

## Clinical assessment of Probiotic mouthwash as adjunct to non-surgical periodontal therapy in patients with stage II grade A periodontitis

Dr. Mohan Krishna Bondili<sup>1</sup>, Dr. Srikanth Adusumilli<sup>2</sup>, Dr. Sathish Manthena<sup>3</sup>, Dr. Penubolu Lakshmi Preethi<sup>4</sup>, Dr. Venkata Naga Sri Harsha Anumolu<sup>5</sup>, Dr. Mulpuri Venkata Ramoji Rao<sup>6</sup>

<sup>1</sup>Postgraduate, Department of Periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of Dental sciences, Chinnaoutpalli, Gannavaram Mandal – 521286

<sup>2</sup>Professor, Department of Periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of Dental sciences, Chinnaoutpalli, Gannavaram Mandal – 521286

<sup>3</sup>Associate professor, Department of Periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of Dental sciences, Chinnaoutpalli, Gannavaram Mandal – 521286

<sup>4</sup>Associate professor, Department of Periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of Dental sciences, Chinnaoutpalli, Gannavaram Mandal – 521286

<sup>5</sup>Associate professor, Department of Periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of Dental sciences, Chinnaoutpalli, Gannavaram Mandal – 521286

<sup>6</sup>Professor & HOD, Department of Periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of Dental sciences, Chinnaoutpalli, Gannavaram Mandal – 521286

### Abstract

**AIM:** To evaluate the effect of probiotic mouthwash with SRP on periodontal indices in patients with stage II, grade A periodontitis.

**Materials & Methods:** Thirty patients were randomly assigned into two groups (n=15) and received SRP treatment along with placebo in one group and probiotic supplementation in the other. After SRP, the test group used probiotic supplemented mouthwash once daily for 21 days. The control group subjects were treated only with SRP. Clinical parameters like PPD, CAL, PI and GI were assessed at baseline, 14 and 21 days.

**Results:** The intra-group analysis using repeated measures ANOVA (Tables 1–4) showed a statistically significant improvement in all periodontal parameters PPD, CAL, PI, and GI across baseline, 14 days, and 21 days in both the probiotic and placebo groups ( $p < 0.05$ ). The probiotic group demonstrated a greater reduction in PPD from a baseline mean of 6.65 mm to 5.44 mm at 14 days and 4.78 mm at 21 days. PPD showed a significant difference favouring the probiotic group ( $p = 0.002$ ), while GI showed significant differences at baseline and 14 days ( $p = 0.049$  and  $0.014$ ), indicating superior periodontal improvement with probiotic mouthwash.

**Conclusion** – The probiotic supplementation as a mouthwash, along with SRP, had a positive effect on periodontal indices in patients with stage II and grade A generalized periodontitis with the probiotic mouthrinse having a great therapeutic potential.

**Keywords** – Probiotic, Grade A, SRP.

## Introduction

Periodontitis is a chronic multifactorial condition, characterized by progressive destruction of supporting structures of the teeth because of host inflammatory responses.

Conventional non-surgical periodontal therapy including scaling and root planing remains gold standard for mechanical removal of plaque and calculus. However, the efficacy of SRP alone is limited in reducing pathogenic microorganisms.

With the threat of widespread antibiotic resistance rendering many antibiotics useless against important diseases, there is an increased necessity not only to minimize antibiotic use and develop novel non antibiotic-based treatments, but also to raise the profile of disease prevention<sup>1</sup>.

In recent years, Probiotics has gained significant interest in dentistry as a natural based approach to modulate the oral microbiome, inhibiting the growth of pathogenic bacteria and reduce inflammation of periodontal tissues.

Only a few studies have investigated probiotics' role in treating periodontitis. This study investigated the effect of probiotic mouthwash along with SRP on periodontal indices in patients with stage II grade A generalized periodontitis<sup>2</sup>. The present study investigated the effect of probiotic supplementation in the form of mouthwash on the clinical indices of probing depth (PD), Gingival index (GI), clinical attachment loss (CAL), and plaque index (PI).

## Materials & Methods

This was a randomized, placebo-controlled, double blind, parallel arm randomized clinical trial to evaluate the effect of probiotic mouthwash with and without SRP on periodontal indices in patients with stage II, grade A periodontitis patients. The informed consent was obtained from the patients during the study period.

The trial period was over 21 days with assessment conducted at i) baseline ii) 14 days and iii) 21 days. Clinical parameters assessed were Probing pocket depth, Clinical attachment level, Plaque index (Loe H & sillness J, 1964) and Gingival index (Sillness J and Loe H, 1963).

## Inclusion criteria

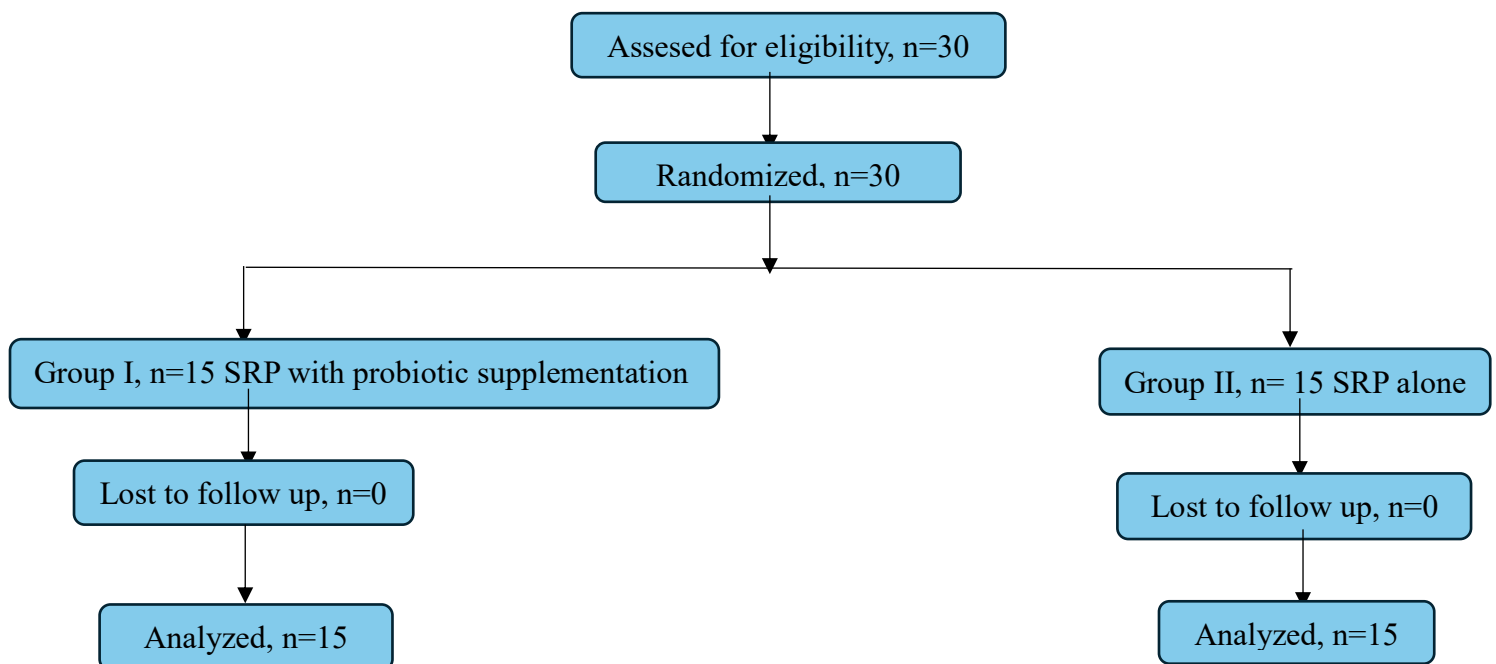
- ✓ Patients between the age group of 18- 60 yrs.
- ✓ Definitive diagnosis of periodontitis, at least four teeth with PPD  $\geq$  5mm and a CAL of  $\geq$  4mm.
- ✓ No recent history of use of antimicrobial agents or any other drugs.
- ✓ Patients having dentition with  $\geq$  20 teeth.

### Exclusion criteria

- ✓ Patients with any systemic conditions
- ✓ Patients allergic to probiotic supplements
- ✓ Patients treated with antibiotics in the past three months<sup>3</sup>.
- ✓ Patients undergoing any periodontal treatment in the past six months.
- ✓ Pregnant and lactating women<sup>6</sup>
- ✓ History of smoking

### Study design

Thirty patients were randomly assigned into two groups (n=15) and received SRP treatment along with placebo in one group and probiotic supplementation in the other. After SRP, the test group used probiotic supplemented mouthwash once daily for 21 days. The control group subjects were treated only with SRP. Clinical parameters like PPD, CAL, PI and GI were assessed at baseline, 14 and 21 days.



### Clinical Parameters

Clinical parameters were assessed by a clinician who is blind to the groups, Clinical parameters such as Probing pocket depth, Clinical attachment level, Plaque index (Loe H & sillness J, 1964) and Gingival index (Sillness J and Loe H, 1963) were assessed at baseline, 14 and 21 days.



**Probiotic  
mouthrinse sample**



**Measuring PPD at  
baseline**



**Measuring PPD at  
14<sup>th</sup> day**



**Measuring PPD at  
21<sup>st</sup> day**

## Observation and Results

### Statistical Analysis Done

All data were entered in Microsoft Excel and analysed using **IBM SPSS Statistics (Version 25.0, IBM Corp., Armonk, NY, USA)**. Descriptive statistics including **mean** and **standard deviation (SD)** were calculated for all clinical parameters (PPD, CAL, PI, and GI) at baseline, 14 days, and 21 days for both groups. To evaluate **intra-group changes over time**, **Repeated Measures ANOVA** was applied separately for the probiotic and placebo groups. Wherever significant differences were detected, **post-hoc pairwise comparisons** were performed using the **Bonferroni correction** to identify specific time-point differences. For **inter-group comparisons** between the probiotic and placebo groups at each time interval, the **Independent Samples t-test** was used. A **p-value < 0.05** was considered statistically significant for all analyses. All tests were two-tailed.

**Table 1: Intra-group Comparison of Probing Pocket Depth (PPD), Clinical Attachment Level (CAL), Plaque Index (PI), Gingival Index (GI) at Baseline, 14 Days and 21 Days Using Repeated Measures ANOVA (Probiotic vs Placebo Groups)**

Repeated measures of ANOVA

Groups	Levels	PPD (Mean ± SD)	CAL (Mean ± SD)	PI (Mean ± SD)	GI (Mean ± SD)
<b>Probiotic mouth wash</b>	Base line	6.65 ± 1.13	6.60 ± 1.30	1.42 ± 0.47	1.38±0.33
	14 days	5.44 ± 1.19	5.68 ± 0.90	1.07 ± 0.32	1.00±0.22
	21 days	4.78 ± 0.83	5.22 ± 0.70	0.88 ± 0.16	0.80±0.16
	F value	489.575	628.727	202.698	407.176
	P value	0.000*	0.000*	0.000*	0.000*
<b>Placebo</b>	Base line	6.46 ± 1.37	6.14 ± 1.31	1.26 ± 0.44	1.10±0.38
	14 days	6.12 ± 1.20	5.76 ± 1.00	1.03 ± 0.29	0.80±0.17
	21 days	5.99± 1.09	5.70 ± 0.83	0.97± 0.18	0.92±0.24
	F value	397.235	487.427	222.462	317.424
	P value	0.000*	0.000*	0.000*	0.000*

*P value <0.05 is considered as statistically significant*

**Table 2: Post-hoc Bonferroni Pairwise Comparison for PPD in Probiotic Mouthwash Group**

Probiotic mouth wash PPD	Sub groups	Mean difference	Standard error	P value
Base line	14 days	1.207*	0.198	0.000*
	21 days	1.867*	0.194	0.000*
14 days	Base line	-1.207*	0.198	0.000*
	21 days	0.660*	0.142	0.001*
21 days	Base line	-1.867*	0.194	0.000*
	14 days	-0.660*	0.142	0.001*

*Post hoc test using Bonferroni correction*

*\*p value <0.05 is considered as statistically significant*

**Table 3: Post-hoc Bonferroni Pairwise Comparison for CAL in Probiotic Mouthwash Group**

Probiotic mouth wash CAL	Sub groups	Mean difference	Standard error	P value
Base line	14 days	0.920*	0.190	0.001*
	21 days	1.380*	0.248	0.000*
14 days	Base line	-0.920*	0.190	0.001*
	21 days	0.460*	0.136	0.013*
21 days	Base line	-1.380*	0.248	0.000*
	14 days	-0.460*	0.136	0.013*

*Post hoc test using Bonferroni correction*

*\*p value <0.05 is considered as statistically significant*

**Table 4: Post-hoc Bonferroni Pairwise Comparison for PI in Probiotic Mouthwash Group**

Probiotic mouth wash PI	Sub groups	Mean difference	Standard error	P value
Base line	14 days	0.347*	0.056	0.000*
	21 days	0.540*	0.088	0.000*
14 days	Base line	-0.347*	0.056	0.000*
	21 days	0.193*	0.064	0.028*
21 days	Base line	-0.540*	0.088	0.000*
	14 days	-0.193*	0.064	0.028*

*Post hoc test using Bonferroni correction*

*\*p value <0.05 is considered as statistically significant*

**Table 5: Post-hoc Bonferroni Pairwise Comparison for GI in Probiotic Mouthwash Group**

Probiotic mouth wash GI	Sub groups	Mean difference	Standard error	P value
Base line	14 days	0.380*	0.060	0.000*
	21 days	0.573*	0.087	0.000*
14 days	Base line	-0.380*	0.060	0.000*
	21 days	0.193*	0.052	0.007*
21 days	Base line	-0.573*	0.087	0.000*
	14 days	-0.193*	0.052	0.007*

Post hoc test using Bonferroni correction

\*p value <0.05 is considered as statistically significant

**Table6: Post-hoc Bonferroni Pairwise Comparison for PPD in Placebo Group**

Placebo PPD	Sub groups	Mean difference	Standard error	P value
Base line	14 days	0.340*	0.073	0.001*
	21 days	0.467*	0.153	0.026*
14 days	Base line	-0.340*	0.073	0.001*
	21 days	0.127	0.111	0.814
21 days	Base line	-.0467*	0.153	0.026*
	14 days	-0.127	0.111	0.814

Post hoc test using Bonferroni correction

\*p value <0.05 is considered as statistically significant

**Table7: Post-hoc Bonferroni Pairwise Comparison for CAL in Placebo Group**

Placebo CAL	Sub groups	Mean difference	Standard error	P value
Base line	14 days	0.380*	0.114	0.015*
	21 days	0.447	0.175	0.070*
14 days	Base line	-.0380*	0.114	0.015*
	21 days	0.067	0.089	1.000
21 days	Base line	-0.447	0.175	0.070*
	14 days	-0.067	0.089	1.000

Post hoc test using Bonferroni correction

\*p value <0.05 is considered as statistically significant

**Table 8: Post-hoc Bonferroni Pairwise Comparison for PI in Placebo Group**

Placebo PI	Sub groups	Mean difference	Standard error	P value
Base line	14 days	0.227*	0.060	0.006*
	21 days	0.287*	0.092	0.023*
14 days	Base line	-0.227*	0.060	0.006*
	21 days	0.060	0.056	0.904
21 days	Base line	-0.287*	0.092	0.023*
	14 days	-0.060	0.056	0.904

*Post hoc test using Bonferroni correction*

*\*p value <0.05 is considered as statistically significant*

**Table9: Post-hoc Bonferroni Pairwise Comparison for GI in Placebo Group**

Placebo GI	Sub groups	Mean difference	Standard error	P value
Base line	14 days	0.300*	0.077	0.005*
	21 days	0.180	0.108	0.356
14 days	Base line	-0.300*	0.077	0.005*
	21 days	-0.120	0.067	0.285
21 days	Base line	-0.180	0.108	0.356
	14 days	0.120	0.067	0.285

*Post hoc test using Bonferroni correction*

*\*p value <0.05 is considered as statistically significant*

**Table 10: Inter-group Comparison of PPD between Probiotic and Placebo Groups at Baseline, 14 Days, and 21 Days Using Independent Sample t-test**

VARIABLE	GROUPS	MEAN	SD	T VALUE	P VALUE
PPD-BASE LINE	Probiotic mouth wash	6.6533	1.13002	0.421	0.677
	Placebo	6.4600	1.37571		
14 DAYS	Probiotic mouth wash	5.4467	1.19455	-1.536	0.136
	Placebo	6.1200	1.20665		
21 DAYS	Probiotic mouth wash	4.7867	.83312	-3.398	0.002*
	Placebo	5.9933	1.09444		

*Independent sample t test*

*\*p value <0.05 is considered as statistically significant*

**Table 11: Inter-group Comparison of CAL between Probiotic and Placebo Groups at Baseline, 14 Days, and 21 Days Using Independent Sample t-test**

VARIABLE	GROUPS	MEAN	SD	T VALUE	P VALUE
CAL-BASE LINE	Probiotic mouth wash	6.6067	1.30738	0.962	0.344
	Placebo	6.1467	1.31142		
14 DAYS	Probiotic mouth wash	5.6867	0.90543	-0.228	0.821
	Placebo	5.7667	1.00971		
21 DAYS	Probiotic mouth wash	5.2267	0.70150	-1.678	0.104
	Placebo	5.7000	0.83751		

*Independent sample t test*

*\*p value <0.05 is considered as statistically significant*

**Table 12: Inter-group Comparison of PI between Probiotic and Placebo Groups at Baseline, 14 Days, and 21 Days Using Independent Sample t-test**

VARIABLE	GROUPS	MEAN	SD	T VALUE	P VALUE
PI-BASE LINE	Probiotic mouth wash	1.4200	0.47087	0.961	0.345
	Placebo	1.2600	0.44045		
14 DAYS	Probiotic mouth wash	1.0733	0.32616	0.351	0.728
	Placebo	1.0333	0.29681		
21 DAYS	Probiotic mouth wash	0.8800	.16562	0.482	0.154
	Placebo	0.9733	.18310		

*Independent sample t test*

*\*p value <0.05 is considered as statistically significant*

**Table 13: Inter-group Comparison of GI between Probiotic and Placebo Groups at Baseline, 14 Days, and 21 Days Using Independent Sample t-test**

VARIABLE	GROUPS	MEAN	SD	T VALUE	P VALUE
GI-BASE LINE	Probiotic mouth wash	1.3800	0.33848	2.056	0.049*
	Placebo	1.1067	0.38816		
14 DAYS	Probiotic mouth wash	1.0000	0.22678	2.636	0.014*
	Placebo	0.8067	0.17099		
21 DAYS	Probiotic mouth wash	0.8067	0.16676	-1.588	0.123
	Placebo	0.9267	0.24044		

*Independent sample t test*

*\*p value <0.05 is considered as statistically significant*

**Figures**

Figure 1. Trend of Probing Pocket Depth (PPD) Scores at Baseline, 14 Days, and 21 Days in Probiotic and Placebo Groups

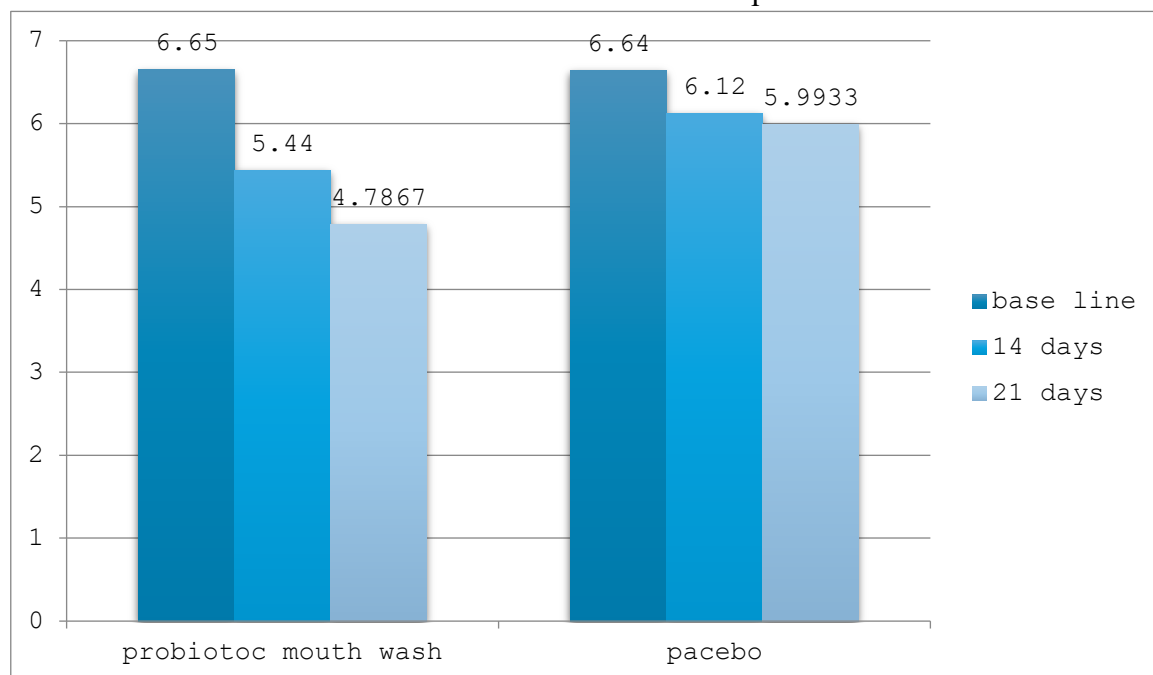


Figure 2. Trend of Clinical Attachment Level (CAL) Scores at Baseline, 14 Days, and 21 Days in Probiotic and Placebo Groups

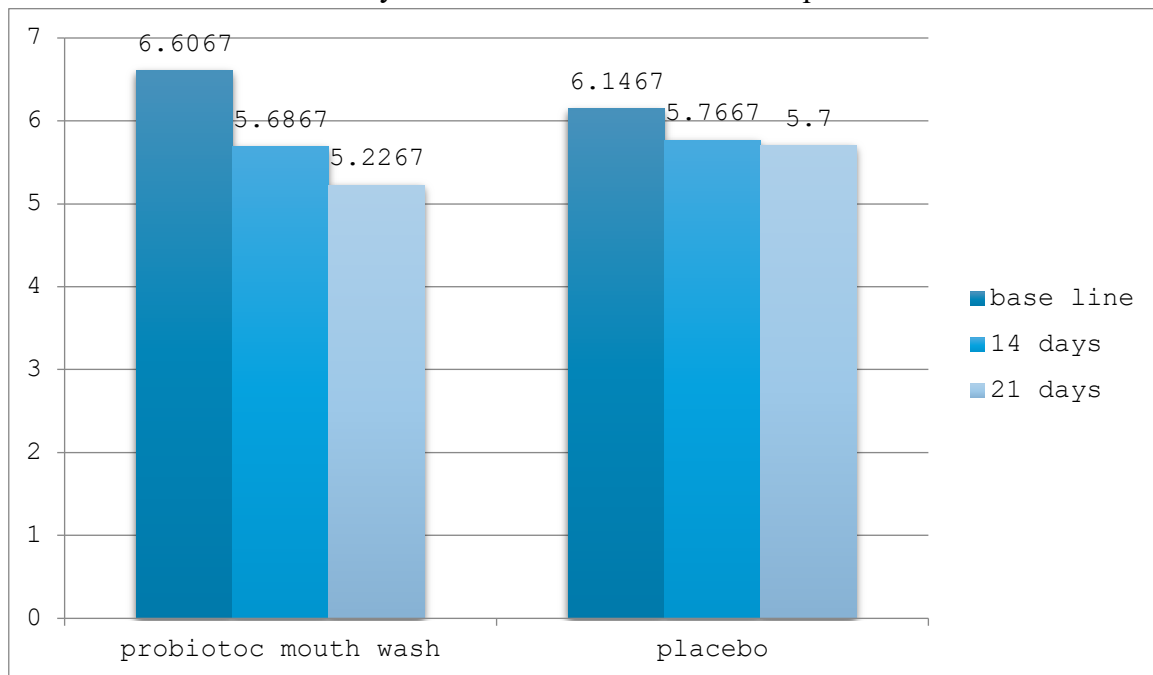


Figure 3. Trend of Plaque Index (PI) Scores at Baseline, 14 Days, and 21 Days in Probiotic and Placebo Groups

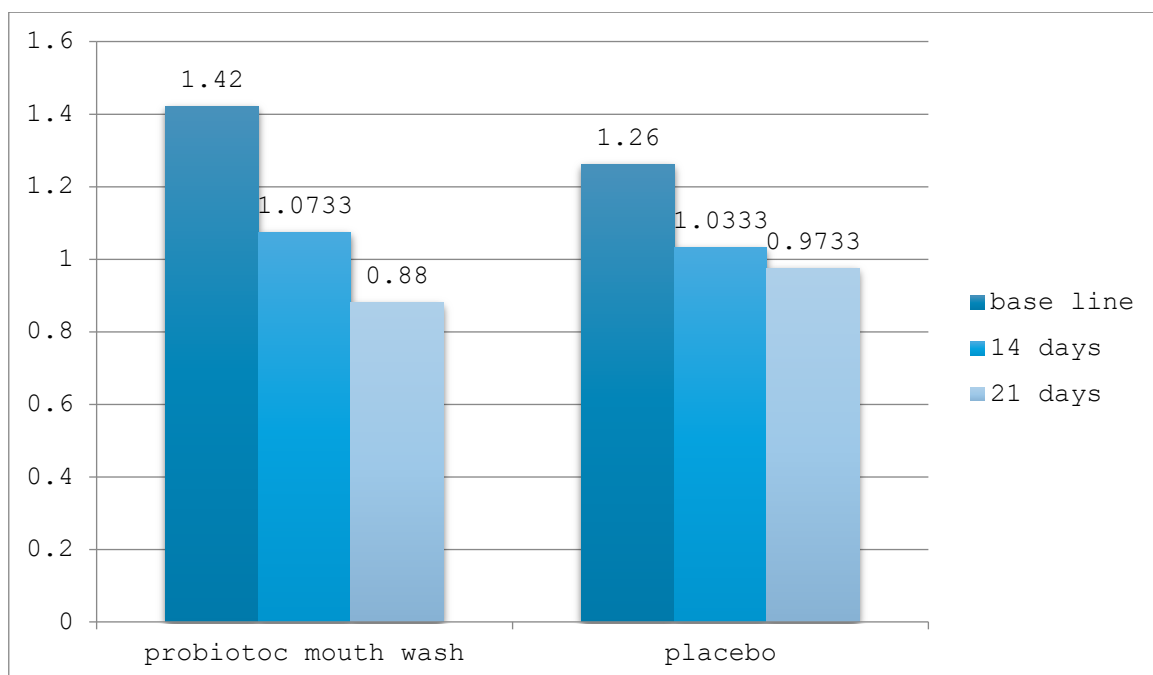
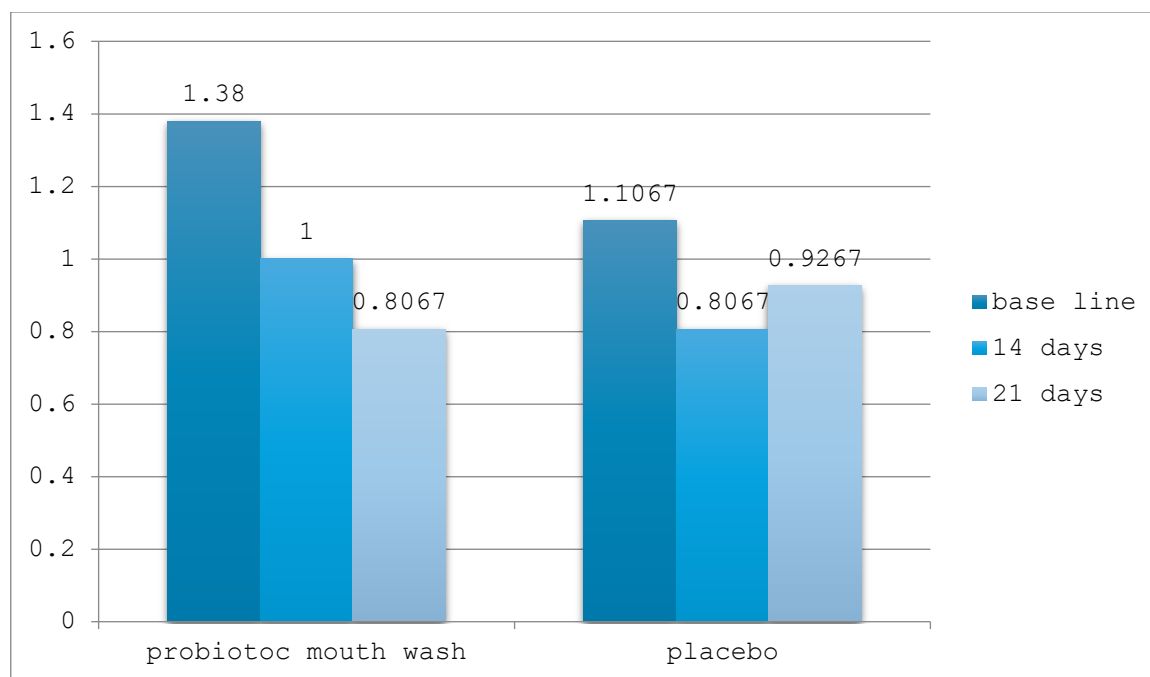


Figure 4. Trend of Gingival Index (GI) Scores at Baseline, 14 Days, and 21 Days in Probiotic and Placebo Groups



### Inference

The intra-group analysis using repeated measures ANOVA (Tables 1–4) showed a statistically significant improvement in all periodontal parameters PPD, CAL, PI, and GI across baseline, 14 days, and 21 days in both the probiotic and placebo groups ( $p < 0.05$ ). The probiotic group demonstrated a greater reduction in PPD from a baseline mean of **6.65 mm** to **5.44 mm** at 14 days and **4.78 mm** at 21 days (Table 1), while the placebo group showed a comparatively smaller reduction from **6.46 mm** to **6.12 mm** and **5.99 mm**, respectively. Similar trends were observed for CAL (Table 2), where the probiotic group improved from **6.60 mm** at baseline to **5.22 mm** at 21 days, compared to the placebo group decreasing from **6.14 mm** to **5.70 mm**. For PI and GI (Tables 3 and 4), the probiotic group again showed greater improvements (PI: **1.42** to **0.88**; GI: **1.38** to **0.80**) compared to the placebo group (PI: **1.26** to **0.97**; GI: **1.10** to **0.92**). Post-hoc Bonferroni comparisons (Tables 5–12) confirmed significant pairwise differences across time points for the probiotic group in all parameters, whereas the placebo group showed fewer significant differences. Inter-group comparisons using independent t-tests (Tables 13–16) revealed no significant differences between groups at baseline for any parameter; however, by 21 days, PPD showed a significant difference favouring the probiotic group ( $p = 0.002$ ), while GI showed significant differences at baseline and 14 days ( $p = 0.049$  and  $0.014$ ), indicating superior periodontal improvement with probiotic mouthwash.

## Discussion

Periodontal diseases are common multifactorial conditions in different communities. One of the most important factors responsible for these diseases is the disruption of the oral cavity microbial flora. Due to the importance of eliminating pathogenic strains in different types of periodontitis, current therapies, including non-surgical treatments such as SRP with or without supplemental treatments, are among the recommended options for recovery. Despite its various benefits, antibiotic therapy leads to the development of resistant strains, and if inappropriate antibiotics are selected, disease recurrence is not unexpected<sup>4</sup>. Other methods, despite their various benefits, are costly, and their success depends on controlling pathogenic bacteria and environmental factors. Therefore, probiotics appears to be a necessity in the treatment of various diseases, including periodontal diseases. Probiotics are living bacteria that affect the host by improving the microbial balance in their body. According to the FDA, probiotics are living microorganisms with health benefits for the host in sufficient amounts. Considering the discrepancies about the effects of different probiotic strains on oral health, this study investigated the effect of probiotic supplementation as a mouthwash along with SRP on periodontal indices in patients with stage II grade A generalized periodontitis. The results show that intra-group analysis using repeated measures showed a statistically significant improvement in all periodontal parameters PPD, CAL, PI, and GI across baseline, 14 days, and 21 days in both the probiotic and placebo groups<sup>7</sup>.

Penal et al studied the effect of a probiotic mouthwash containing *Lactobacillus salivarius* and *Lactobacillus reuteri* on changing the periodontal indices of patients with chronic periodontitis and reported that the application of probiotics in the mouthwash and subgingival form along with SRP treatment for 15 days could significantly reduce the plaque index and BOP in three months. The study also showed that both SRP + placebo and SRP +probiotic treatments significantly reduced the mean PD and CAL in patients, with no significant difference between the two groups. In our study, changes in pocket depth were significant between the two test and control groups; however, in the study by Penal et al, these changes were not significant. The difference between the results could be attributed to a higher mean of patients' pocket depths and a wider variety of bacteria, which reduces the therapeutic effects of probiotics<sup>10</sup>.

Teughles et al studied 30 patients >35 years of age with chronic periodontitis and reported that *L. reuteri* could significantly reduce medium and deep pockets in 12 weeks. Further investigations also showed that *P. gingivalis* levels significantly decreased due to the use of probiotics, consistent with the present study, and indicating that by increasing the duration of probiotic use, it is possible to decrease pocket depths.

In the present study, the test group (SRP + Probiotic) demonstrated a greater reduction in PPD from a baseline mean of 6.65 mm to 5.44 mm at 14 days and 4.78 mm at 21 days (Table 1), while the placebo group showed a comparatively smaller reduction from 6.46 mm to 6.12 mm and 5.99 mm, respectively. Specifically, the additional reduction in the test group suggests that probiotics may enhance the healing of the pocket epithelium. Similar trends were observed for CAL (Table 2), where the probiotic group improved from 6.60 mm at baseline to 5.22 mm at

21 days, compared to the placebo group decreasing from 6.14 mm to 5.70 mm. This greater gain in clinical attachment level in the probiotic group indicated that the intervention does not reduce inflammation, but potentially promotes a stable connective tissue attachment<sup>12</sup>.

For PI and GI (Tables 3 and 4), the probiotic group again showed greater improvements (PI: 1.42 to 0.88; GI: 1.38 to 0.80) compared to the placebo group (PI: 1.26 to 0.97; GI: 1.10 to 0.92). Our findings showed a marked decrease in Gingival index (GI) and Plaque index (PI) in both the groups, confirming the efficacy of mechanical debridement. However, the significantly lower GI scores in the probiotic group suggests that probiotic strains exerted an anti-inflammatory effect that persisted beyond the immediate post operative period of non-surgical periodontal therapy, likely by inhibiting the recolonization of marginal plaque<sup>14</sup>.

A longitudinal look at our data reveals that while both groups improved by the 7<sup>th</sup> day, the test group maintained significantly more stable clinical parameters through the follow-up.

This shift is particularly important for the stage II patients where the goal of the therapy is to arrest disease progression and prevent further bone loss<sup>16</sup>.

Despite the positive clinical outcomes, this study is not without limitations. Firstly, the use of a mouthwash delivery system may offer limited subgingival penetration compared to local drug delivery in deeper stage II pockets only Grade A periodontitis is considered as it is characterized by a slow rate of bone loss and high host resistance, the introduction of beneficial bacteria may be particularly effective. Our findings suggest that in these patients, probiotics help maintain a state of homeostasis longer than mechanical cleaning alone. While SRP physically removes the biofilm, the probiotic mouthwash acts as biological barrier that delays the recolonization of periopathogens and the results may not apply to the patients with Grade B and C periodontitis. These patients often have different microbial profiles and host immune responses that might not respond as favourably to simple probiotic adjunct<sup>18</sup>.

The follow-up period may not be sufficient to determine the long-term stability of the shifted microbiome. Additionally, the absence of microbiological and immunological assays (GCF cytokine levels) prevents a definitive conclusion regarding the biological mechanism of the observed improvements in reduction of specific pathogens like *Porphyromonas gingivalis*.

Therefore, within the constraints of the study, this literature concludes that probiotic supplementation as a mouthwash, along with SRP, had a positive effect on periodontal indices and produced promising results in enhancing periodontal outcomes compared to conventional non – surgical periodontal therapy.

## Conclusion

The probiotic supplementation as a mouthwash, along with SRP, had a positive effect on periodontal indices in patients with stage II and grade A generalized periodontitis with the probiotic mouthrinse having a great therapeutic potential.

**Conflict of Interest-** None

## References

1. **Ghasemi S, Babaloo AR, Mohammadi B, Esmailzadeh M.** Evaluating the effect of probiotic supplementation in the form of mouthwash along with scaling and root planing on periodontal indices in patients with stage III and grade A generalized periodontitis: A randomized clinical trial. *Journal of Advanced Periodontology & Implant Dentistry.* 2020 Dec 9;12(2):73.
2. **Mani A, Mani S, Saini SR.** Efficacy of oral probiotics as an adjunct to scaling and root planing in nonsurgical treatment outcome of generalized chronic periodontitis patients: a clinico-microbiological study. *International Journal of Experimental Dental Science.* 2011 Apr 1;6(1):6-13.
3. **Alshareef A, Attia A, Almalki M, Alsharif F, Melibari A, Mirdad B, Azab E, Youssef AR, Dardir A.** Effectiveness of probiotic lozenges in periodontal management of chronic periodontitis patients: clinical and immunological study. *European journal of dentistry.* 2020 May;14(02):281-7.
4. **Paul GT, Gandhimadhi D, Babu SK.** A double-blind, placebo-controlled study to assess the clinical and microbiological effects of a probiotic lozenge as an adjunctive therapy in the management of chronic periodontitis. *CHRISMED Journal of Health and Research.* 2019 Jan 1;6(1):57-63.
5. **Ikram S, Raffat MA, Baig S, Ansari SA, Borges KJ, Hassan N.** Clinical efficacy of probiotics as an adjunct to scaling and root planning in the treatment of chronic periodontitis. *Annals Of Abbasi Shaheed Hospital and Karachi Medical & Dental College.* 2019 Mar 31;24(1):31-7.
6. **Poulose M, Gujar D, Panicker S, Rokade S, Guruprasad M, Gopalakrishnan D.** Efficacy and viability of subgingival application of probiotics as an adjunct to scaling and root planing in periodontitis. *Indian Journal of Dental Research.* 2024 Jan 1;35(1):59-64.
7. **Yilmaz FÇ, Görgin NÇ.** The role of probiotics and dietary interventions in the treatment of periodontitis: a pilot randomized controlled clinical trial. *BMC Oral Health.* 2025 Jul 31;25(1):1287.
8. **Minić I, Pejčić A, Bradić-Vasić M.** Effect of the local probiotics in the therapy of periodontitis A randomized prospective study. *International Journal of Dental Hygiene.* 2022 May;20(2):401-7.
9. **Penala S, Kalakonda B, Pathakota KR, Jayakumar A, Koppolu P, Lakshmi BV, Pandey R, Mishra A.** Efficacy of local use of probiotics as an adjunct to scaling and root planing in chronic periodontitis and halitosis: A randomized controlled trial. *Journal of research in pharmacy practice.* 2016 Apr 1;5(2):86-93.
10. **Kanagaraj SS, Elavarasu S, Thangavelu A, Subaramoniam MK, Dutta T, Ramasamy DK.** The evaluation of probiotic as an adjunct to scaling and root planing in chronic periodontitis patients-a clinical, microbiological and biochemical study. *Int J Oral Health Dentistry.* 2019; 5:32-6.
11. **Morales A, Gandolfo A, Bravo J, Carvajal P, Silva N, Godoy C, Garcia-Sesnich J, Hoare A, Diaz P, Gamonal J.** Microbiological and clinical effects of probiotics and antibiotics on nonsurgical treatment of chronic periodontitis: a randomized placebo-controlled trial with 9-month follow-up. *Journal of Applied Oral Science.* 2018;26:e20170075.
12. **Ikram S, Hassan N, Baig S, Borges KJ, Raffat MA, Akram Z.** Effect of local probiotic (*Lactobacillus reuteri*) vs systemic antibiotic therapy as an adjunct to non-surgical periodontal treatment in chronic periodontitis. *Journal of investigative and clinical dentistry.* 2019 May;10(2):e12393.
13. **Ranjith A, Nazimudeen NB, Baiju KV.** Probiotic mouthwash as an adjunct to mechanical therapy in the treatment of stage II periodontitis: A randomized controlled clinical trial. *International Journal of Dental Hygiene.* 2022 May;20(2):415-21.
14. **Dhaliwal PK, Grover V, Malhotra R, Kapoor A.** Clinical and Microbiological Investigation of the Effects of Probiotics Combined with Scaling and Root Planing in the Management of Chronic Periodontitis: A Randomized, Controlled Study. *Journal of the International Academy of Periodontology.* 2017 Jul 1;19(3):101-8.
15. **Shah MP, Gujjari SK, Chandrasekhar VS.** Evaluation of the effect of probiotic (Inersan®) alone, combination of probiotic with doxycycline and doxycycline alone on aggressive periodontitis—a clinical and microbiological study. *Journal of clinical and diagnostic research: JCDR.* 2013 Mar 1;7(3):595.
16. **Martin-Cabezas R, Davideau JL, Tenenbaum H, Huck O.** Clinical efficacy of probiotics as an adjunctive therapy to non-surgical periodontal treatment of chronic periodontitis: a systematic review and meta-analysis. *Journal of clinical periodontology.* 2016 Jun;43(6):520-30.

17. **Hu D, Zhong T, Dai Q.** Clinical efficacy of probiotics as an adjunctive therapy to scaling and root planning in the management of periodontitis: a systematic review and meta-analysis of randomized controlled trails. *Journal of Evidence Based Dental Practice.* 2021 Jun 1;21(2):101547.
18. **Ikram S, Hassan N, Raffat MA, Mirza S, Akram Z.** Systematic review and meta-analysis of double-blind, placebo-controlled, randomized clinical trials using probiotics in chronic periodontitis. *Journal of investigative and clinical dentistry.* 2018 Aug;9(3):e12338.
19. **Manas A, Swain JR, Kantale SA, Seshadri PR, Kouser S, Tyagi U.** Probiotics, tetracycline fibres and chlorhexidine gel's effectiveness in treating chronic periodontitis as a supplement to scaling and root planning. *Bioinformation.* 2024 Aug 31;20(8):933.
20. **Şahin T, Akca GÜ, Özmeriç N.** The role of probiotics for preventing dysbiosis in periodontal disease: a randomized controlled trial. *Turkish Journal of Medical Sciences.* 2024;54(1):357-65.
21. **Retamal-Valdes B, Teughels W, Oliveira LM, da Silva RN, Fritoli A, Gomes P, Soares GM, Temporão N, Furquim CP, Duarte PM, Doyle H.** Clinical, microbiological, and immunological effects of systemic probiotics in periodontal treatment: study protocol for a randomized controlled trial. *Trials.* 2021 Apr 15;22(1):283.
22. **Kumar S, Madurantakam P.** Limited evidence shows short-term benefit of probiotics when used as an adjunct to scaling and root planing in the treatment of chronic periodontitis. *Evidence-Based Dentistry.* 2017 Dec;18(4):109-10.
23. **Meenakshi SS, Varghese S.** Adjunctive effect of probiotic (*Lactobacillus casei* Shirota) to scaling and root planing in the management of chronic periodontitis. *Drug Invention Today.* 2018 Aug 1;10(8):1381-6.
24. **Laleman I, Yilmaz E, Ozcelik O, Haytac C, Pauwels M, Herrero ER, Slomka V, Quiryne M, Alkaya B, Teughels W.** The effect of a streptococci containing probiotic in periodontal therapy: a randomized controlled trial. *Journal of clinical periodontology.* 2015 Nov;42(11):1032-41.
25. **Liu S, Song T, Zhao J, Yao J.** Effect of probiotics combined with periodontal basic therapy on inflammatory factors in gingival crevicular fluid in patients with moderate periodontitis. *Medicine.* 2025 Dec 26;104(52):e46471.
26. **Butera A, Gallo S, Maiorani C, Molino D, Chiesa A, Preda C, Esposito F, Scribante A.** Probiotic alternative to chlorhexidine in periodontal therapy: evaluation of clinical and microbiological parameters. *Microorganisms.* 2020 Dec 29;9(1):69.
27. **Ausenda F, Barbera E, Cotti E, Romeo E, Natto ZS, Valente NA.** Clinical, microbiological and immunological short, medium and long-term effects of different strains of probiotics as an adjunct to non-surgical periodontal therapy in patients with periodontitis. Systematic review with meta-analysis. *Japanese Dental Science Review.* 2023 Dec 1;59:62-103.
28. **Ghazal M, Ahmed S, Farooqui WA, Khalid F, Riaz S, Akber A, Shabbir S, Khan FR, Sadiq A.** A placebo-controlled randomized clinical trial of antibiotics versus probiotics as an adjuvant to nonsurgical periodontal treatment among smokers with Stage III, Grade C generalized periodontitis. *Clinical advances in periodontics.* 2023 Sep;13(3):197-204.
29. **Tapashetti RP, Ansari MW, Fatima G, Bhutani N, Sameen N, Pushpalatha HM.** Effects of probiotics mouthwash on levels of red complex bacteria in chronic periodontitis patients: a clinico-microbiological study. *The Journal of Contemporary Dental Practice.* 2022 Jun 24;23:320-6.
30. **Invernici MM, Salvador SL, Silva PH, Soares MS, Casarin R, Palioto DB, Souza SL, Taba Jr M, Novaes Jr AB, Furlaneto FA, Messoria MR.** Effects of Bifidobacterium probiotic on the treatment of chronic periodontitis: A randomized clinical trial. *Journal of clinical periodontology.* 2018 Oct;45(10):1198-210.