ORIGINAL RESEARCH

Assessment of the Changes in the Salivary Profile and Its Clinical Correlation in Children with Acute Lymphoblastic Leukemia Undergoing Chemotherapy: A Follow-up Study

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Abstract

Aim: To assess the changes in salivary profile and its clinical correlation in patients with acute lymphoblastic leukemia (ALL) undergoing chemotherapy.

Materials and methods: Children who have been diagnosed with ALL undergoing chemotherapy at Bharati Hospital, Pune, were included in the study. Those children were included who fulfilled the following inclusion and exclusion criteria. Stimulated salivary samples were collected in sterile vials at 1-, 3-, and 6-month intervals and ware assessed for salivary pH and buffering capacity. Caries and oral manifestations were also checked at each interval.

Results: A total of 25 children with ALL undergoing chemotherapy were included to participate in the study. The results were analyzed using Statistical Package for the Social Sciences software. There was a statistically significant difference in the change in salivary pH during the 1st and 6th months of chemotherapy (*p*-value of 0.001). Salivary buffering capacity was also found to be low in these patients during the 1st month of chemotherapy, which gradually increased during the entire course of chemotherapy (*p*-value of 0.011). Progression of dental caries was seen during the entire course of treatment.

Conclusion: All the major changes were seen in the 1st month, that is, the induction phase of chemotherapy. Hence, we can say this is the most affected phase of chemotherapy.

Clinical significance: The parents and children should be educated and motivated to maintain proper oral hygiene. Whenever possible, all preventive dental procedures should be undertaken before the start of chemotherapy to avoid future complications.

Keywords: Acute lymphocytic leukemia, Chemotherapy, Oral Manifestations, Saliva.

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Introduction

Leukemia is a malignant disease of blood-forming tissues such as the bone marrow and causes a large number of immature blood cells to be produced and enter the bloodstream.[1,2] Among all the other childhood cancers, it accounts for about 33.3% and is the most common childhood cancer in India.[3] Management of children with acute lymphoblastic leukemia (ALL) is done using four types of standard procedures, among which chemotherapy remains the mainstay of the treatment, and though it increases the survival rate in children with ALL, it causes oral complications like oral mucositis, gingival bleeding, hyperplasia, and opportunistic infections like oral candidiasis, primary herpetic gingivostomatitis, caries, cheilitis, xerostomia, and dry lips.[4] Chemotherapy adversely affects the salivary glands, altering the quality and quantity of saliva. Several chemotherapeutic agents cause damage to the mucosa, which affects the dividing cells of the basal epithelium; direct contact of these agents with connective tissues can lead to their extensive damage.

Taking the above aspects into consideration, the present study was undertaken to assess the changes in salivary profile and its clinical correlation in patients with ALL undergoing chemotherapy.

Materials and Methods

Children who have been diagnosed with ALL undergoing chemotherapy in Bharati Hospital, Pune, were included in the study. The study was conducted after it was approved by the Institutional Ethical Committee. The information sheet, child assent and consent forms were given to the parents of these children, the proposed risks and benefits were explained in detail, and only those participants who were willing were included in the study. Those children were included who fulfilled the following inclusion and exclusion criteria.

Inclusion Criteria

- Children between the age group of 3 and 13 years detected with ALL and in whom chemotherapy has been initiated.
- Children who have not been diagnosed with any other systemic disease other than ALL.

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Exclusion Criteria

- Healthy children.
- Children with ALL who were critically ill and uncooperative.

Methodology

- A total of 25 children who have been diagnosed with ALL undergoing chemotherapy in Bharati Hospital, Pune, were included in the study.
- A detailed history was recorded every time before the examination.
- Stimulated salivary samples were collected in sterile vials at 1-, 3-, and 6-month intervals.
- Clinical assessment: Recording caries by using the Mount and Hume caries classification system, gingival health and oral hard and soft tissue changes were checked at each interval.
- The collected saliva was assessed for pH and buffering capacity.

The pH was assessed using a digital pH meter and was compared with the chart (Fig. 1).

- Highly acidic: 5.0–5.8
- Moderately acidic: 6.0–6.6
- Healthy saliva: 6.8–7.8

Salivary buffering capacity was assessed using the Erickson method.

Results

A total of 25 children with ALL undergoing chemotherapy were included to participate in the study. The mean age-group of children were 7.12 ± 3.75 (Table 1). A total of 21 patients were followed for 6 months because of the dropout of samples. Salivary buffering capacity was also found to be low in these patients during the first month of chemotherapy, which gradually increased during the entire course of chemotherapy (*p*-value of 0.011) (Table 2). There was a statistically significant difference in the change in salivary pH during the 1st and 6th month of chemotherapy (*p*-value of 0.001) using repeated analysis of variance (ANOVA) tests (Table 3). Progression of dental caries was seen during the entire course of treatment.

Fig. 1: Digital pH meter

Table 1: Demographic details

Variable	*Category*	*Mean/n (%)*
Age	–	7.12 ± 3.75 (range: 3–13 years)
Gender	Male	10 (47.6%)
	Female	11 (52.4%)

Discussion

Earlier, leukemia was considered a rare disease; however, it is increasing in incidence and prevalence slowly and steadily. Though chemotherapy and radiotherapy have increased the survival rate and are widely accepted,[5,6] these treatment modalities lead to oral complications and have an impact on the developing dentition and on orofacial growth.[3] In this present study, children between the age group of 3 and 13 who were detected with ALL and in whom chemotherapy has been initiated were included. There were 10 male children and 11 female children. The total sample size was 25, but as four children expired after the first sample was taken, they were excluded from the study.

Salivary pH

The mean salivary pH was found to be acidic during the first month of chemotherapy, which gradually increased during the 3rd and 6th months of chemotherapy (Tables 2 and 3). The reason for low salivary pH could be the affected salivary gland function due to chemotherapeutic drugs. The other reasons could be the frequent episodes of nausea and vomiting in these patients, poor oral hygiene, and anxiety during the sample taking. The low salivary pH was in accordance with the study done by other authors,[7–10] who also reported decreased salivary pH with an increase in consumption of sweet foods and the effect of cytotoxic drugs on salivary gland function. A study done by Mitchell et al.[11] also showed a significant reduction in salivary pH pre and postchemotherapy. Contrary to these findings, a study done by Costa et al.[12] showed a constant salivary pH of around 6.7, even during the entire chemotherapy, where the authors concluded that reduction in pH could be due to unhygienic oral conditions and not directly related to chemotherapies. According to this study, there was a statistically significant difference in the change in salivary pH during the 1st and 6th months of chemotherapy (Table 3).

Salivary Buffering Capacity

The buffering capacity of saliva was also found to be low in these patients during the 1st month of chemotherapy, which gradually increased during the entire course of chemotherapy (Table 2). This was similar to the study done by Jacobson et al.,[2] who also showed the buffering capacity to be significantly low in children postchemotherapy when compared to prechemotherapy and healthy children. This was similar to the findings of Avşar et al.,[6] who

Table 2: Mean salivary pH and buffering capacity

Interval	*Mean for salivary pH*	*Mean for buffering capacity*	*SD for salivary pH*	*SD for buffering capacity*	*F-value*	*p-value*
1 month	6.14	6.14	1.17	1.17	20.619	0.001*
3 months	6.56	6.56	1.14	1.14		
6 months	6.74	6.74	0.91	0.91		

Repeated measure ANOVA test; * indicates significant difference at $p \leq 0.05$

also found that salivary buffering capacity was significantly lower in patients who have undergone chemotherapy. They concluded that hyposalivation has an effect on the buffering capacity of saliva, and these patients are at a higher risk of demineralization and the development of dental caries. There were no reported studies that assessed salivary pH and buffering capacity during the course of chemotherapy. Most of the studies compared the pH and buffering capacity pre and postchemotherapy, but in this study, both these parameters were checked at 1-, 3-, and 6-month intervals of chemotherapy in which salivary pH and buffering capacity returned to normal at 6 months of chemotherapy.

Dental Caries

Progression of dental caries was seen during the entire course of treatment. Only 14 teeth out of 181 showed caries progression during 1–3-month intervals, whereas five teeth out of 181 showed caries progression from 3- to 6-month intervals (Table 4). The reason for progression could be decreased salivary pH, decreased salivary buffering capacity, neglected dental health, inaccessible dental treatment, frequent hospitalizations, and oral mucositis, which causes difficulty in brushing and maintaining oral hygiene. These results were similar to the study done by Pajari et al.[13] and Hegde et al.,[10] who also showed a higher incidence of dental caries in these children. Also, a study done by Dubey et al.[9] revealed that leukemic patients had significantly higher caries than patients with diabetes and asthma. Bassir et al.[14] reported no significant difference in sum of the number of decayed, missing due to caries, and filled teeth (DMFT) of both groups, which was contradictory to the findings of the present study. Author[6,9,12] concluded that dental caries could be due to sanitarian education and parents' awareness. In all of the studies, DMFT/decayed, extraction needed, filled teeth was taken into account as an index to calculate dental caries. As this index has its own limitations, in the present study, Mount and Hume were taken as an index to calculate dental caries.

Oral Manifestations

Oral mucositis was observed during the 1st month of chemotherapy, which resolved during the 3rd and 6th month of chemotherapy. It is seen that the prevalence of mucositis in pediatric patients is even greater than in adults; this may be because of rapid cell division in this patient population.[3] Mucositis was more common in the prepubertal age group than the younger age group in the present study. Also, it was more common in girls than boys. Contrary to this, a study done by Carreón-Burciaga et al.[15] concluded that the severity of mucositis was higher in children below 6 years of age (73.33%), and the mucosa is still developing in children of this age group. Although mucositis appeared to occur more in boys than in girls, sex was not a statistically significant factor in the development of mucositis. Limitations of the study were there was a dropout rate, and as the Mount and Hume index is considered in this particular study, it was not possible sometimes to examine all teeth. A larger sample size with a longer follow-up and more studies would be recommended in future.

Table 3: Pairwise comparison of change in salivary pH

Interval	*Difference in salivary pH*	*p-value*
1 vs 3 months	0.42	0.001*
1 vs 6 months	0.60	0.001*
3 vs 6 months	0.18	0.038*

Post hoc least significant difference test; * indicates significant difference at $p \leq 0.05$

Table 4: Assessment of caries progression

Duration	*Caries progressed out of total teeth at 1 month (n = 181)*	*%*
1–3 months	14/181	7.7
3–6 months	5/181	2.8

Conclusion

The conclusions drawn out from this study are:

- There was a statistically significant difference between salivary pH at 1- and 6-month intervals (*p*-value of 0.001).
- With respect to the salivary buffering capacity, it was also found to be low during the 1st month, which gradually increased in the 3rd and 6th months of chemotherapy (*p*-value of 0.011).
- Progression of dental caries was also seen along the course of chemotherapy.
- With respect to oral manifestations, oral mucositis was the most common, which was seen in prepubertal girls within 4–5 days after the start of chemotherapy.
- In conclusion, all the major changes were seen in the 1st month, that is, the induction phase of chemotherapy. Hence, we can say this is the most affected phase of chemotherapy; thus, the parents and children should be educated and motivated to maintain proper oral hygiene.
- Whenever possible, all preventive dental procedures should be undertaken before the start of chemotherapy to avoid future complications.
- This was the study where a 6-month follow-up was undertaken to assess the minute changes which are occurring during chemotherapy.

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