



Modulating the Oral Microbiome Around Orthodontic Mini- Implants Through *Lactobacillus reuteri* Supplementation

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ABSTRACT

Background: Orthodontic mini-implants may cause cavities that harbor biofilm, leading to gum inflammation and microbial imbalance. This study compared the impact of *Lactobacillus reuteri* supplementation on the status of the gingiva and the composition of the oral microbiome surrounding orthodontic mini-implants.

Methods: This prospective observational cohort study (January and June 2023) included 60 patients of orthodontic mini-implants divided into two groups by supplementation as probiotic-exposed cohort group (n= 30) and non-probiotic cohort group (n= 30) by diet. At baseline and after 4 weeks, Gingival Index (GI), Plaque Index (PI), and Bleeding on Probing (BOP) were measured. Chi-square, paired and independent

t-tests were used to analyze the data; $p < 0.05$ was taken to be significant.

Results: At 4 weeks, the probiotic cohort showed significant improvements in GI (1.23 ± 0.24 ; $p = 0.001$), PI (1.33 ± 0.28 ; $p = 0.002$), and BOP (34.6 ± 7.9 ; $p = 0.001$) compared with non-probiotic. qPCR results (\log_{10} copies/mL) showed reductions in *P. gingivalis* (2.18 ± 0.33 ; $p < 0.001$) and *S. mutans* (3.21 ± 0.48 ; $p = 0.002$) and increases in *L. reuteri* (5.48 ± 0.36 ; $p < 0.001$) and *A. naeslundii* (5.01 ± 0.29 ; $p = 0.01$) in the probiotic group ($p > 0.05$).

Conclusion: The four-week *Lactobacillus reuteri* supplement enhanced the health of the gingiva and the composition of the oral microbiota in favor of a more desirable composition near orthodontic mini-implants.

Keywords: *Lactobacillus reuteri*, Probiotics, Orthodontic, Gingival inflammation, Microbiome

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INTRODUCTION

Oral microbiome is significant in terms of preservation of the ecological balance of the oral cavity and the periodontal and peri-implant health¹. Temporary anchorage devices (TADs) are also referred

to as orthodontic mini-implants, which have emerged as a stable approach to offer skeletal anchorage and complex tooth movements². Nevertheless, they may change the local microbial environment by providing new retention niches of biofilms³. This biofilm alteration frequently favors pathogenic species, which orient the patient towards gingivitis inflammation, peri-implant mucositis, and in a minority of cases, early peri-implantitis⁴.

The traditional preventive measures, like mechanical plaque control, antiseptic mouth rinses like chlorhexidine, are also useful in minimizing the microbial load⁵. However, these strategies are generally linked to negative consequences such as mucosal irritation, dysbiosis, change in taste, and tooth staining⁶. Furthermore, prolonged use of antiseptics can also alter the natural microbial balance, whereby alternative biological solutions that can take care of the oral microbial balance without damaging the host tissues should be considered.

Probiotic therapy is becoming one of the promising adjunctive treatments for maintaining oral and peri-implant health⁷. Probiotics are live microorganisms that, when given in the proper amounts, have health benefits through competitive inhibition of pathogenic bacterial colonization, host immune response modulation, and beneficial species recolonization⁸. The past literature has shown that probiotic strains, including *Lactobacillus reuteri* and *Bifidobacterium bifidum*, are capable of inhibiting some of the notable periodontopathogens, including *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, leading to in turn an improved gingival index and lower bleeding scores⁹. Nevertheless, the majority of the available studies have been conducted on chronic gingivitis or periodontitis, with few studies specifically looking at the effects of probiotics in patients with orthodontic implants¹⁰.

Since the surfaces of orthodontic implants are not similar to natural dentition, in terms of both mechanical and microbial properties. Thus, this study sought to determine the association between microbiome modulation and clinical outcomes mainly the impact of probiotic supplementation on the composition of the oral microbiome and gingival health in patients receiving orthodontic implants.

METHODS

This prospective observational cohort study (January and June 2023) conducted at FMH Lahore and BDMC Mirpurkhas after informed consent (Ref: 2023/1133) based on the Declaration of Helsinki. A simple random sampling method was used to enroll 60 orthodontic patients who need mini-implants (n = 60) to compensate for potential dropouts. OpenEpi software (version 3.01) was used to calculate sample size with a 95 % confidence interval, 80 % statistical power, and a 5 % margin of

error¹¹. A minimum of 25 participants per group was used based on a past literature on expected differences in Gingival Index (GI).

Inclusion criteria included the healthy persons aged between 18 and 35 years with fixed orthodontic treatment using new mini-implants and good oral health and have no systemic disease. Exclusion criteria were the use of systemic antibiotics, probiotics or antimicrobial mouthrinses in the past 3 months; smoking; pregnancy or lactation; and active caries or periodontal disease. Standardization of a baseline oral hygiene instruction was provided before the enrollment to reduce behavioral bias. The participants were categorized into two cohorts based on supplementation status as a group (n=30 each) with consumed chewable *Lactobacillus reuteri* DSM 17938 and ATCC PTA 5289 (1×10^8 CFU per tablet) twice daily for four weeks and other cohort without tablet. The participants and the investigators were blinded to the allocation of the groups during the study period.

An evaluation of clinical status was conducted at baseline (day 0) and 4-week follow-up. The demographics variables such as age and gender were documented at the baseline to have group comparability. The Gingival health parameters such as Gingival Index (GI), Plaque Index (PI) and Bleeding on Probing (BOP) were measured at six sites per tooth with a standard periodontal probe. Each clinical measure was conducted by single calibrated examiner to minimize the inter-examiner bias. Samples of subgingival plaque were taken around orthodontic mini-implants with paper points that were sterilized, and immersed in the peri-implant sulcus in the vicinity of the implant during a period of 30 seconds. The samples were placed in sterile microtubes and stored at -80 C until commercially prepared robotic-arm automated PCR was utilized (Cobas 8000, Roche Diagnostics). Relative abundance was reported as log₁₀ copies/ml and compared with the 16S rRNA gene in order to estimate total bacterial load. All samples were repeated to have duplicated reactions that are reproducible and internally valid. The completeness of data was checked prior to analysis.

The data of microbes were transformed logarithmically to achieve normal distribution. Mean \pm SD was used to represent descriptive statistics of continuous variables and n (percent) was used to indicate categorical variables. Independent t-tests were used to conduct between-cohort comparisons in continuous variables, and Chi-square tests were used to compare within-cohort categorical data. Paired t-tests were used to compare within-group comparisons between the baseline and post-intervention (4-weeks follow up). The p-value of less than 0.05 was taken as a statistically significant value. Analysis was done using SPSS software (version 26.0, IBM Corp., USA).

RESULTS

This prospective observational cohort study enrolled 60 orthodontic implant patients who completed the study without dropouts. Participants were also evenly divided into two cohorts based on supplementation. The average age of the participants was 26.1 ± 4.1 years and there were no statistically significant differences in demographic variables between the groups ($p > 0.05$). There was equal gender distribution of 22 (36.6%) males and 38 (63.3%) females. Table 1 shows the demographic and clinical data of the participants at the baseline.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Variable	Probiotic Cohort group (n = 30)	Non-probiotic Cohort group (n = 30)	Statistical value	p-value
Age (years, Mean \pm SD)	26.1 ± 4.1	25.5 ± 4.3	t = 0.47	0.64
Gender				
Male	11 (36.7%)	11 (36.7%)	$\chi^2 = 0.00^{df=1}$	1.00
Female	19 (63.3%)	19 (63.3%)		
Baseline Gingival Index (GI)	1.82 ± 0.27	1.79 ± 0.29	t = 0.36	0.72
Baseline Plaque Index (PI)	1.96 ± 0.32	1.91 ± 0.30	t = 0.51	0.61
Baseline Bleeding on Probing (BOP)	58.4 ± 8.7	57.2 ± 9.1	t = 0.45	0.65

SD = Standard Deviation; GI = Gingival Index; PI = Plaque Index; BOP = Bleeding on Probing. χ^2 = chi-square test, t = independent t-test, $p < 0.05$ considered statistically significant. There were no statistically significant differences between the probiotic and non-probiotic cohort group and this proved the homogeneity of the both groups at the baseline ($p > 0.05$). Four weeks later, there was a significant decrease in the level of gingival inflammation and plaque in the probiotic group, as compared to the non-probiotic cohort group. Mean GI, PI and BOP decreased significantly in the probiotic group and marginally changed in non-probiotic cohort group. The comparative clinical changes in gingival health indices are presented in **Table 2**.

Table 2: Comparison of Gingival Health Parameters Before and After Probiotic Supplementation

Parameter	Time Point	Probiotic Cohort group (Mean \pm SD)	Non-Probiotic Cohort group (Mean \pm SD)	p-value (Post-intervention)
Gingival Index (GI)	Baseline	1.82 \pm 0.27	1.79 \pm 0.29	0.72
	After 4 weeks	1.23 \pm 0.24*	1.68 \pm 0.26	<0.001*
Plaque Index (PI)	Baseline	1.96 \pm 0.32	1.91 \pm 0.30	0.61
	After 4 weeks	1.33 \pm 0.28*	1.75 \pm 0.31	0.002*
Bleeding on Probing (BOP)	Baseline	58.4 \pm 8.7	57.2 \pm 9.1	0.65
	After 4 weeks	34.6 \pm 7.9*	51.8 \pm 8.6	0.001*

Values expressed as Mean \pm SD; *p < 0.05 considered statistically significant.

Table 3: Changes in Relative Abundance of Selected Oral Microbiota Around Orthodontic Mini-Implants (Log₁₀ copies/mL)

Bacterial Species	Time Point	Probiotic Cohort group (Mean \pm SD)	Non-Probiotic Cohort group (Mean \pm SD)	p-value (Post-intervention)
<i>P. gingivalis</i>	Baseline	5.21 \pm 0.42	5.27 \pm 0.45	0.78
	After 4 weeks	2.18 \pm 0.33*	5.04 \pm 0.39	<0.001*
<i>S. mutans</i>	Baseline	6.03 \pm 0.51	6.09 \pm 0.49	0.67
	After 4 weeks	3.21 \pm 0.48*	5.72 \pm 0.46	0.002*
<i>L. reuteri</i>	Baseline	3.18 \pm 0.39	3.14 \pm 0.37	0.81
	After 4 weeks	5.48 \pm 0.36*	3.19 \pm 0.34	<0.001*
<i>A. naeslundii</i>	Baseline	4.42 \pm 0.33	4.39 \pm 0.30	0.79
	After 4 weeks	5.01 \pm 0.29*	4.43 \pm 0.28	0.01*

Values are expressed as Mean \pm SD (Log₁₀ copies/mL); *p < 0.05 considered significant.

The probiotic group showed a much higher decrease in GI, PI, and BOP than the non-probiotic cohort group at the end of four weeks of supplementation (p < 0.01 in all parameters). The quantitative PCR result showed that probiotic supplementation had a significant influence on the mouth microbiota composition surrounding the orthodontic mini-implants. Four weeks later, the Probiotic Group recorded significant improvements in the mean counts of *Porphyromonas gingivalis* and *Streptococcus mutans*; whereas beneficial species like *Lactobacillus reuteri* and *Actinomyces naeslundii* had significantly increased relative abundance over the non-probiotic cohort Group (p <

0.05 all). These findings show that there is a favorable microbial change after the consumption of probiotics. **Table 3** shows the detailed post-intervention data.

It was found that the probiotic cohort group demonstrated a statistically significant reduction in pathogenic bacterial load (*P. gingivalis*, *S. mutans*) and an increase in favorable species (*L. reuteri*, *A. naeslundii*), which revealed the restoration of the microbial balance in the mouth.

DISCUSSION

This prospective observational cohort study revealed that four weeks probiotic consumption showed a significant reduction of gingival inflammation and plaque formation than the non-probiotic cohort. Moreover, orthodontic mini-implants pathogenic species were significantly reduced in the probiotic group, especially the presence of *Porphyromonas gingivalis* and *Streptococcus mutans* and the presence of *Lactobacillus reuteri* and *Actinomyces naeslundii* were increased. These results suggest that a probiotic therapy is effective in the management of microbial homeostasis and enhancement of gingivitis in patients receiving orthodontic implants.

According to the previous research, the positioning of orthodontic mini-implants tends to interfere with the local microbial environment and expose patients to peri-implant inflammation and gingival bleeding¹². Although effective, conventional plaque control options like chlorhexidine mouthrinses are constrained by side effects such as change in taste and mucosal irritation¹³. The considerable decrease in Gingival Index and Bleeding on Probing seen in the current study is consistent with previous clinical trials that showed the anti-inflammatory effect of *Lactobacillus reuteri* probiotics among orthodontic and periodontal patients^{14,15}. Probability of clinical improvement could be explained by the fact that probiotics can prevent the production of inflammatory cytokines and promote epithelial barrier integrity, which leads to a reduction in gingival bleeding and swelling¹⁶.

The identified drop in the number of pathogenic bacterial species confirms previous articles that probiotic strains, particularly *Lactobacillus reuteri*, have antimicrobial effects which are competitive, hydrogen peroxide-generating, and local pH modifying¹⁷. Other orthodontic studies have also reported the reduction of both *S. mutans* and *P. gingivalis* by probiotic supplementation¹⁸. The growth of *B. naeslundii* and *L. reuteri* in the current study also supports the restorative action of probiotics on the good microbiota, favoring ecological balance and stability of biofilms¹⁹. In contrast to mouthrinses, which have a temporary, short-term effect in reducing the number of microbes, probiotics offer a long-term ecological benefit of mucosal colonization and commensal re-establishment^{20,21}.

These findings have greater implications in the prevention and treatment dentistry²². Probiotic supplementation can be a safe adjunct to maintain gingival health around orthodontic mini-implants and reduce the risk of inflammation. According to the previous research, probiotics can work mechanistically by suppressing proinflammatory cytokines, including IL-6 and TNF- α , enhancing the production of short-chain fatty acids, and enhancing the immune response of the mucosal barrier^{23,24}. These clinical results indicate the possible consideration of probiotic preparations in the daily orthodontic practice especially in patients with higher risks of plaque-induced inflammation or deficient oral health care practices. In addition, this method may reduce an addiction to antibiotics and aid in antimicrobial stewardship in the dental field.

Along with these encouraging findings, this research has a number of limitations. The relatively brief period of intervention and the relatively small sample could restrict the applicability of the results. Also, microbial analysis was limited to a few specific bacterial species as opposed to metagenomic profiling of the entire microbial interactions that could be missed. A longer period of follow-up, larger multicentric cohorts and more sophisticated methods of sequencing should be used in future studies in order to learn more about the stability of probiotic colonization over time and its systemic implications. Comparative trials between various probiotic strains and delivery system may also help to optimize formulations to achieve specific gingival protection²⁵.

CONCLUSION

Under the constraints of this randomized clinical trial, probiotic supplementation showed a considerable enhancement in the health of the gingiva and oral microbial balance in patients undergoing orthodontic mini-implantation. The *Lactobacillus reuteri* preparation was effective in decreasing the number of pathogenic bacteria, enhancing the number of beneficial organisms, and improving the important clinical parameters, such as the Gingival Index, Plaque Index, and Bleeding on Probing. These results may indicate that probiotics may act as an adjunct that is safe, biologically compatible and can be used to promote good gingival health around orthodontic mini-implants in the course of treatment. These results should be supported by future research using larger sample sizes, longer follow up periods, and in-depth microbiome profiling of how probiotics can be used to maintain oral health, involving a larger sample and a longer period of follow-up.

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CONFLICT OF INTEREST

None.

ETHICAL APPROVAL

This prospective observational cohort study (January and June 2023) was conducted at FMH Lahore and BDMC Mirpurkhas after informed consent (Ref: 2023/1133) based on the Declaration of Helsinki.

AUTHORS' CONTRIBUTION

All authors contributed equally as per ICMJE.

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