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Research Article

Impact of Microbial Intake for Gums and Periodontal Health in Children Receiving Chemotherapy

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Abstract: Probiotics comprised of living microorganisms and are devoid of any detrimental impacts on health. When consumed in sufficient amounts, they provide nutritional advantages. The prevalent oral infections primarily target the periodontal and dental tissues inside the mouth cavity. This study aims to investigate the effectiveness of oral probiotics in combating bacteria associated with periodontal and dental diseases. Moreover, it aims to evaluate the gum and periodontal well-being of children receiving chemotherapy following the intake of oral probiotics. Seventy children, aged 4 to 16 years and undergoing chemotherapy, were randomly assigned to either the control or test group, which received probiotics, over a period of ninety days. Various evaluations, including the examination of gum and teeth-supporting structures, oral cleanliness, and testing for caries activity, were conducted at different intervals. SPSS 19.0 was utilized for statistical analysis. Among participants in the treatment group, the administration of oral probiotics resulted in a noteworthy reduction in biofilm accumulation over the observation period ($P < 0.05$). The test group exhibited an improvement in the condition of the gums and supporting structures of the teeth ($P < 0.05$). A caries activity assessment was conducted using the Snyder test. Among the children in the research group, 10 were found to have a score of 1, while eight exhibited a score of 2. None of the children in the research group displayed a score of 3. The findings indicated that consistent intake of oral probiotics leads to a significant decrease in the build-up of biofilm, the production of tartar, and the occurrence of tooth decay within the experimental group.

Keywords: Oral hygiene index, dental caries, Dental Biofilm probiotics and Chemotherapy

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1. INTRODUCTION

Several Cancer Institute defines pediatric cancer as a cancer that develops in individuals from infancy to 15 years of age. These tumors are uncommon and exhibit distinct characteristics compared to malignancies that occur in adults, including their rate of development, ability to spread, methods of therapy, and how they respond to treatment. Pediatric cancer, often referred to as childhood cancer, and is more frequently observed in western countries than in developing nations such as India. In impoverished regions, pediatric cancer constitutes just 2% of all malignancies[1]. Each year, approximately 50,000 children in India receive a cancer diagnosis, with leukemia accounting for 45to 55% of cases and lymphoma accounting for 15 to 20%[2]. The age group most often impacted is children aged 5 to 14 years. Boys are disproportionately impacted compared to females. Acute lymphoblastic leukemia (ALL), which impacts 3 to 4 per 100,000 children under the age of 15, stands as the predominant form of leukemia[3]. Chemotherapy is the primary treatment for acute lymphoblastic leukemia. Chemotherapeutic medications have detrimental effects on killing proliferating cells, which encompass those found in the bone marrow, hair follicles, and the linings of the oral cavity and gastrointestinal tract. These drugs influence the usual microbiota present in the oral environment. Oral adverse reaction symptoms occur in around 40% to 90% of children who take chemotherapy. The predominant symptoms include mucositis, xerostomia (dry mouth), discomfort, parageusia (impaired taste sensitivity), opportunistic infections, dental caries and salivary gland dysfunction [4]. In 1965, Stillwell and Lilly introduced the term "probiotics," derived from the Greek word meaning "life".[5] In 2001, the World Health Organization (WHO) provided a definition for probiotics as "live microorganisms, when consumed in appropriate amounts, confer health benefits to the individual". These microorganisms release various chemicals, such as hydrogen peroxide and bacteriocins, which have clear bactericidal properties. They function by competitively inhibiting the adherence of harmful bacteria to mucosal locations, hence preventing their colonization. By adjusting the redox potential, they alter the pH, consequently affecting the survival capability of microbes in the oral environment. Probiotics ultimately stimulate the innate immune response in humans and modify their immunological processes, including both cellular and humoral components[6]. Lactogenic bacteria may alter immunological competent cells such as T cells and macrophages[7]. This might potentially affect the generation of cytokines in these cells, which in turn may have an effect on the overall immunological response of people. The use of different mixtures of probiotic strains results in a synergistic impact, which is employed to enhance the advantageous outcomes. Patients receiving chemotherapy and radiation for cancer treatment have a weakened immune system[8]. An imbalance in homeostasis occurs, leading to the development of several strains that are resistant to treatment and the invasion of harmful microbes. Disturbances in the balance of the oral microbiome can lead to the development of dental cavities, gum issues, and various infections like mucositis and oral candidiasis. Research indicates that probiotics can play a significant role in restoring balance and minimizing the negative effects of chemotherapy. These helpful microbes are both affordable and easily accessible to people. They play a role in preserving the equilibrium of microorganisms in the mouth through their natural colonization. Research has investigated the impact of probiotics in preventing and minimizing chemotherapy-related problems, namely diarrhea and mucositis. Insufficient research has been conducted to assess the efficacy of giving oral probiotics to children receiving cancer treatments like chemotherapy and radiation. The outcomes of this investigation could offer significant understandings to both researchers and individuals contemplating the incorporation of oral probiotics as an adjunctive therapy for addressing oral side effects stemming from chemotherapy in children. The research had two primary objectives: the aim to evaluate the antibacterial effectiveness of oral probiotics against microorganisms associated with periodontal and dental tissue ailments and, to assess the oral health status of gum and periodontal tissues in children undergoing chemotherapy by employing oral probiotics.

2. MATERIALS AND METHODS

2.1. Subjects

The research retained its approval and was carried out in accordance with the ethical guidelines set forth by the Institutional Ethical Board (IRB A22/014/ dated 4 june 2023), The parents of the children provided informed permission, which was gained via both verbal and written means. There were no financial grants provided for this research.

2.2. Sample size and Population

The sample size was calculated using the formula

$$n = (2 (Z\alpha + Z [1-\beta])2 \times p \times q/d2)\ ^{9}$$

"n" represents the sample size and is denoted by Z (1-β), a constant determined by convention based on the study's power. α, error and Zα represent a constant determined by convention based on the acceptable. The threshold for alpha (P-value) has been established at less than 0.05. The study's "power" is represented as (1-β), where β is equal to 0.2. A power of 0.8 is needed to accept the null hypothesis, which is the lowest acceptable power level. The effect size (ES) was determined based on previously published data, with a value of 20%, and a dropout rate of 32% was applied to each group. The findings from the prior research indicated a 10% scope. A significant reduction of up to 20% in the incidence of dental caries activity was considered substantial for evaluating the effectiveness of oral probiotics. Based on these calculations, it was established that each research group should comprise 35 children. As a result, 70 children were enrolled in the study, selected from those aged 4 to 16 who have been diagnosed with Acute Lymphoblastic Leukemia and Lymphoma and are currently undergoing treatment at the Government Cancer Hospital (Annal Gandhi Memorial Government Hospital , Tiruchirappali , india). The research excluded children who had not begun chemotherapy or those who had finished their treatment.

2.3. Study design

The research was a prospective study carried out between August 2023 and November 2023, with a cohort of 70 children. The inclusion criteria were (1) children aged 4 to 16 undergoing chemotherapy (2) Willing children or parents to participate in the study (3) Diagnosed with Acute

Lymphoblastic Leukemia and Lymphoma (4) currently undergoing treatment at the Government Cancer Hospital. The exclusion criteria were (1) Children having oral cancer (2) mouth deformities (3) Existing tartar or gum infection before the cancer diagnosis (4) Unwilling children or parents to participate in the study (5) Children experiencing severe pain discomfort due to chemotherapy (6) Diagnosed with cancer other than Acute Lymphoblastic Leukemia and Lymphoma (7) Not undergoing treatment at the Government Cancer Hospital (8) Children prescribed with antibiotics. The research participants were divided into two groups, each comprising 35 youngsters, using a simple randomization technique involving a raffle. The test group was provided with oral probiotics (Probiotic product (BLISM18 (BLISS Technologies)), based on Streptococcussalivarius M18, 2.5 billion CFU) in addition to an oral hygiene kit containing a toothbrush and toothpaste, whereas the control group solely received the oral hygiene package, comprising only a toothbrush and toothpaste. Detailed medical histories, including treatment specifics, were documented. Comprehensive documentation was maintained concerning the oral hygiene habits of the participants, and their intake of food items containing lactic acid was duly recorded. Children were advised to avoid consuming probiotic-rich foods for a month prior to the commencement of the trial. Parents were actively educated and encouraged to acquire the correct brushing technique for their children. The test group was directed to consume two lozenges of probiotics after the act of teeth brushing. The research group was instructed to repeat this method for a length of 90 days. The control group participants were instructed to perform regular teeth cleaning as part of their routine without using oral probiotics. Both the research and control groups had scheduled check-ups after 90 days. [Figure 1].

2.4. *Oral examination*

The oral investigation of both the research and control group was conducted using sterile mouth mirrors and disposable sterile gloves. The baseline and subsequent time points of 15, 30, 45, 60, 75, and 90 days were used to record the numbers of decaying, missing, and filled teeth. Information pertaining to oral hygiene, dental plaque, and factors concerning saliva (including pH, buffering ability, and rate of salivary flow) was gathered at specific intervals. These parameters were utilized to ascertain potential risk factors linked to tooth decay. The assessment of participants' oral hygiene utilized the Oral Hygiene Index-Simplified (OHI-S), a measurement devised by Greene and Vermilion. This parameter has two components: the DIS and the Tartar index. Each of them is determined numerically, indicating the quantity of DIS or DCS on the tooth surfaces being measured. Any side effect due to probiotics consumption was not reported by any subjects.

2.5. *Statistical analysis*

The statistics was gathered by a competent examiner who was both trained and expertise, and the data collected gave Kappa value of 0.86. No participants withdrew from the research. The collected data underwent statistical analysis through SPSS version 10.0. A paired t-test was used to evaluate the values before and after the intervention within a single group. Additionally, a Chi-square test was applied to examine the grouping variable. Subsequently, an ANOVA test was performed to analyze factors between the initial and subsequent examinations. Statistical significance was assessed with a threshold set at p-values of 0.05 or lower.

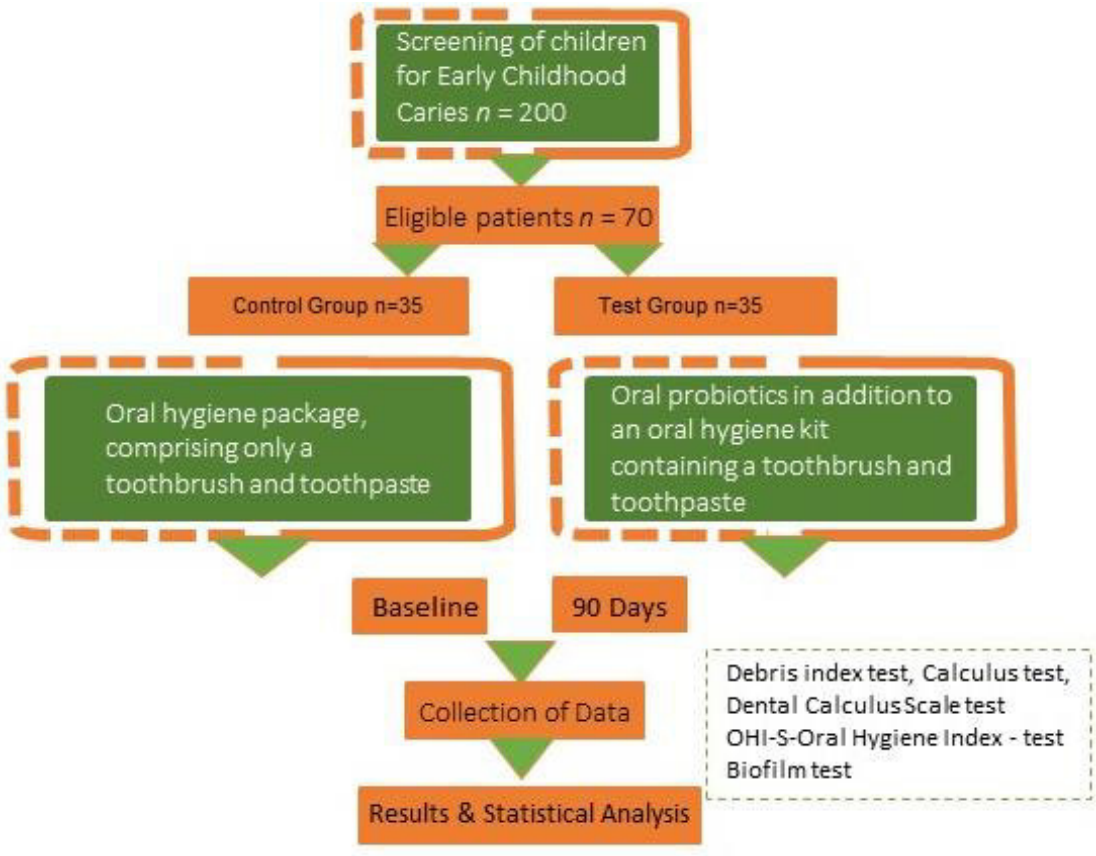


Fig-1: Study design investigating the impact of probiotics on periodontal health.

3. RESULTS AND DISCUSSION

Annually, an estimated 38 to 124 out of every million children in India are diagnosed with pediatric cancer[10]. Acute lymphoblastic leukemia is the most prevalent form of cancer in children, with lymphoma being the second most cancer. Chemotherapy is the primary course of treatment for those cancers. Numerous severe adverse effects, including alopecia, tiredness, hematological toxicity, and gastrointestinal toxicity, occur during chemotherapy. Chemotherapy also disrupts the indigenous microbiota in the body and this modification results in diverse and adverse consequences such as diarrhea and mucositis. Recent researches has shown that probiotics have positive impacts on regulating the immunological response of the host, boosting antioxidant activity, breaking down possible cancer-causing substances, and enhancing the natural microbiota[11]. Dental Biofilm is a community of bacteria that forms a biofilm on the tooth's surface[12]. The intricate polymer structure, originating from both the host and bacterium, encases microorganisms. Dental biofilm is crucial in initiating dental and periodontal diseases by providing an environment favorable for disease-causing bacteria to flourish and protecting them from antimicrobial agents. Inadequate and sporadic removal of dental biofilm can result in a range of oral health problems such as dental caries, gingivitis, and periodontitis. Probiotics mitigate biofilm formation by counteracting free radicals, regulating mucosal lining permeability, and modulating the body's immune response[13]. Various studies have revealed that probiotics have a key role in preventing and managing mucositis, halitosis, candidiasis, dental, and periodontal illnesses. In our study, a cohort of thirty adolescents consumed oral probiotics for a 90-day duration. Table 1 presents the demographic profiles (Baseline) of the participants, indicating no statistically significant variances between the study and control groups. Table 2 emphasizes a significant change in the biofilm index between these groups, with evidence indicating a significant decrease in biofilm index after 90 days of oral probiotic consumption. On day 90, there was a decrease in the average values of test group for DCS index, tartar index, and OHI-S compared to day 0. In contrast, the mean value of salivary pH increased from the initial baseline day 0 to day 90. The study unveiled a significant difference in biofilm and tartar indices across various observation days, with a substantial decrease in biofilm index from the initial measurement to day 90 and a notable change in tartar index after 90 days of probiotic use. By the 90th day, a declining pattern in the average levels of DCS and OHI-S was evident when compared to both day 0 and day 90. Moreover, the mean salivary pH showed an upward trend from day 0 to 90, as illustrated in Graph 1. Table 3 illustrates the decrease in caries activity observed in the test group throughout the 90-day duration. The evaluation of caries activity using the Snyder test revealed a score of 1 in 10 children and a score of 2 in eight children, while none of the children in the test group exhibited a score of 3. [Graph 2].

Table 1: Features of participants- Baseline

Variables	Control group (Mean±SD)	Test group (Mean±SD)	*P*
Age,	3.3±1.4	3.2±1.1	0.619
DIS	1.2±0.6	0.4±0.6	0.623
DCS	1.7±0.6	1.4±0.6	0.626
OHI-S	2.2±0.6	1.8±0.6	0.644
Biofilm Index	2.3±0.7	2.1±0.5	0.557
pH Saliva	5.2±0.7	5.2±0.3	0.811
Gender			0.778
Male	14	13	
Female	16	17	

OHI-S=Simplified oral hygiene index, DIS- Debris index simplified, DCS- Dental Calculus Scale, SD=Standard deviation

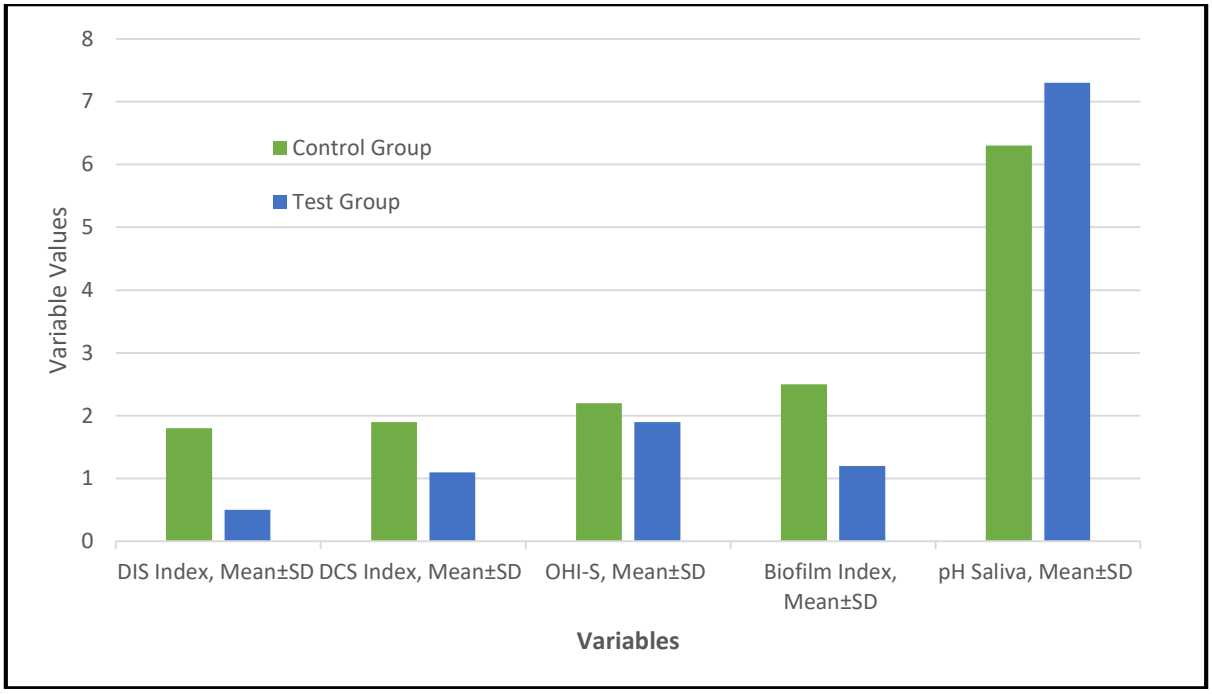
Table 2: Correlation of characteristics between the treated and untreated groups on day 90

Variables	Control group (Mean±SD)	Test group (Mean±SD)	*P*
DIS Index,	1.8±0.6	0.5±0.6	0.601
DCS Index	1.9±0.6	1.1±0.6	0.742
OHI-S	2.2±0.6	1.9±0.6	0.614
Biofilm Index	2.5±0.7	1.2±0.6	0.624
pH Saliva	6.3±0.7	7.3±0.4	0.811

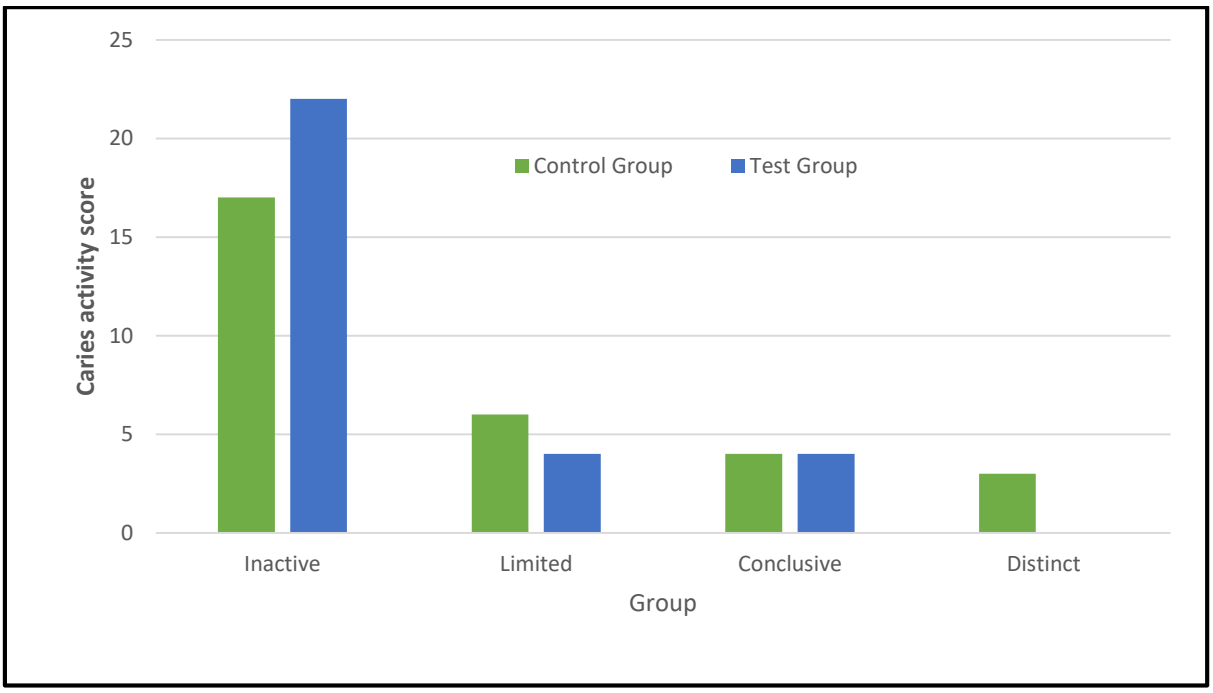
OHI-S=Oral hygiene index-simplified, P=Probability, DIS- Debris index simplified, DCS- Dental Calculus Scale, SD=Standard deviation

Table 3: Correlation of dental decay test between control and test group at day 90

Group		Caries activity score		
	dmft	Limited (Score 1)	Conclusive (Score 2)	Distinct (Score 3)
Control Group	3.6±0.5	6	4	3
Test Group	3.6±0.5	4	4	0



Graph 1: Correlation of parameters between the control and test group at day 90



Graph 2: Comparison of caries activity test results between that was subjected to treatment and the group that was not treated on the 90th day.

Probiotics hinder the binding of harmful microorganisms to tissues. By regulating NFkB pathways, they decrease Promoting the production of anti-inflammatory cytokines such as Interleukins-10 (IL-10) and host defense peptides like beta-defensin while also generating pro-inflammatory cytokines[14]. Furthermore, it boosts the immune system by fortifying the defenses of Immunoglobulin A (IgA) and play a role in the development of dendritic cells[15]. The bacterium generates bacteriocins, which have the ability to eliminate or impede the proliferation of harmful microorganisms. Probiotics disrupt this processes by which oral bacteria adhere to proteins, hence inhibiting the production of biofilm. research has shown that probiotics enhance the treatment-induced mucositis[16]. There is insufficient evidence available regarding the effects of oral probiotics on dental caries activity, salivary pH, and oral hygiene in children undergoing chemotherapy. At the conclusion of the 90-day trial, the test group had a significant decrease in Biofilm. The calculus index had a substantial decrease after daily use of oral probiotics. The research group exhibited an elevation in the pH level of their saliva. This event can be elucidated by the notion that probiotics harbor advantageous and non-pathogenic bacteria existing within the dental biofilm, offering defense to oral and dental structures[17]. Furthermore, the casein phosphopeptide present in probiotics neutralizes the acid generated by cariogenic bacteria and promotes the remineralization process[18]. Earlier studies have demonstrated the beneficial effect of probiotics in reducing caries activity in typically healthy children[19]. The children in our

research showed a high level of tolerance towards the oral probiotics, and no participants withdrew from the trial. The research group also saw a decrease in caries activity. The current research was carried out on pediatric patients afflicted with lymphoma undergoing chemotherapy. The study was constrained by its limited sample size and brief duration. The results of this investigation provide positive support for the efficacy of oral probiotics in reducing biofilm, dental caries activity, and increasing salivary pH. The combination of probiotics with appropriate oral hygiene practices may be suggested as an effective approach to minimize tooth decay.

4. CONCLUSION

Our current work has shown that oral probiotics have a substantial role in reducing biofilm and increasing salivary pH. Utilizing oral probiotics in conjunction with oral hygiene equipment is an effective method for decreasing the buildup of biofilm and tartar in children receiving chemotherapy.

5. AUTHORS CONTRIBUTION STATEMENT

Dr. Anieta Merin Jacob conceptualized the manuscript; Dr. Ammar A. Razzak Mahmood gathered the data about this work. Dr. Narendranath S and Dr D Abisheik Johnson Babu analyzed these data, and provided necessary inputs were given towards the design of the manuscript. Finally, Dr D Abisheik Johnson Babu supervised and executed the entire study, critically revising, editing, and communicating the manuscript. All authors discussed the methodology and results and contributed to the final manuscript.

6. CONFLICT OF INTEREST

Conflict of interest declared none.

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