 leukemic children were statistically significant when compared with control group ( $p < 0.001$ ). The decreases in total salivary antioxidants levels were highly significant in group 3 leukemic children when compared with group 1 leukemic children and control group. (ANOVA,  $p < 0.001$ ). (Table 1).

The oral hygiene of study group was deteriorated when compared with the control group and the increased values were statistically highly significant ( $p = 0.004$ ). Among the study group, decreased oral hygiene of group 3 was statistically highly significant (ANOVA,  $p < 0.001$ ). (Table 2, Graph 1).

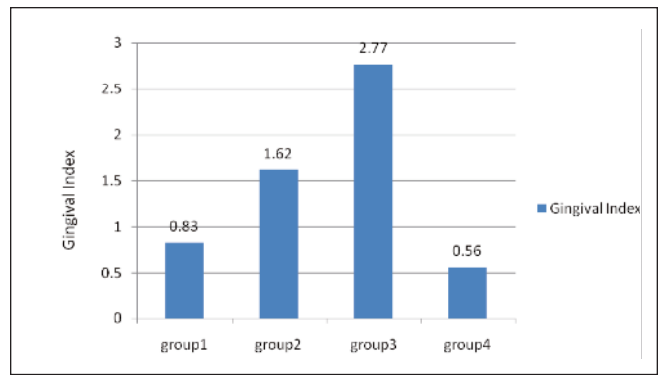
The gingival health was deteriorated in all three groups with higher mean value in group 3 leukemic children who were for more than 2 weeks of chemotherapy which was statistically significant (ANOVA,  $p < 0.001$ ). (Table 2, Graph 2).

**Table 2.** Mean values of Oral hygiene index, Gingival health status, and Dental caries experience (DMFT/dft) in study group and control group.

	Groups	Mean	SD	p-value (One way ANOVA)
Oral hygiene index	Group 1	1.17	0.52	<0.001(vhs)
	Group 2	1.39	0.49	
	Group 3	2.15	0.76	
	Group 4 (control)	1.13	0.34	
Gingival health status	Group 1	0.83	0.58	<0.001(vhs)
	Group 2	1.62	0.49	
	Group 3	2.77	0.50	
	Group 4 (control)	0.56	0.57	
Dental Caries experience (DMFT/dft)	Group 1	0.87	0.67	<0.001(vhs)
	Group 2	1.65	0.60	
	Group 3	3.40	0.88	
	Group 4 (control)	0.70	0.87	



**Graph 1.** Graph showing the mean values of oral hygiene index among all groups



**Graph 2.** Graph showing the mean values of Gingival index among all groups

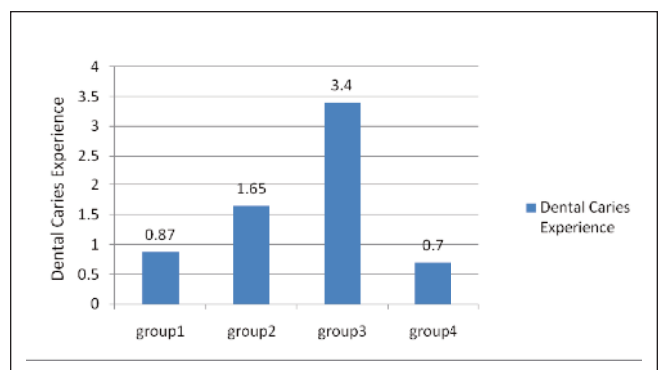
The dental caries experience was higher in all three groups with highest mean value in group 3 leukemic children who were for than 2 weeks of chemotherapy which was statistically significant (ANOVA,  $p < 0.001$ ). (Graph 3).

**DISCUSSION**

Leukemia is a common type of malignancy.<sup>1</sup> Nearly 75% of childhood leukemia's are of Acute Lymphoblastic type (ALL) which is a debilitating disease suppressing children's general and dental health, rendering them immunocompromised.<sup>2,3</sup> Children treated with chemotherapy forming a part of treatment schedule for the same, exhibit acute complications in the oral cavity and long term complications in dental and craniofacial development. Higher prevalence of dental diseases like dental caries, oral mucositis, gingival inflammation are reported for children with leukemia when compared to systemically healthy children.<sup>2,4</sup> Similar findings were observed in the present study with increased severity of disease process.

Patients were found to be at various levels of risks for developing oral problems, which could be due to the time lapse between the onset of the pathology and the clinical diagnosis of the condition among them. Other factors influencing are related to the drug, type of the malignancy, patient's age and the level of oral health before and during the therapy.<sup>4</sup>

Chemotherapy causes decrease in salivary flow rate in cancer patients which can be attributed to the fact that salivary gland hypoplasia occurs in patients receiving



**Graph 3.** Graph showing the mean values of Dental caries experience among all groups

chemotherapy.<sup>4</sup> Ebstein *et al*<sup>10</sup> showed decreased salivary output in patients receiving chemotherapeutic agents similar to our study, where the most affected group was the one who received chemotherapy for more than 2 weeks. Housseiny *et al* also showed dry mouth as a main complain in 56.7% of ALL children examined.<sup>17</sup>

The mean salivary pH receiving chemotherapy for more than 2 weeks or less than that was 6.5, whereas control group had mean salivary pH of 7.5. Ingestion of cytotoxic drugs for cancer decreases the salivary flow, and induces vomiting<sup>13</sup> to the patient, which was seen in the present study. The decrease in salivary pH can also be correlated to the decreased salivary flow rate in these children which further reduces the salivary buffering capacity, thereby reducing the salivary pH.<sup>14</sup>

The oral health status in leukemic patients was found to be deteriorated as compared to the control group and the deterioration increased with the duration of chemotherapy. This is due to the fact that the mucosal inflammation seen during chemotherapy, may reduce the ability to maintain proper oral hygiene.<sup>4,10</sup> Gingival inflammation was also found to be increased with the duration of chemotherapy. Being infectious in nature, gingival diseases may cause significant morbidity and mortality in these children during the periods of chemotherapy, which may suppress the bone marrow making the subject susceptible to infection.<sup>13</sup>

The dental caries experience in leukemic children were found to increased when compared with control which is in agreement with earlier study by Nasim and Hegde (2007).<sup>15</sup> The increase in dental caries could be due to the fact that maintenance of oral hygiene was difficult for the patients who were on chemotherapy due to increased oral mucosal inflammation.<sup>13</sup>

The degenerative diseases that afflict humanity have their origin in deleterious free radical reactions. Reactive Oxygen Species (ROS) are related to both the arrest of growth and start of cell differentiation. Human cancer is accompanied by a strong oxidative predominance in blood. In cancer, ingestion of drugs has been reported to cause increased production of oxygen free radicals through auto-oxidation. Generation of oxygen free radicals by auto-oxidation is widely believed to be one of the main causes of oxidative stress in cancer.<sup>5,6</sup>

It was established from our study that total salivary antioxidant levels were increased in leukemic children prior to the induction of chemotherapy, followed by decreased salivary antioxidant levels as chemotherapy was induced. But this decrease in total antioxidant levels was seen more in leukemic children who were for more than 2 weeks of chemotherapy. This is in agreement with a study carried out by Bag chi *et al*<sup>5</sup> which showed decreased salivary antioxidant levels in oral cancer patients with increased oxidative stress.<sup>5</sup>

The key to success in maintaining a healthy oral cavity during cancer therapy is patient compliance. Consequently, it is vital to educate the caretaker and child about the importance of oral care to minimize discomfort and maximize the

chances for a successful outcome. Recent clinical trials have found that antioxidant supplementation can significantly improve immune response.<sup>16</sup> Supplementation with the antioxidant vitamins improved the immune responses in individuals suffering from cancer and which were exposed to sources of free radicals.<sup>16</sup> Although our study establishes the role of antioxidants in oral health of leukemia patients but further studies are required with larger sample size to confirm these findings. Nevertheless this study hopefully shall begin the journey.

## CONCLUSION

In the present study following observations were made in Acute Lymphoblastic Leukemic children in comparison with their healthy siblings:

- The oral health status and gingival health status was deteriorated.
- The salivary flow rate and salivary pH was decreased.
- There was increase in dental caries experience.
- The salivary total antioxidant levels deteriorated.

**Table 3.** Oral Care guidelines for children with Acute Lymphoblastic Leukemia.

<p><b>A) To Parents &amp; Children</b><sup>12,18</sup></p> <ol style="list-style-type: none"> <li>1) Brush the teeth with suggested soft toothbrush and toothpaste and to place the toothbrush on their teeth at a 45 degree angle against the gums and move it back and forth gently in short strokes for 90 seconds.</li> <li>2) Gently clean and massage the tongue with the toothbrush.</li> <li>3) Rinse the mouth with nonalcoholic mouth rinses and with 60ml of 5% sodium bicarbonate solution for 30seconds and then to spit out the solution.</li> <li>4) Spicy and rough food items to be avoided. Food items rich in antioxidants, vitamins A, C, E should be supplemented.</li> <li>5) Symptomatic treatment with topical anesthetics can be carried out for pain relief from oral mucositis.</li> </ol> <p><b>B) To the Pediatric dentist</b><sup>5</sup></p> <ol style="list-style-type: none"> <li>1) <b>Before Chemotherapy-</b> Any infection in oral cavity should be reduced to a significant degree prior to induction of chemotherapy by comprehensive oral health care.</li> <li>2) <b>During chemotherapy-</b> <ul style="list-style-type: none"> <li>• Proper anticipatory guidance should be given to the parents which focuses on oral hygiene measures during each stage of child development.</li> <li>• Dental caries management can be done by caries control protocol.</li> <li>• Antioxidant supplementations in diet.</li> </ul> </li> </ol>
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