Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Probiotics As An Adjunct To Mechanical Debridement On Non-Surgical Management Of Gingivitis And Periodontal Diseases – A Systematic Review And Meta-Analysis

Dr. Tasmiya Khan*[1], Dr. Chanchal Bherwani[2], Dr. Arvind Shetty[3], Dr. Ankita Deshmukh[4], Dr. Juhi Gundavda[5], Dr. Poonam Rai[6]

[*1] Third year Resident of Department of Periodontology and Oral Implantology, DY Patil University School of Dentistry
[2]Associate Professor, Department of Periodontology and Oral Implantology, DY Patil University School of Dentistry
Email ID: chanchal.bherwani@dypatil.edu
[3]Head of Department, Department of Periodontology and Oral Implantology, DY Patil University School of Dentistry
Email ID: aravind.shetty@dypatil.edu
[4]Associate Professor, Department of Periodontology and Oral Implantology, DY Patil University School of Dentistry
Email ID: dr.ankitad2011@gmail.com
[5]Senior Lecturer, Department of Periodontology and Oral Implantology, DY Patil University School of Dentistry
Email ID: juhi.gundavda@dypatil.edu
Professor, Department of Periodontology and Oral Implantology, DY Patil University School of Dentistry
Email ID: poonam.rai@dypatil.edu
***Corresponding author:**
Dr. Tasmiya Khan
Email ID: mds.tasmiya@gmail.com

Cite this paper as: Dr. Tasmiya Khan, Dr. Chanchal Bherwani, Dr. Arvind Shetty, Dr. Ankita Deshmukh, Dr. Juhi Gundavda, Dr. Poonam Rai, (2025) Probiotics As An Adjunct To Mechanical Debridement On Non-Surgical Management Of Gingivitis And Periodontal Diseases – A Systematic Review And Meta-Analysis. *Journal of Neonatal Surgery*, 14 (32s), 2375-2396.

1. INTRODUCTION

Specific microorganisms can cause periodontitis, an infection that results in periodontium damage and inflammation.[1] The primary causative agent in the microbial biofilm is thought to be one pathogenic bacterium.[2] As of right now, the disease is thought to progress in phases: lengthy intervals of disease remission between sporadic, relatively brief episodes of severe tissue destruction followed by partial healing. A symmetrical pattern of alveolar bone loss and pocket development is observed in the subsequent tissue disintegration, which is shared by numerous kinds of periodontitis, despite the seeming random distribution of disease activity episodes.[3]

The most prevalent type of periodontal disease, known as chronic periodontitis, causes periodontal abnormalities, sporadic pain, and ultimately tooth loss. A combination of acquired, inherited, and environmental variables are considered periodontitis risk factors. Therefore, the key elements for the development of chronic periodontitis are microbial plaque and host response.[1]

The disease is very common, with prevalence rates ranging from 20 to 50% around the globe (Messora et al., 2021).[4] The disease, which affects the general public, can lower quality of life, cause tooth loss and impairment, and affect chewing and appearance (Messora et al., 2021).[4]

When bone and attachment loss are observed at 30% of the analysed oral sites, the condition is classified as generalised periodontitis; when less than 30% of the evaluated sites are afflicted, it is referred to as localised periodontitis. Although the disease activity typically progresses slowly, behavioural, local, and systemic factors might influence the rate of change. Patients in their adult and senior years are more likely to develop chronic periodontitis due to local causes, particularly tooth plaque.[1]

The goal of periodontal therapy is to reverse the inflammatory process by removing the bacterial deposits. Periodontal disease is often treated with non-surgical and/or surgical care, with a focus on mechanical debridement. When a new microbial community with a higher proportion of host-compatible microorganisms is generated and the levels, proportions, and percentage of sites colonised by various periodontal pathogens are effectively reduced following therapy, improvements in clinical parameters are attained.[5]

Non-surgical periodontal therapy, however, may not be adequate to eradicate periodontal infections found in soft tissues and/or in locations inaccessible to periodontal instrumentation, nor to stop pathogenic microorganisms from frequently recolonizing treated areas.[6] Novel adjunct techniques like antibiotic therapy, phototherapy, laser therapy, homoeopathy, and probiotics have been explored as ways to improve the effectiveness and durability of traditional periodontal treatment (scaling and root planing, SRP).[7]

Antibiotic usage has successfully changed the oral microbiota's balance by eradicating harmful and undesired microorganisms. But it also gets rid of the good bacteria, which encourages the development of resistant microbes. Other microbial replacement therapies that have the potential to restore a healthy oral microenvironment are therefore of interest (Gupta et al., 2017).[8] For the treatment of periodontal disorders, non-surgical mechanical debridement (NSMD) is still done with hand equipment as curettes and ultrasonic scalers. On the other hand, compared to NSMD alone, adjunct therapies such probiotic therapy (PT) have been shown to increase the overall anti-inflammatory efficacy of NSMD. [9]

Live bacteria and yeasts, known as probiotics, are beneficial to health when consumed or administered topically. Probiotics are used to treat a wide range of illnesses, such as pancreatitis, cancer, mood disorders (including depression), and ulcerative colitis. Additionally assessed has been the function of physical therapy (PT) in the treatment of clinical and experimentally produced periodontal inflammatory diseases (PIC). [9]

Probiotics are believed to function through a multitude of mechanisms, such as the production of antimicrobial compounds against periodontopathogens, the exclusion and competition with potential pathogens for nutrients and epithelial cell adhesion, local and systemic immunomodulation, and the improvement of the mucosal barrier function.[2] One of these target mechanisms of probiotics is systemic immunomodulation, which controls the production of pro- and anti-inflammatory cytokines. [10]

Numerous in vitro and in vivo research have looked into the therapeutic effects of probiotics in periodontology. The effectiveness of probiotics as a supplement to supra- and subgingival instrumentation in the treatment of periodontal disease has been investigated in recent research.[6] Messora et al[11] evaluated the impact of oral PT administration on the management of ligature-induced periodontitis (LIP) in rats in an experimental investigation. Rats in the test (PT) and control (no PT) groups were put to sleep after 44 days, or around six weeks, and their jaws were examined using a histomorphometry technique. Alveolar bone loss (ABL) was found to be substantially greater in the control group compared to the test group. According to the study's findings, PT lowers ABL in rats with LIP.

Probiotics have been studied in relation to periodontal disease in a number of studies. The outcomes are debatable. This research showed that using probiotics to treat various periodontal disorders reduced the levels of periodontopathogens and clinical indicators.[10] Research indicates that probiotics may help reduce the number of harmful bacteria and/or act as adjunct anti-inflammatory agents during periodontal therapy. [5]

Therefore, this systematic review and meta-analysis were aimed to answer the following question: Is there any difference in the efficacy of probiotics adjunct to non-surgical periodontal treatment among adults with chronic periodontitis?

2. METHODS

A systematic review of literature and meta-analysis was performed. This study followed the (PRISMA 2020) Preferred Reporting Items for Systematic Review 2020, the Cochrane Handbook for systematic reviews of interventions, version 5.1.0. and 4th Edition of the JBI Reviewer's Manual and was registered at **INPLASY registration number: INPLASY2023110088**

Eligibility criteria:

[A] Inclusion criteria:

a. Population –
    i. Studies including adult population with chronic periodontitis irrespective of gender, socio-economic status, nationality, etc
b. Intervention –
    i. Studies including use of probiotic therapy along with scaling and root planning (SRP) for treatment of chronic periodontitis

c. Comparison –
   i. Studies including use of scaling and root planning (SRP) for treatment of chronic periodontitis.

d. Outcome –
   i. Primary outcome as clinical parameters such as clinical attachment loss, pocket depth, plaque index, gingival recession, etc.

e. Study design –
   i. Studies published in any language where English translation is possible.
   ii. Studies published between 1-1-2000 to 31-10-2023
   iii. Clinical trials, in-vivo studies, randomized clinical trials, controlled clinical trial, non-randomized clinical trials, Quasi experimental studies, non-experimental studies, cohort studies, cross-sectional studies
   iv. Studies with full-text articles were included.

[B] Exclusion criteria:

i. Studies not fully available in the database.
ii. Observational studies, Review reports, case series, in-vitro and animal studies were excluded.
iii. Studies providing only abstract and not full text.
iv. Studies involving valid comparison group only.

Search strategy

Studies were selected based on the PICOS inclusion criteria in the review protocol. Two reviewers assessed titles and abstracts to identify potentially eligible studies. Any queries were discussed with a third reviewer.

- The preferred reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for conducting a meta-analysis were followed.
- The electronic data resources consulted for elaborate search were Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, CINAHL, EMBASE, PsycINFO, Scopus, ERIC, ScienceDirect with controlled vocabulary and free text terms. (Table 1)
- Articles published from 01/01/2000 until 31/10/2023 were searched, without any restriction concerning the publication's language.
- Following keywords and MeSH terms were used in combination with Boolean operators in the advanced search option.

Focused review question:

Is there any difference in the efficacy of probiotics adjunct to non-surgical periodontal treatment among adults with chronic periodontitis?

Search Strategy in PubMed:

((("probiotics"[MeSH Terms] OR "probiotics"[All Fields]) AND (scaling[All Fields] AND ("root planing"[MeSH Terms] OR ("root"[All Fields] AND "planing"[All Fields]) OR "root planing"[All Fields]))) AND ("chronic periodontitis"[MeSH Terms] OR ("chronic"[All Fields] AND "periodontitis"[All Fields]) OR "chronic periodontitis"[All Fields])) AND ("randomized controlled trial"[All Fields] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized clinical trials"[All Fields] OR "randomised clinical trials"[All Fields])

The above mentioned was the final search history for the databases accessed till the month of October 2023.

Selection of studies

The title and the abstract of each study were reviewed and critically assessed by two independent reviewers. The methods used to apply the selection criteria were the following:

i. integration of the searched outcomes to delete duplicate entries
ii. examination of titles and abstracts to delete clearly irrelevant articles
iii. recovery of the full text of potentially relevant articles
iv. binding and gathering of multiple articles of the very same study

v. examination of the articles' full text to verify the degree of compliance that the studies had with the eligibility criteria

vi. establishing connection with researchers, if necessary, to clarify the study's eligibility

vii. deciding about the study's inclusion and proceeding with data gathering.

Data extraction

Two reviewers independently extracted data from the included studies. Disagreements were again resolved through discussion. Data gathered was carried out using a verification list of items that were considered for data extraction. The main items of this list were as follows:

1. Authors, Year and Title of study
2. Country
3. Study design
4. Sample size
5. Age group of participants
6. Gender
7. Intervention
8. Comparison
9. Outcomes
10. Methods of outcome assessment
11. Conclusion and other items

Details regarding the publication and the study, the participants, settings, the interventions, the comparators, the outcome measures, study design, statistical analysis and results, and all other relevant data (funding; conflict of interest etc.) were carefully and accurately extracted from all included studies. Data extraction was done and accurately recorded in the excel sheets for all the primary outcomes separately.

Critical appraisal of retrieved studies

For randomized controlled trials, Cochrane RoB-2 tool[2] was used for quality assessment.

According to this tool, risk of bias is assessed at study level under seven domains:

1. Random sequence generation
2. Allocation concealment
3. Blinding of participants and personnel
4. Blinding of outcome assessment
5. Incomplete outcome data
6. Selective reporting
7. Other bias

The overall risk for individual studies was assessed as low, moderate or high risk based on domains and criteria. The study was assessed to have a low overall risk only if all domains were found to have low risk. High overall risk was assessed if one or more of the six domains were found to be at high risk. A moderate risk assessment was provided to studies when one or more domains were found to be uncertain, with none at high risk.

Risk of bias was evaluated using RevMan (Review Manager Version 5.3) software.

Meta-analysis

Meta-analysis was conducted on the studies that provided information on similar outcomes at same follow-up period.

Quantitative assessment was done using Review Manager version 5.4

Assessment of Heterogeneity:

Clinical heterogeneity refers to differences between studies with regards the participants, interventions, comparators, settings, and outcomes. Methodological heterogeneity refers to the study design and the methodological quality of the studies (risk of bias).

The I square statistic (I^2) represents the percentage of the variability in effect estimates that is due to heterogeneity. I^2 is the proportion of observed dispersion of results from different studies included in a meta-analysis that is real, rather than spurious.

Heterogeneity was considered statistically significant if $P < 0.05$. A rough guide to the interpretation of I^2 given in the Cochrane handbook is as follows:

(1) from 0 to 30%, the heterogeneity might not be important;

(2) from 30% to 60%, it may represent moderate heterogeneity;

(3) from 50% to 90%, it may represent substantial heterogeneity;

(4) from 75% to 100%, there is considerable heterogeneity.

3. RESULTS

Study selection:

The initial electronic database search on PubMed/MEDLINE, Cochrane library and DOAJ resulted in 6489 titles. Eight hundred eighty four articles were duplicates. After screening the abstracts, 120 relevant titles were selected by two independent reviewers and 5485 were excluded for not being related to the topic. Hand searching of the reference lists of the selected studies did not deliver additional papers. After pre-screening, application of the inclusion and exclusion criteria and handling of the PICO questions, 18 studies remained. Eighteen studies were included in the qualitative synthesis which were subjected for data extraction and statistical analysis. **(Figure 1)**

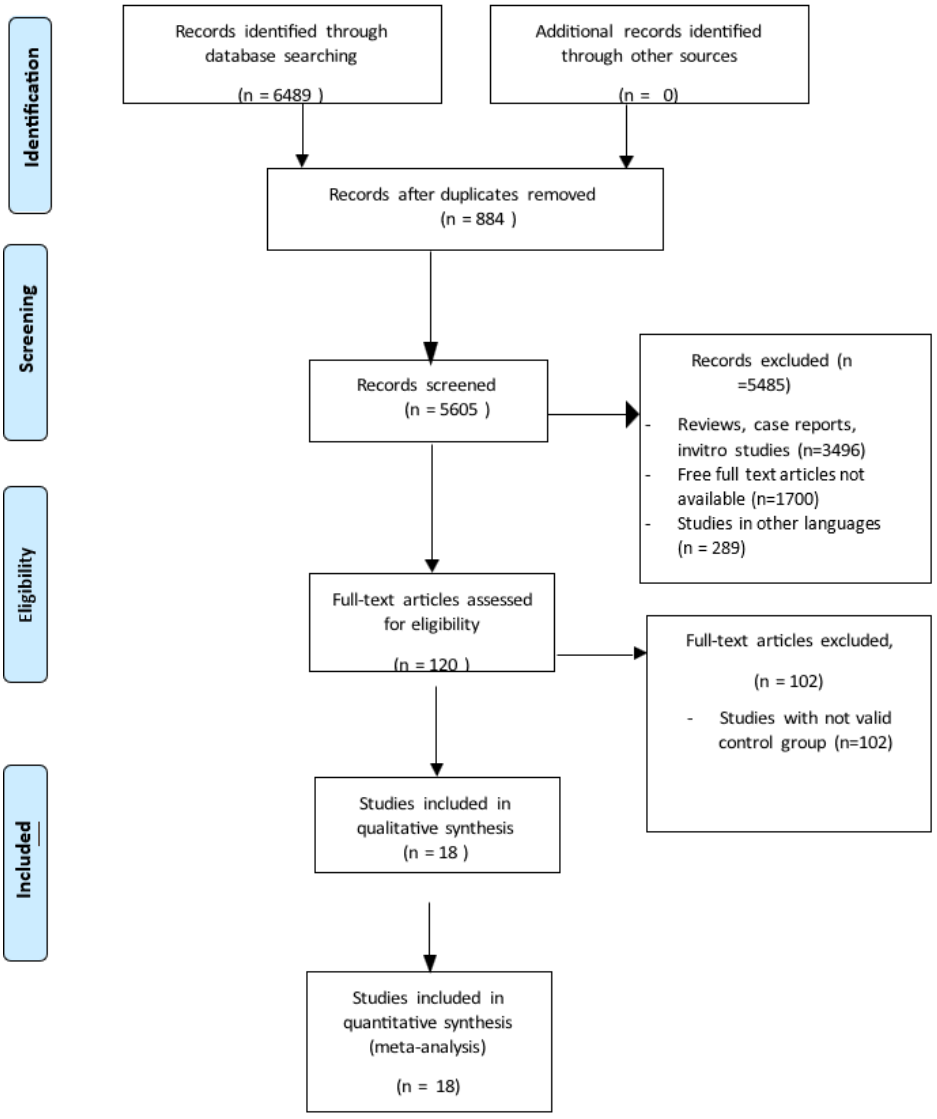

Figure 1: PRISMA flow diagram

Study characteristics

All the studies included in systematic review were randomized controlled trial, of which one was split-mouth design[21] and remaining were parallel arm design. These studies were conducted in different parts of world with one in Belgium[13], three in Turkey[10,15,6], Istanbul[14], one in Chile[5], Brazil[16,18,20,4], China[18], Egypt[1,22], Slovenia[20], Italy[7], Iasi[21], Saudi Arabia[9], one in India[23]. The conclusions of all studies indicated that use of probiotic therapy as adjunct to SRP is more beneficial as compared to SRP alone.

Table 2: Characteristics of included studies

	Study ID	Place of study	Study design	Sample size	Age	Probiotic organism used	Control	method of delivery	Dosage	outcomes assessed	Follow-up	Authors conclusions
1	**Teughels 2013**	Belgium	RCT double blind	30 15/15	-	L. reuteri strains DSM17938 and ATCC PTA5289	SRP	lozenge	twice a day	PPD, GR, BOP, CAL, PI	3,6,9,13 weeks	The results indicate that oral administration of L. reuteri lozenges could be a useful adjunct to SRP in chronic periodontitis.
2	**Ince 2015**	Turkey	RCT double blind	30	35-50	L. reuteri	SRP	lozenges	twice a day for 3 weeks	PI, GI, BOP, CAL, PD	21,90,180,360 days	L. reuteri containing lozenges may be a useful supplement in moderately deep pockets of CP patients
3	**Tekce 2015**	Istanbul	RCT double blind	40 20/20	41.4 +- 8.86	L. reuteri	SRP	lozenges	twice a day for 3 weeks	PI, GI, BOP	0,21,90,180,360 days	L. reuteri-containing lozenges may be a useful adjuvant agent to slow re-colonization and improve clinical outcomes

												of chronic periodontitis.
4	**Yilmaz 2015**	Turkey	RCT double blind	48 24/24	39-58	Streptococcus oralis KJ3, Streptococcus uberis KJ2 and Streptococcus rattus JH145	SRP	tablet	twice a day for 12 weeks	PI, GI, BOP	12 weeks, 24 weeks	No differences were detected when comparing the adjunctive use of a placebo or the investigated streptococci containing probiotic tablet after SRP
5	**Morales 2016**	Chile	RCT double blind	28 14/14	35-68	L. rhamnosus SP1	SRP	probiotic sachet	150 mL	CAL, PD, BOP, plaque	3,6,9 months	The results of this trial indicate that oral administration of L. rhamnosus SP1 resulted in similar clinical improvements compared with SRP alone
6	**Invernici 2018**	Brazil	RCT	41 20/21	> 30 years	B. lactis HN019	SRP	lozenges	10mg	CAL, PPD, GR	1 month, 3 months	The use of B. lactis HN019 as an adjunct to SRP promotes additional clinical, microbiological, and immunological benefits in the

												treatment of chronic periodontitis
7	**Pelekos 2019**	China	RCT double blind	41 21/20	53.3 +- 9.6	L. reuteri DSM17938 and L. reuteri ATCC PTA5289	SRP	lozenges	twice a day	CAL, PPD, GR	3,6 months	The adjunctive use of probiotics with NSPT did not show any additional clinical effectiveness when compared to NSPT alone in the management of periodontitis
8	**Theodoro 2019**	Brazil	RCT	28 14/14	45.07+- 6.31	L. reuteri DSM 17938,	SRP	lozenge	twice a day for 3 weeks	PD, BOP, GR, CAL	3 months	The adjuvant use of L. reuteri in the treatment of chronic periodontitis was effective in controlling gingival inflammation because reduced bleeding on probing which means reduced gingival inflammation and was effective in reducing deep pocket in

												manner clinically relevant.
9	**Alsharef 2020**	Egypt	RCT	40	25-58	Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum, Lactobacillus rhamnosus, and Lactobacillus salivarius.	SRP	lozenges	twice a day	PI, BI, PPD, CAL,MMP8	1 month	The current study has suggested an improvement in periodontal parameters in both groups, especially in patients treated with probiotic lozenges
10	**Pudgar 2020**	Slovenia	RCT double blind	40 20/20	25-80	L. brevis (CECT7480), L. plantarum (CECT7481)	SRP	gel and lozenges		PI, BI, PD, GR, CAL, BOP	3month	Probiotics containing L. brevis and L. plantarum strains were associated with increased odds for healing of gingival bleeding but reduction of the odds for healing of diseased sites

11	**Ramos 2021**	Brazil	RCT	30 15/15	35-50	Lactobacillus reuteri (DSM 17938 and ATCC PTA 5289	SRP	lozenges	twice a day	PI, CAL, BOP, PD, GR	1,3 months	After three months, none of the adjuvant therapies provided any additional benefit for subgingival instrumentation
12	**Bilourou 2022**	Brazil	RCT double blind	24 12/12	55.67+-10.87	2% w/v of Lacticasei bacillus casei 01	SRP	milk	100 mL in morning for 15 days	PD, CAL, oral health related quality of life	1,30,90,180 days	Probiotic milk drinks (L. casei) may be used as an adjuvant therapy to mechanical control for the treatment of periodontitis with improvements in biofilm control and inflammation.
13	**Butera 2022**	Italy	RCT double blind	40 20/20	18-70	Lactobacillus and Bifidobacterium species	SRP+CHX	toothpaste		BOP, PPD, CAL, Gingival recession	3,6 months	
14	**Sufaru 2022**	Iasi	split mouth RCT	40 40/40	48.65+-6.62	L. reuteri DSM 17938	SRP	local application of solution 0.2mL	-	PD, BOP, CAL	3 months	Local delivery of L. reuteri DSM 17938 associated to conventional non-surgical therapy demonstr

												ated significant improvements of periodontal attachment and a reduction of gingival bleeding in patients with stage 3–4 periodontitis.
15	**Alhamoudi 2023**	Saudi arabia	RCT	37 19/18	37.6 +- 2.5	not mentioned	SRP	-	-	PD, PI, GI, CAL, salivary cortisol	6 weeks	NSMD continues to be the "gold standard" and most reliable treatment strategy for managing Periodontal Inflammatory Conditions.
	Nasr 2023	Egypt	RCT	18	24-57	Lactobacillus brevis and plantarum	SRP	Prolac San® Gel syringe	-	GI, PI, PPD, CAL,IL-10	1,3 months	Adjunctive topically applied probiotic gel exhibited anti inflammatory effect through the significant expression of IL-10 after treatment of stage I and II grade A periodontitis

												patients.
16	**Ozener 2023**	Turkey	RCT double blind	30 15/15	41.4 +- 6.8	Bifidobacterium animalis subsp. lactis DN-173010	SRP	yoghurt	110g	PI, GI, BOP, PD, CAL, TVC	1month, 3 months	The administration of probiotics has shown beneficial effects, albeit limited, on clinical and microbiological outcomes in the management of periodontitis patients
17	**Shetty 2023**	India	RCT	62 32/30	18-72	Lactobacillus and Bifidobacterium species	SRP	chewable tablet	7 days	plaque index, bleeding index, probing depth, CAL	1,3 months	The use of a blend of probiotics containing lactobacillus and Bifidobacterium strains in the form of chewable probiotic tablets, as an attachment to SRP compromises supplementary medical assistances during the therapy /medication of patients with periodonti

												tis at various stages and grades and varying states of disease.

Quality assessment of included studies

The included studies were subjected to Cochrane RoB-2 tool for quality assessment. Among the eighteen included studies, nine showed Low risk[4,5,7,9,10,13,14,19,20], four studies showed moderate risk[6,15,18,23] and five showed high risk of bias[1,16,18,21,23].

In studies by Pelekos 2019, Alshareef 2020, Sufaru 2022 and Shetty 2023 information relating to randomization and allocation concealment was not mentioned which led to high risk of bias in these studies.

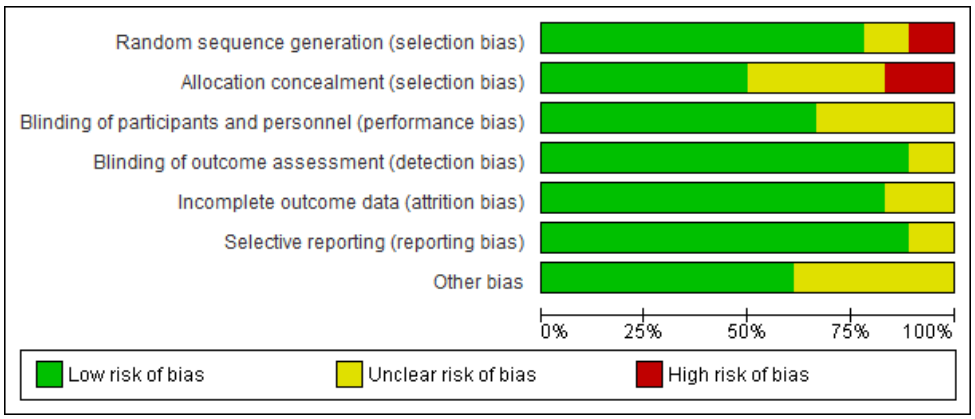

Figure 2: Risk of bias graph

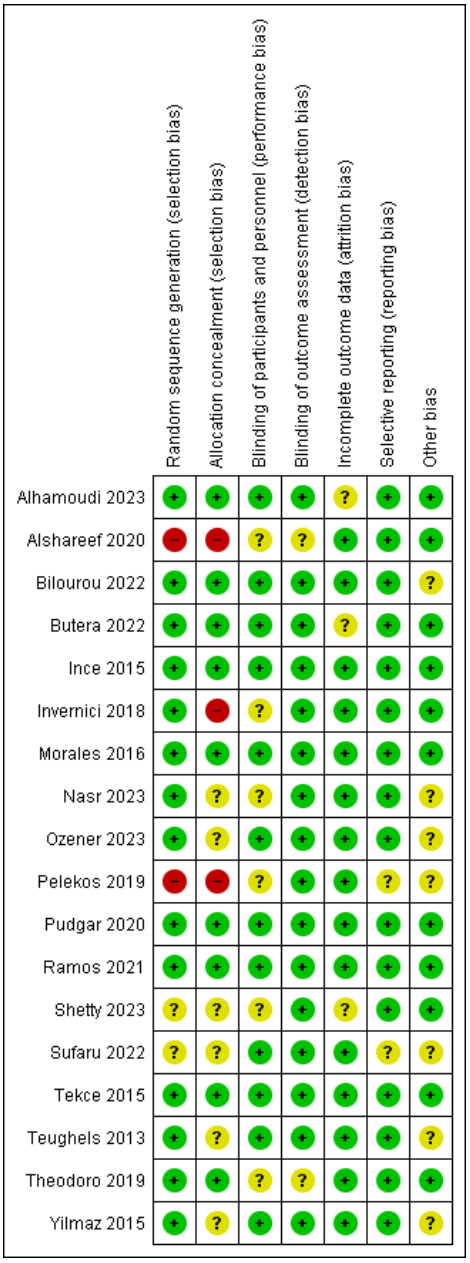

Figure 3: Risk of bias summary

Sr. No.	Study ID	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Risk of bias
1.	**Teughels 2013**	low	unclear	low	low	low	low	Low	**Low**
2.	**Ince 2015**	low	low	low	low	low	low	Low	**Low**
3.	**Tekce 2015**	low	low	low	low	low	low	Low	**Low**
4.	**Yilmaz 2015**	low	unclear	low	low	low	low	Unclear	**Moderate**
5.	**Morales 2016**	low	low	low	low	low	low	Low	**Low**
6.	**Invernici 2018**	low	high	unclear	low	low	low	Low	**High**
7.	**Pelekos 2019**	high	high	unclear	low	low	u	Unclear	**High**
8.	**Theodoro 2019**	low	low	unclear	unclear	low	low	Low	**Moderate**
9.	**Alshareef 2020**	high	high	unclear	unclear	low	low	Low	**High**
10. [12]	**Pudgar 2020**	low	low	low	low	low	low	Low	**Low**
11. [13]	**Ramos 2021**	low	low	low	low	low	low	Low	**Low**
12.	**Bilourou 2022**	low	low	low	low	low	low	Unclear	**Low**
13.	**Butera 2022**	low	low	low	low	unclear	low	Low	**Low**
14.	**Sufaru 2022**	unclear	unclear	low	low	low	unclear	Unclear	**High**
15.	**Alhamoudi 2023**	low	low	low	low	unclear	low	Low	**Low**
16.	**Nasr 2023**	low	unclear	unclear	low	low	low	Unclear	**Moderate**
17.	**Ozener 2023**	low	unclear	low	low	low	low	Unclear	**Moderate**
18.	**Shetty 2023**	unclear	unclear	unclear	low	unclear	low	Low	**High**

Meta-analysis

Data synthesis was carried out using a descriptive synthesis, with a summary of the characteristics of each included study. For quantitative synthesis, a summary of the combined estimate related to the success or failure of treatment was used as dichotomous outcome.

Effect measures

Effect measures refer to statistical constructs that compare outcome data between two intervention groups. For this quantitative analysis, Standardized mean difference (SMD) was used as effect measure.

1. Plaque index

Four studies evaluated plaque index at 1 month follow-up. A total of 51 participants were evaluated in probiotic group and 46 in control group. The pooled SMD value was -0.90[-1.50, -0.30] indicating that the **plaque index was reduced in probiotic group as compared to control group at 1 month follow-up**. Overall the results were statistically significant ($p<0.05$) with 47% heterogeneity. Random effects model was used for analysis.

Six studies evaluated plaque index at 3 month follow-up. A total of 90 participants were evaluated in probiotic group and 85 in control group. The pooled SMD value was -0.55[-1.26, 0.17] indicating that the **plaque index was reduced in probiotic group as compared to control group at 3 month follow-up**. Overall the results were not statistically significant ($p>0.05$) with 80% heterogeneity. Random effects model was used for analysis.

Four studies evaluated plaque index at 6 month follow-up. A total of 66 participants were evaluated in probiotic group and 66 in control group. The pooled SMD value was -0.86[-1.70, -0.02] indicating that the **plaque index was reduced in probiotic group as compared to control group at 6 month follow-up**. Overall the results were statistically significant ($p<0.05$) with 80% heterogeneity. Random effects model was used for analysis.

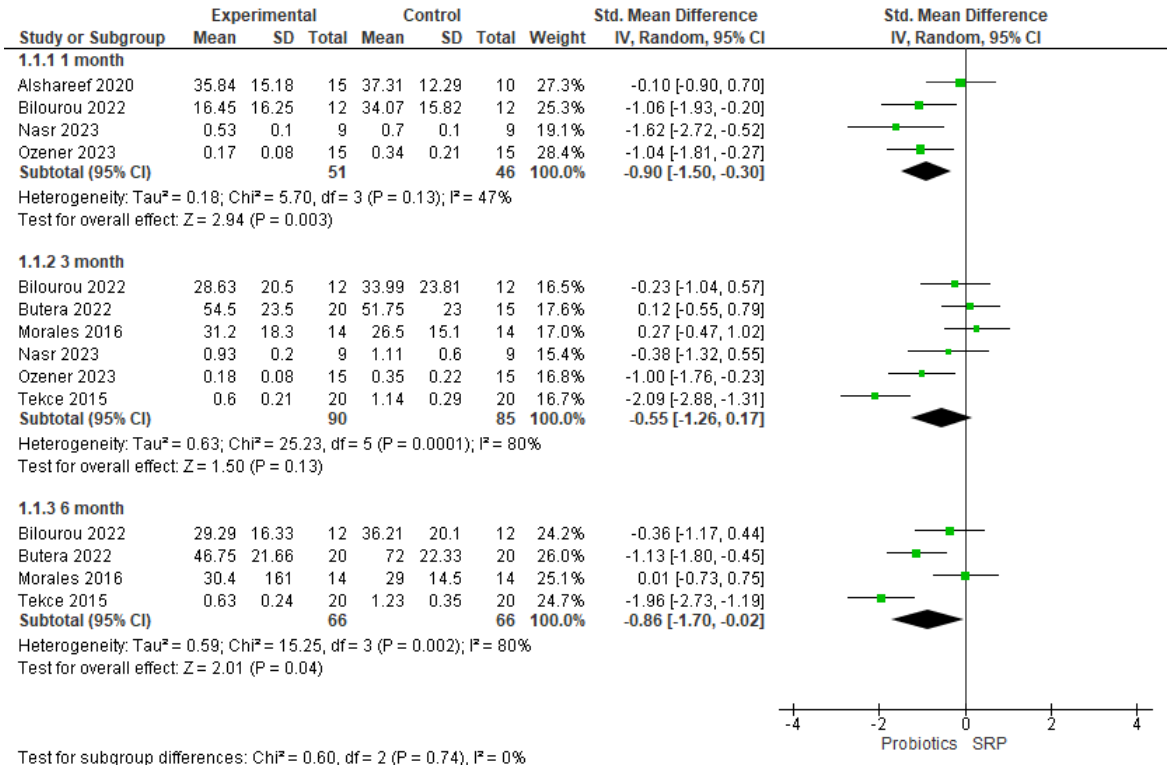

Figure 4: Forest plot for plaque index

2. Pocket depth

Six studies evaluated pocket depth at 1 month follow-up. A total of 81 participants were evaluated in probiotic group and 76 in control group. The pooled SMD value was -0.23[-0.54, 0.09]mm indicating that the **pocket depth was reduced in probiotic group as compared to control group at 1 month follow-up**. Overall, the results were not statistically significant ($p>0.05$) with 0% heterogeneity. Random effects model was used for analysis.

Eleven studies evaluated pocket depth at 3-month follow-up. A total of 206 participants were evaluated in probiotic group and 205 in control group. The pooled SMD value was-0.44[-0.74, -0.13]mm indicating that the **pocket depth was reduced**

in probiotic group as compared to control group at 3-month follow-up. Overall, the results were statistically significant (p<0.05) with 56% heterogeneity. Random effects model was used for analysis.

Five studies evaluated pocket depth at 6-month follow-up. A total of 87 participants were evaluated in probiotic group and 86 in control group. The pooled SMD value was -0.72[-1.35, -0.09]mm indicating that the **pocket depth was reduced in probiotic group as compared to control group at 6 month follow-up**. Overall, the results were statistically significant (p<0.05) with 74% heterogeneity. Random effects model was used for analysis.

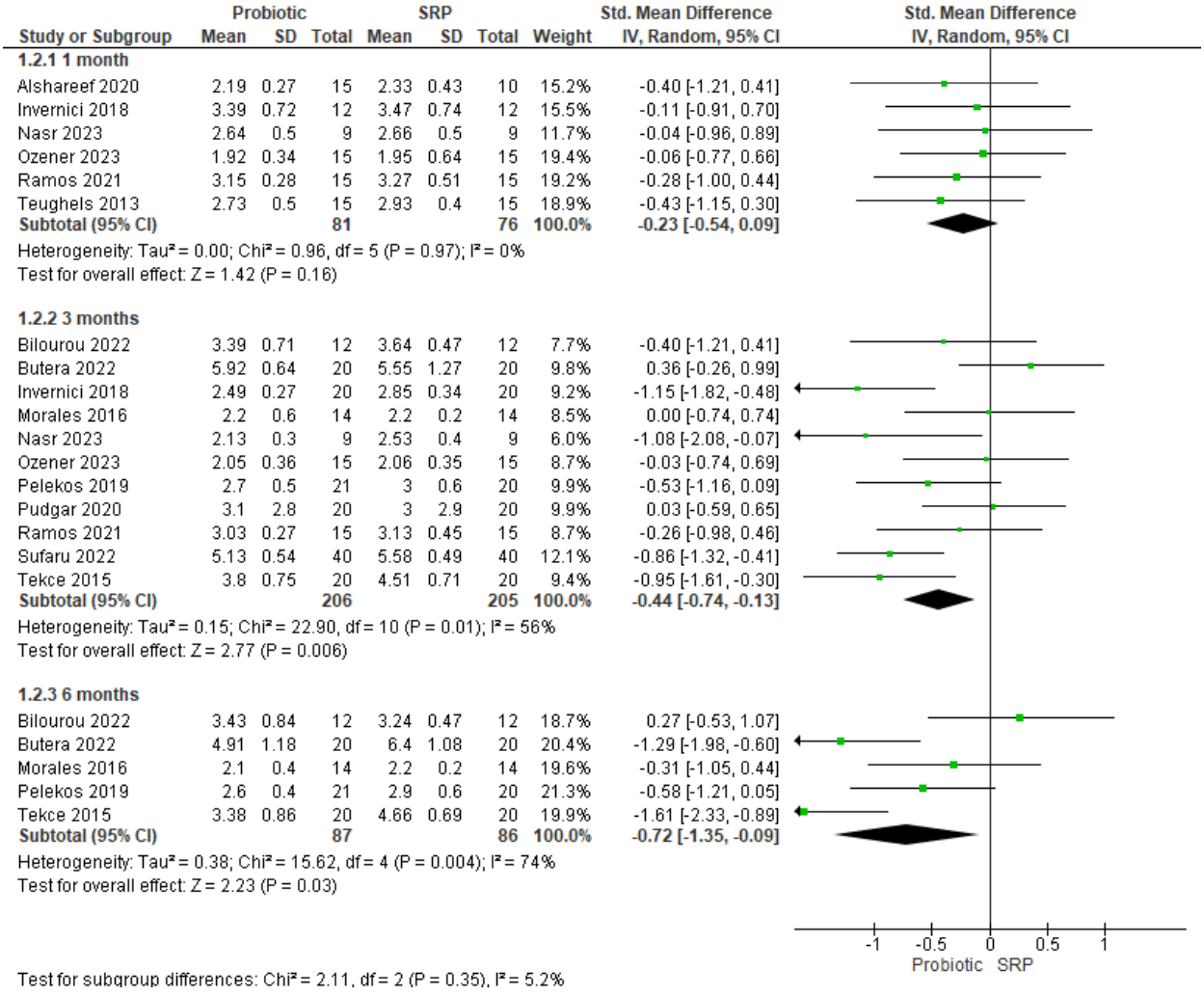

Figure 5: Forest plot for pocket depth

3. Clinical attachment loss

Seven studies evaluated clinical attachment loss at 1 month follow-up. A total of 101 participants were evaluated in probiotic group and 97 in control group. The pooled SMD value was -0.20[-0.49, 0.09]mm indicating that the **CAL was reduced in probiotic group as compared to control group at 1 month follow-up**. Overall, the results were not statistically significant (p>0.05) with 5% heterogeneity. Random effects model was used for analysis.

Ten studies evaluated clinical attachment loss at 3-month follow-up. A total of 186 participants were evaluated in probiotic group and 186 in control group. The pooled SMD value was -0.39[-0.73, -0.05]mm indicating that the **CAL was reduced in probiotic group as compared to control group at 3-month follow-up**. Overall, the results were statistically significant (p<0.05) with 61% heterogeneity. Random effects model was used for analysis.

Four studies evaluated clinical attachment loss at 6-month follow-up. A total of 67 participants were evaluated in probiotic group and 66 in control group. The pooled SMD value was -0.58[-0.93, -0.23]mm indicating that the **CAL was reduced in probiotic group as compared to control group at 6-month follow-up**. Overall, the results were statistically significant (p<0.05) with 0% heterogeneity.

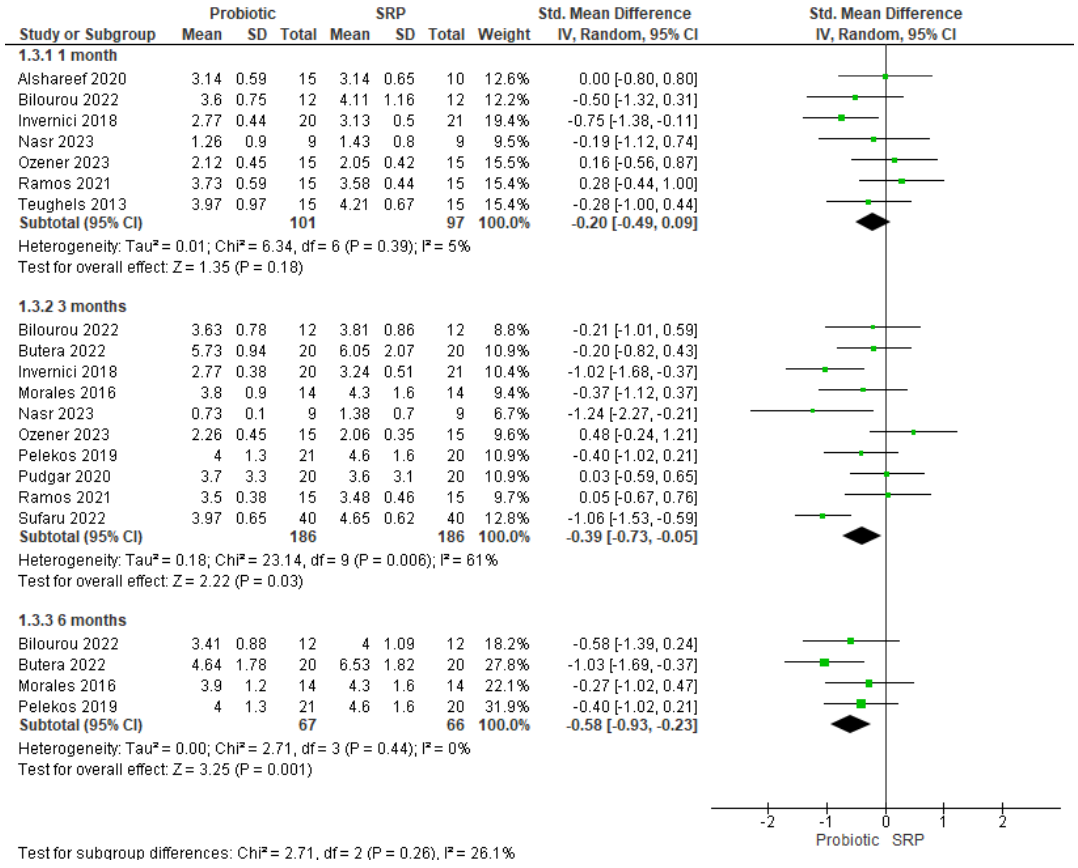

Figure 6: Forest plot for CAL

4. Gingival recession

Three studies evaluated gingival recession at 1-month follow-up. A total of 67 participants were evaluated in probiotic group and 66 in control group. The pooled SMD value was 0.07[-0.55, 0.69]mm indicating that the **recession was greater in probiotic group as compared to control group at 1-month follow-up**. Overall, the results were not statistically significant (p>0.05) with 0% heterogeneity.

Four studies evaluated gingival recession at 3-month follow-up. A total of 75 participants were evaluated in probiotic group and 76 in control group. The pooled SMD value was 0.08[-0.25, 0.40]mm indicating that the **recession was greater in probiotic group as compared to control group at 3-month follow-up**. Overall, the results were not statistically significant (p>0.05) with 0% heterogeneity.

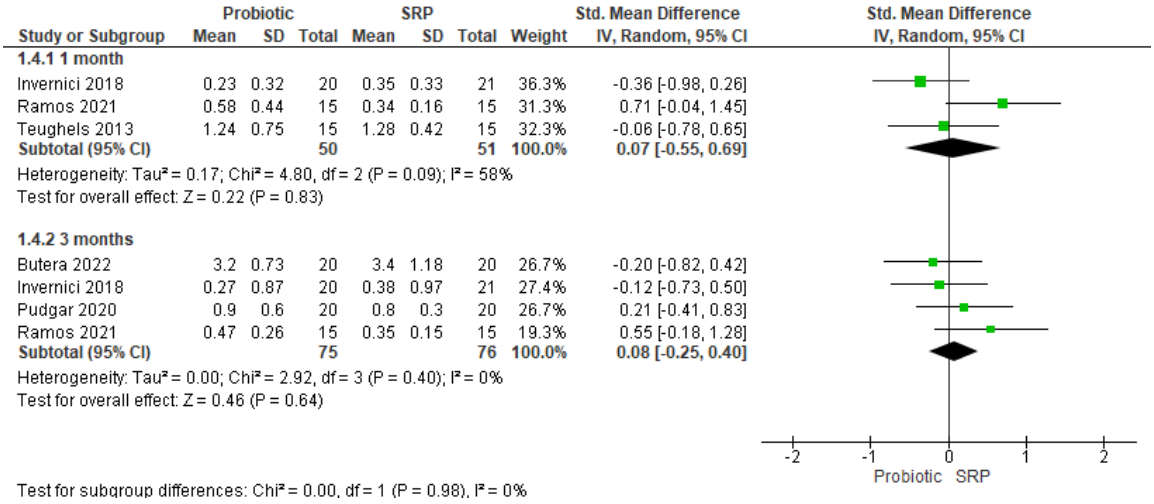

Figure 7: Forest plot for gingival recession

5. Bleeding on probing

Two studies evaluated BOP at 1-month follow-up. A total of 27 participants were evaluated in probiotic group and 27 in control group. The pooled SMD value was -2.37[-5.09, 0.35] indicating that the **BOP was reduced in probiotic group as compared to control group at 1-month follow-up.** Overall, the results were not statistically significant (p>0.05) with 92% heterogeneity.

Six studies evaluated BOP at 3-month follow-up. A total of 122 participants were evaluated in probiotic group and 121 in control group. The pooled SMD value was -1.10[-1.86, -0.35] indicating that the **BOP was reduced in probiotic group as compared to control group at 3-month follow-up.** Overall, the results were statistically significant (p<0.05) with 85% heterogeneity.

Four studies evaluated BOP at 6-month follow-up. A total of 66 participants were evaluated in probiotic group and 67 in control group. The pooled SMD value was -0.94[-2.24, 0.36] indicating that the **BOP was reduced in probiotic group as compared to control group at 6-month follow-up**. Overall, the results were not statistically significant (p>0.05) with 91% heterogeneity.

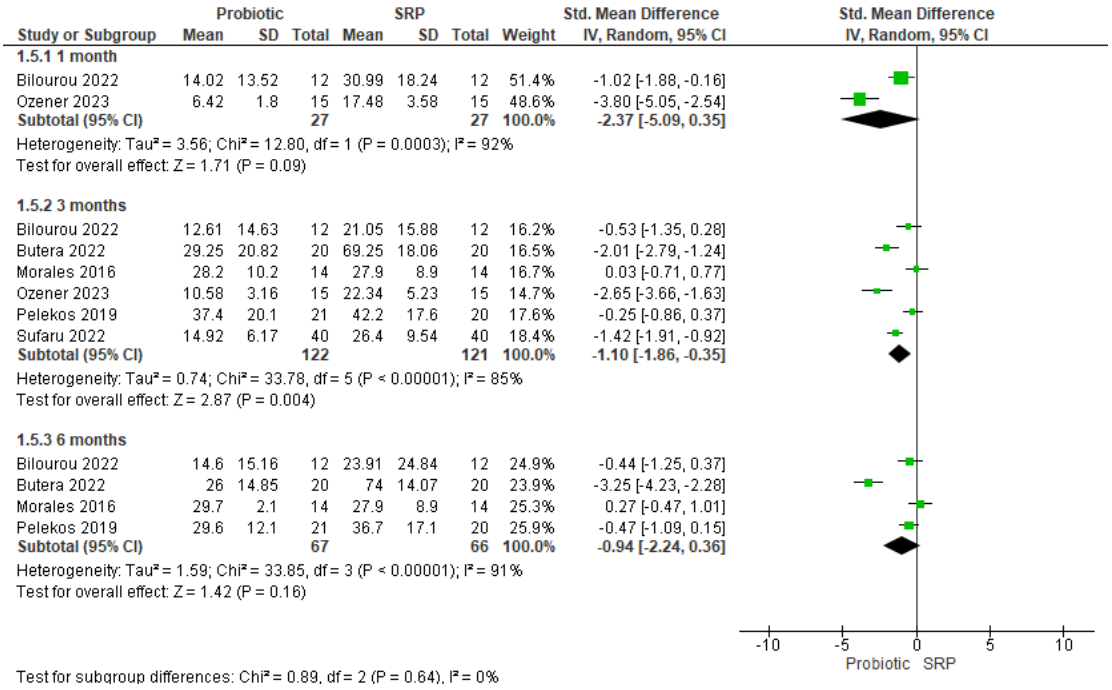

Figure 8: Forest plot for BOP

4. DISCUSSION

Bacterial colonisation, inflammation, adaptive immune responses, and both hard and soft periodontal tissues are all thought to play a role in the multifactorial nature of periodontitis. Periodontal disease treatment options include nonsurgical and surgical care, with a focus primarily on mechanical debridement and, in certain circumstances, the use of antibiotics. The complete spectrum of periodontal infections that invaded and localised in the periodontal tissues was the target of these therapeutic techniques. A novel therapy approach for periodontal disease was required due to the emergence of antibiotic resistance and the recurring recolonization of managed sites by pathogenic organisms.[1]

The cornerstone of periodontal therapy, which aims to eliminate the etiologic cause and restore a biologically suitable root surface for healing, is still non-surgical periodontal therapy. Thus, it not only serves as the initial treatment option for periodontal disease but also promotes tissue health.[3]

Local delivery of probiotics was used as an additional treatment to basic periodontal care. It has the potential to function as a monotherapy or adjuvant treatment, contributing to the prevention of infections as well as the disruption of microbial pathways that lead to inflammatory immunological diseases. The scientific community is becoming more interested in probiotics as a preventive strategy for a variety of disorders, including periodontal diseases, due to their ease of administration and the lack of side effects documented in the literature.[3]

Probiotics have been shown to have a number of effects on host immunity, including reducing or inhibiting the development of harmful bacteria, changing cell proliferation and apoptosis, and modifying pro-inflammatory and anti-inflammatory cytokines. These effects have been documented in the literature.[1]

The clinical effectiveness of probiotics in conjunction with nonsurgical periodontal therapy for the treatment of periodontitis has been the subject of multiple clinical investigations.[1] Thus, this systematic review and meta-analysis of the literature sought to analyse if there is any difference in the efficacy of probiotics adjunct to non-surgical periodontal treatment among adults with chronic periodontitis.

The overall risk of bias was low in the studies conducted by Teughels et al[13], Ince et al[10], Tekce et al[14], Morales et al[5], Pudgar et al[19], Ramos et al[20], Bilourou et al[4], Butera et al[7] and Alhamoudi et al[9]. The studies by Yilmaz et al[15], Theodoro et al[18], Nasr et al[3] and Ozener et al[6] showed moderate overall risk of bias.

Whereas 5 of the studies included in this systematic review and meta-analysis showed a high risk of bias which included the studies by Invernici et al[16], Pelekos et al[17], Alshareef et al[1], Sufaru et al[21] and Shetty et al.[23]

The method of delivery of probiotics in all the studies was through lozenges except the studies done by Yilmaz et al[15], Morales et al[5], Bilourou et al[4], Butera et al[7], Sufaru et al[21], Nasr et al[3], Ozener et al[6] and Shetty et al[23] in which it was given in the form of tablet, satchet, milk, toothpaste, applied locally or as a gel.

Most of the studies used *Lactobacillus reuteri* as an adjunct to SRP in chronic periodontitis including the studies by Teughels et al[13], Ince et al[10], Tekce et al[14], Pelekos et al[17], Theodoro et al[18], Ramos et al[20], Sufaru et al[21]. The studies done by Pelekos et al[17] and Alshareef et al[1] showed high risk of bias regarding the random sequence generation and allocation concealment, whereas the other studies had a low risk of bias.

The study by Invernici et al[16] showed a high risk of bias in allocation concealment. All the studies scored low risk of bias in blinding of participants and personnel except for the studies by Theodoro et al[18], Pelekos et al[17], Alshareef et al[1], Nasr et al[3] and Shetty et al[23] who had it as unclear.

The randomized controlled trials by Theodoro et al[18] and Alshareef et al[1] showed an unclear risk of bias whereas the other studies included showed a low risk of bias of blinding of outcome assessment. All of the included studies a low risk of bias for incomplete outcome data excluding the studies by Butera et al[7], Alhamoudi et al[9] and Shetty et al[23] where it was unclear.

A low risk of bias was seen in selective reporting in all the included studies but unclear in the studies by Pelekos et al[17] and Sufaru et al[21]. All the included studies assessed bleeding on probing, plaque index, pocket depth, clinical attachment loss and gingival recession as the outcomes to check the effectiveness of the probiotics.

The randomized controlled trials by Ince et al[10], Tekce et al[14] and Theodoro et al[18] had a dosage of the probiotics twice a day for 3 weeks which resulted as a useful supplement in controlling the gingival inflammation and slowing down the re-colonization in chronic periodontitis.

Lactobacillus and *Bifidobacterium* species used by Alshareef et al[1] and Shetty et al[23] had shown that improvement in periodontal
parameters at various stages and grades and varying states of disease. *Lactobacillus reuteri* used in the randomized controlled trials of Teughels et al[14], Ince et al[10], Tekce et al[14], Theodoro et al[18], Sufaru et al[21] demonstrated a significant improvement of periodontal attachment and a reduction of gingival bleeding in patients.

But in the studies by Pelekos et al[17] and Ramos et al[20] the use of *Lactobacillus reuteri* did not show any additional clinical effectiveness when compared to NSPT alone in the management of periodontitis. Yilmaz et al[15] had conducted a randomized controlled trial using the *Streptococcus spp* concluding that there was no difference detected when comparing the adjunctive use of a placebo or the investigated streptococci containing probiotic tablet after SRP.

After following up the patients for 9 months in the study of Morales et al[5] with the probiotic *L.rhamnosus,* the results of this trial indicate that oral administration of L. rhamnosus SP1 resulted in similar clinical improvements compared with SRP alone. The study by Invernici et al[14] using B. lactis HN019 as an adjunct to SRP concluded that it promotes additional clinical, microbiological, and immunological benefits in the treatment of chronic periodontitis.

The *L. brevis and L. plantarum* used in the study of Pudgar et al[19] indicates an increased odds for healing of gingival bleeding but reduction
of the odds for healing of diseased sites, but in the study of Nasr et al[2] exhibited anti-inflammatory effect through the significant expression of IL-10 after treatment of stage I and II grade A periodontitis patients.

It can also be seen through the study of Bilourou et al[4] that probiotic milk drinks (L. casei) can be used as an adjuvant therapy to mechanical control for the treatment of periodontitis with improvements in biofilm control and inflammation.

The Bifidobacterium animalis subsp. Lactis in the study of Ozener et al[6] showed a beneficial effect, albeit limited, on clinical and microbiological outcomes in the management of periodontitis patients.

Meta-analysis was conducted on the studies that provided information on similar outcomes. The overall risk of bias was low in the studies conducted by Teughels et al[13], Ince et al[10], Tekce et al[14], Morales et al[5], Pudgar et al[19], Ramos et al[20], Bilourou et al[4], Butera et al[7] and Alhamoudi et al[9]. The studies by Yilmaz et al[15], Theodoro et al[18], Nasr et al[3] and Ozener et al[6] showed

moderate overall risk of bias.

Whereas 5 of the studies included in this systematic review and meta-analysis showed a high risk of bias which included the studies by Invernici et al[16], Pelekos et al[17], Alshareef et al[1], Sufaru et al[21] and Shetty et al[23].

The plaque index was reduced in probiotic group as compared to control group at 1, 3 and 6 months follow-up with statistically significant ($p<0.05$) results at 1 and 6 months with 47% heterogeneity and 80% heterogeneity, respectively.

The results were statistically significant ($p<0.05$) at 3 and 6 months follow up with 56% heterogeneity and 74% heterogeneity, respectively showing reduction in pocket depth in probiotic group as compared to control group, but not statistically significant ($p>0.05$) with 0% heterogeneity at 1 month follow up.

Clinical attachment loss was reduced in probiotic group as compared to control group at 1, 3 and 6 months follow-up which was statistically significant ($p<0.05$) at 3 and 6 months follow up with 61% heterogeneity and 0% heterogeneity, respectively. Recession was greater in probiotic group as compared to control group at 1and 3-months follow-up which was not statistically significant ($p>0.05$) with 0% heterogeneity.

The bleeding on probing was reduced in probiotic group as compared to control group at 1, 3 and 6-months follow-up with statistically significant ($p<0.05$) results with 85% heterogeneity at 3 months follow-up.

Accordingly, favourable outcomes have been attained, supporting the use of probiotics for their immunomodulatory properties. It is also vital to make comparisons with various treatments, including photoactivation therapy or antibiotic consumption. Probiotic use in conjunction with less invasive techniques like ozone and photo biomodulation may also yield further intriguing findings on the subject.[7]

5. CONCLUSION

Reduced probing pocket depth, increased attachment level, and decreased bleeding on probing suppuration are the objectives of periodontal therapy. To accomplish the therapeutic results, a new microbial population is required. Given the advantages of probiotics, this therapy may be a good complement to or replacement for periodontal treatments. Probiotic use in dental care applications is on the rise. There is mounting evidence that using probiotic strains now available can improve oral health. Therefore, suggesting a treatment that combines non-surgical therapy and probiotic consumption may lead to improved regulation of bacterial plaque and thereby support a successful periodontal treatment. They may also have an impact on immunological markers. To completely optimise and quantify the magnitude of this advantage, more study is required.

Probiotics are a viable treatment option for periodontal problems even if research into their potential advantages for periodontal health is still in its early stages. According to the results, this systematic review pointed out that there is an improvement in periodontal parameters in patients managed by nonsurgical periodontal treatment and probiotic lozenges than in patients managed by nonsurgical periodontal treatment only.

REFERENCES

[1] Alshareef A, Attia A, Almalki M, Alsharif F, Melibari A, Mirdad B, et al. Effectiveness of probiotic lozenges in periodontal management of chronic periodontitis patients: clinical and immunological study. Eur J Dent. 2020;14(2):281–7. doi:10.1055/S-0040-1709924 onlinelibrary.wiley.com+9researchgate.net+9academia.edu+9

[2] Butera A, Gallo S, Pascadopoli M, Maiorani C, Milone A, Alovisi M, et al. Paraprobiotics in non-surgical periodontal therapy: clinical and microbiological aspects in a 6-month follow-up domiciliary protocol for oral hygiene. Microorganisms. 2022;10(2):337. doi:10.3390/microorganisms10020337 researchgate.net+2pubmed.ncbi.nlm.nih.gov+2mdpi.com+2

[3] Edrees MF, Nasr HK, Mowafy IM, Bakry AM. Evaluation of the effect of topically applied probiotics on interleukin-10 and osteoprotegerin as an adjunctive treatment of Stage I and II Grade A periodontitis cases. Al-Azhar Assiut Dent J. 2023 Mar 6;6(1):63–72.

[4] Bilouro FC, Rocha RS, Guimaraes JT, Pimentel TC, Magnani M, Esmerino EA, et al. Probiotic milk drink as adjuvant therapy for the treatment of periodontitis: a randomized clinical trial with 180 days follow-up. Food Sci Technol. 2022 May 2;42:e17922.

[5] Morales A, Carvajal P, Silva N, Hernandez M, Godoy C, Rodriguez G, et al. Clinical effects of Lactobacillus rhamnosus in non-surgical treatment of chronic periodontitis: a randomized placebo-controlled trial with 1-year follow-up. J Periodontol. 2016;87(8):944–52.

[6] Özener HÖ, Kuru L, Kadir T, Kuru B. Bifidobacterium animalis subsp. lactis as adjunct to non-surgical periodontal treatment in periodontitis: a randomized controlled clinical trial. Clin Oral Investig. 2023;27(5):1965–72. doi:10.1007/s00784-023-04870-1

[7] Butera A, Gallo S, Pascadopoli M, Maiorani C, Milone A, Alovisi M, et al. Paraprobiotics in non-surgical periodontal therapy: clinical and microbiological aspects in a 6-month follow-up domiciliary protocol for oral hygiene. Microorganisms. 2022;10(2):337. doi:10.3390/microorganisms10020337 onlinelibrary.wiley.com

[8] Gupta ND, Sharma S, Sharma VK. Probiotic–an emerging therapy in recolonizing periodontal pocket. J Oral Biol Craniofac Res. 2017 Jan 1;7(1):72–3.

[9] Alhamoudi N, Abduljabbar T, Vohra F, Javed F. Influence of mechanical debridement with adjunct probiotic therapy on clinical status and salivary cortisol levels in patients with periodontal inflammation. 2023;? :8360–70.

[10] İnce G, Gürsoy H, İpçi ŞD, Cakar G, Emekli-Alturfan E, Yılmaz S. Clinical and biochemical evaluation of lozenges containing Lactobacillus reuteri as an adjunct to non-surgical periodontal therapy in chronic periodontitis. J Periodontol. 2015;86(6):746–54. doi:10.1902/jop.2015.140612 sciencedirect.com+4bmcoralhealth.biomedcentral.com+4oraljournal.com+4professional.sunstargum.com+1adm.org.mx+1

[11] Messora MR, Oliveira LF, Foureaux RC, Taba Jr M, Zangerônimo MG, Furlaneto FA, Pereira LJ. Probiotic therapy reduces periodontal tissue destruction and improves the intestinal morphology in rats with ligature-induced periodontitis. J Periodontol. 2013;84(12):1818–26.

[12] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg. 2021;88:105906. doi:10.1016/j.ijsu.2021.05.005

[13] Teughels W, Durukan A, Ozcelik O, Pauwels M, Quirynen M, Haytac MC. Clinical and microbiological effects of Lactobacillus reuteri probiotics in the treatment of chronic periodontitis: a randomized placebo-controlled study. J Clin Periodontol. 2013;40(11):1025–35.

[14] Tekce M, İnce G, Gürsoy H, Dirikan Ipci S, Cakar G, Kadir T, et al. Clinical and microbiological effects of probiotic lozenges in the treatment of chronic periodontitis: a 1-year follow-up study. J Clin Periodontol. 2015;42(4):363–72. doi:10.1111/jcpe.12387 adm.org.mx+1professional.sunstargum.com+1

[15] Laleman I, Yilmaz E, Ozcelik O, Haytac C, Pauwels M, Herrero ER, et al. The effect of a streptococci-containing probiotic in periodontal therapy: a randomized controlled trial. J Clin Periodontol. 2015;42(11):1032–41.

[16] Invernici MM, Salvador SL, Silva PHF, Soares MSM, Casarin R, Palioto DB, et al. Effects of Bifidobacterium probiotic on the treatment of chronic periodontitis: a randomized clinical trial. J Clin Periodontol. 2018;45(10):1198–210. doi:10.1111/jcpe.12995 onlinelibrary.wiley.com

[17] Pelekos G, Ho SN, Acharya A, Leung WK, McGrath C. A double-blind, parallel-arm, placebo-controlled and randomized clinical trial of the effectiveness of probiotics as an adjunct in periodontal care. J Clin Periodontol. 2019;46:1217–27.

[18] Theodoro LH, Cláudio MM, Nuernberg MAA, Miessi DMJ, Batista JA, Duque C, et al. Effects of Lactobacillus reuteri as an adjunct to the treatment of periodontitis in smokers: randomized clinical trial. Benef Microbes. 2019;10(4):375–84.

[19] Pudgar P, Povšič K, Čuk K, Seme K, Petelin M, Gašperšič R. Probiotic strains of Lactobacillus brevis and Lactobacillus plantarum as adjunct to non-surgical periodontal therapy: 3-month results of a randomized controlled clinical trial. Clin Oral Investig. 2021;25(3):1411–22.

[20] Ramos TCS, Vilas Boas ML, Nunes CMM, Ferreira CL, Pannuti CM, Santamaria MP, et al. Effect of systemic antibiotic and probiotic therapies as adjuvant treatments of subgingival instrumentation for periodontitis: a randomized controlled clinical study. J Appl Oral Sci. 2022;30:e202101–11.

[21] Sufaru IG, Lazar L, Sincar DC, Martu MA, Pasarin L, Luca EO, et al. Clinical effects of locally delivered Lactobacillus reuteri as adjunctive therapy in patients with periodontitis: a split-mouth study. Appl Sci. 2022;12(5):*.

[22] Dibiase AT, Nasr IH, Scott P, Cobourne MT. Duration of treatment and occlusal outcome using Damon3 self-ligated and conventional orthodontic bracket systems in extraction patients: a prospective randomized clinical trial. Am J Orthod Dentofac Orthop. 2011;139(2):e111–6. doi:10.1016/j.ajodo.2010.07.020

[23] Shetty S, Khan DKM, Khayat MMN, Hakami SA, Alsaadawi LS, Alsibale DB. Clinical evaluation of chewable probiotic tablets as an adjunct to non-surgical periodontal therapy in the treatment of periodontal disease-a pilot project. J Coast Life Med. 2023;11(1):3092–104.