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Research Article

The Effect of Doxycycline-Coated Bioactive Glass Added Chewing-Gum on Periodontitis Biomarker

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ABSTRACT
Objective: Owing to the efficacy of doxycycline and fluoride their synergetic effect will be evaluated for the control of periodontitis by adding doxycycline coated on fluoride contain bioactive glass incorporated in chewing gum and observe its effect on the level of IL6 biomarker expression.
Design: A cross-sectional study was conducted on 20 cases of stage 2 and 3 periodontitis, by purposive convenience sampling between January and February 2024 at the Combined Military Hospital (CMH) Kohat, the Institute of Pathology and Diagnostic Medicine (IPDM) and the dental material laboratory at Khyber Medical University. A sample size of 20 was determined using a 95% confidence level and a 5% confidence interval, calculated via OpenEpi, Version 3. Oral cavity was examined for gingival index and periodontal pocket depth following collection of saliva by passive droll method. The patients were provided with prepared chewing gum, twice a day for one month and at a baseline and one month following periodontal therapy, biochemical evaluations (ELISA) of saliva was carried out.
Results: Overall, the gingival index and periodontal pocket was reduced. IL-6, a chief marker for inflammation, its levels are generally lower after treatment compared to before therapy. The average IL-6 level before the intervention/treatment across all patients is 37.563pg/ml. After the intervention/treatment across all patient theIL6 level decrease to 32.0495pg/ml. The decrease in the mean IL-6 levels from 37.563 pg./ml (Pre-treatment) to 32.0495pg/ml (post-treatment) suggests a positive effect of the treatment/intervention on reducing IL-6 levels among the patients.
Conclusion: The chewing gum containing Doxycycline loaded Bioactive Glass has considerably decrease the IL6 level of Periodontitis Patients.

Keywords: Periodontitis, Interleukin-6, Bioactive Glass, Doxycycline, Chewing Gum.

INTRODUCTION

Periodontitis is an illness that first alters the gingival tissue and, if neglected, expands to associated apical tissues, disrupting the normal state of equilibrium of the bone and ultimately resulting in tooth loss(Zhang, Liu, Afzali, & Graves, 2024). Formation of dental plaque, a bacterial-filled thick film that forms on teeth and gums, is the main factor. Periodontitis is caused by a variety of microorganisms that interact with the body's immune system to harm tissue. Gingivitis, bone loss, and the complete expression of periodontitis are caused over time by a concoction of Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola (Wang, Chen, & Liu, 2025). There are three separate classes of periodontitis. Periodontitis as a definite indicator of underlying illnesses, Periodontitis that is necrosing and Periodontitis(Fernandes & Fernandes, 2024).

Inflammatory mediators and cytokines are released by periodontal bacteria, which prompts the host defense response and results in periodontal tissue disintegration. It has been shown that a wide network of cytokines plays an important role in the development of periodontitis, leading to soft tissue damage and bone resorption(Matos-Sousa et al., 2024). Interleukin-6 (IL-6) is a kind of signaling molecule known as a cytokine that is produced by a variety of cell types, including immune cells, in response to infection and

inflammation(Tang, Zhong, Li, Ji, & Zhang, 2025). The fluid within periodontal pockets and the gingival tissues of people with periodontitis have more advance levels of IL-6, contributes to the disease's chronic inflammatory response. It is believed that IL-6 aids in the periodontal tissues deterioration. Increased levels of IL-6 during periodontitis may trigger excessive osteoclast activity, which will contribute to bone loss around the teeth(Zhao et al., 2024).

Maintenance of the patient's current periodontal tissues and improvement of their gingival health are the main objectives of periodontal therapy. In the present, dentifrices and antibacterial mouthwashes are used in conjunction with mechanical cleaning techniques like brushing and flossing to treat periodontal disease. Root planning and mechanical scaling are two non-surgical periodontitis therapy options(Kimberly Ann Obiedo, 5-13-2024). In addition to nonsurgical periodontal care, antibiotic prescriptions have been made. such as amoxicillin/metronidazole, azithromycin, clindamycin, and clarithromycin (Yuarindias, (2025)). Tetracycline, along with its related compounds doxycycline and minocycline, can be used to prevent and suppress the advancement of periodontal disease when used in sub-antimicrobial dosages, according to current studies(Sher Singh, 2021).

Biomaterials are also used in the treatment of periodontitis. One of the most popular materials for periodontitis is bioactive glass because it interacts with living tissue to encourage healing and regeneration(Nicholson, 2022). In order to promote bone regeneration, particularly in interproximal bone defects, bioactive glass has been widely employed in periodontal surgical treatments. This is advantageous because it has a hemostatic impact on trabecular bone(Faleh Abushahba, 2023). Furthermore, bioactive glass is used in endodontic management. If pulp capping or partial pulpotomy is recommended for an exposed dental pulp(Merve Abaklı İnci, 2022). Bioactive glasses can be used for a variety of purposes, particularly in dentistry. These glasses can be used as particles, homogeneous forms, permeable or solid structures in a variety of uses, such as revitalization or for the management of hypersensitivity. It is possible to improve some characteristics of bioactive glasses, such their antibacterial properties, by introducing various components into the glass(Tayana Takeshova, 2025).

Sugar free chewing gum has constructive effect on periodontal health. According to studies, chewing sugar-free gum can stimulate saliva production, lessen plaque, neutralize acids, restore enamel, clean the mouth of food particles, and relieve the discomfort associated with dry mouth. In fact, chewing sugar-free gum has been discovered to be one of the most well-liked treatments for xerostomia(Hayslett, February 2025,). It has been found that the baking soda (sodium bicarbonate) in chewing gum can lessen plaque, gingivitis, and extrinsic stains when chewed two to three times daily.[15]

The addition of medications to chewing gum has improved periodontal health care. Gum-driven medications may be introduced as potential treatments for oral illnesses. This is because of their capacity to deliver the appropriate local doses of active substances, short contact times, biocompatibility, chemical structures that degrade, and capacity to maintain an emboss condition(Kazem Alemzadeh 1, 2025).

Periodontitis is a serious gum infection that damage the soft tissue around the teeth. Periodontitis has been treated using different techniques like scaling root planning medication(doxycycline) and Fluoride containing biomaterials treatment. Owing to the efficacy of doxycycline and fluoride their synergetic effect will be evaluated for the control of periodontitis by adding doxycycline coated on fluoride contain bioactive glass incorporated in chewing gum and observe its effect on the level of IL6 biomarker expression.

MATERIALS AND METHODS

Ethical Approval

Before any data was collected, the IPDM, KMU ethical board granted ethical clearance. The study was then carried out with the institutional advanced studies and research board NO: KMU/IPDM/IEC/2023/21 giving its approval. The patients' informed consent was documented using a prestructured form.

Reagents Apparatus (Equipment and software)

The reagents and apparatus utilized in this study are listed in Table 1. The chemical reagents were used as such without any further modification and purification.

Table 1: List of chemical reagents.

Materials	Brand Name	CAS No

Absolute ethanol	Sigma Aldrich	-
Diabase ammonium phosphate	Daejung	7783-34-4
calcium nitrate tetrahydrate	Daejung	13477-34-4
Tetra ethyl ortho silicate (TEOS)	Daejung	78-10-4
Sodium fluoride	Hanna instruments	-
Doxycycline hyclate	Pfizer	-
Chewing gum	Hilal foods	-

Preparation of Fluoride Based Bioactive

Three different solutions were carefully synthesized to create fluoride based bioactive glass. In a 200 ml beaker, 12.02 ml of tetraethyl orthosilicate (TEOS) and 37.5 ml of ethanol were added. The mixture was then stirred for 10 minutes at 300 rpm using a magnetic stirrer. In a 100 ml beaker, 6.5 g of calcium nitrate tetrahydrate,.342 sodium fluoride, and 15 ml ethanol were combined to create Solution B. The mixture was then stirred for 10 minutes at 400 rpm using a magnetic stirrer. Lastly, Solution C was made by adding 50 ml of distilled water and 0.209 g of ammonium phosphate diabase to a beaker. The pH was then adjusted to 11 using liquid ammonia, and the mixture was magnetically stirred for ten minutes at 300 rpm. The next steps were adding Solution B to Solution A gradually while using a probe sonicator. After that, Solution C was added drop by drop using a syringe. All of these procedures were carried out within a specific sonication parameter: 40 amplitudes, 7 seconds on, 3 seconds off, and a total of 10 minutes of sonication. This 25-minute synthesis sequence lays the groundwork for the synthesis of fluoride based bioactive glass, paying close attention to variables that are essential to obtaining the right qualities and attribute.

Coating of Bioactive Glass with Doxycycline

The synthesis technique of fluoride-based bioactive glass was adapted from the established protocol reported by Nawshad Muhammad et al{Shah, 2023 #171}.

Doxycycline tablets (24000mg) were crushed and stir in water up to 3 hours at 400 rpm to make sure the dissolution of Doxycycline in liquid part. After stirring it was subjected to centrifuge at 12000 rpm to remove un-dissolved materials. The bioactive glass was added into the liquid part and stir it for 24 hrs to make sure the surface adsorption of doxycycline on bioactive glass (confirmed with Uv/vis spectrophotometry)

Doxycycline Coated Bioactive Glass Added Chewing Gum

The 1200 candies were divided into four equal halves in which every part containing 300 candies so that material could be easily prepared and completely mixed with one another. Fluoride based bioactive glass (38 g) was divided into 4 equal part each part having weight of 9.5g and mixed each half of candies to prepared chew gums of desired proportions. The procedure followed for the preparation of medicated candies is discussed such as a) A microwave oven was preheated to 100 degrees centigrade for 5 minutes, b) A heat-resistant bowl of glass containing 300 candies was then placed in the oven and heated for 30 minutes at 100 degrees centigrade until complete melting, c) Doxycycline (6000 mg) and 9.5 g of fluoride-based bioactive glass was added to the molten candy mixture following the melting process. d) These three components were continuously mixed by hand, following a strict protocol, until a complete homogenized mix was achieved. The process was repeated for further three batches, and subsequently a modified candy weighing 3.2 gm, appropriately shaped, and wrapped individually within a wrapping sheet for administration to the patients. The prepared candies were then distributed among 20 patients participating in the research; hence each patient is supposed to have a total of 60 candies. The designed distribution was dosage of two candies per day for the period of one month.

Ethics Approval and Consent to Participate: This research was done according to the Declaration of Helsinki. The Institutional Ethical Committee, Institute of Pathology and Diagnostic Medicine Khyber Medical University on March 15, 2024, granted ethical approval (Approval Reference Number: KMU/IPDM/IEC/2023/2.1. All participants gave written informed consent before participating in the study.

Study Design and Study Setting

In this Cross-sectional study, a total of 20 cases by purposive Convenience Sampling of stage 2

and 3 periodontitis were diagnosed and included in the study between January and February of 2024. The research procedure was carried out at Combined military hospital (CMH) Kohat**,** Institute of pathology and diagnostic medicine (IPDM) Khyber Medical University Peshawar and dental material lab Khyber Medical university. Using 95% confidence level and confidence interval of 5, the sample size calculated, using an open Epi. Results from OpenEpi, Version 3, open-source calculator SSMean (22).

1. **Inclusion Criteria**

- Patients having stage 2 moderate and stage 3 periodontitis.
- Non-diabetic patients will include in criteria.
- Age 30 and 60 male genders only.
- Patients who are agree to take part in the research

2. **Exclusion Criteria**

- Patients with infectious diseases, malignant tumors
- In the last six months, a history of periodontal therapy

Data Collection Procedure

Clinical findings recorded on data collection spreadsheets included plaque index (PI), bleeding on probing (BOP), sulcus/probing pocket depth (PPD) measurements, and clinical attachment loss (CAL). A standardized periodontal probe was used to measure the probing depths and attachment loss of each tooth, with the exception of third molars, at six distinct sites: buccal, distolingual, lingual, mesiolingual, and distobuccal. Measurements of attachment loss and probing pocket depths from the edge of marginal gingiva are taken at the cementoenamel junction to the bottom of the pocket. After the previously indicated measures were taken, a radiographic examination supported the preliminary diagnosis.

Patients with periodontitis were categorized using the new classification that the 2017 International World Workshop proposed, which was based on stage and grade. The severity (mainly periodontal breakdown and periodontitis-related tooth loss) and complexity of management (pocket depth, infrabony defects, tooth mobility, furcation defects, masticatory deficiency) were taken into consideration when defining the stages of the disease. The grade definitions of periodontitis were also based on this information. Fig 1 is showing a classic and progressive case, a 45-year-old male patient of chronic periodontitis presented with chief complaint as gingival bleeding and pain. The clinical examination revealed that periodontal pockets with an average depth of 4-5mm, and the intraoral view showed a poor level of oral hygiene (POH), with significant accumulation of dental calculus and plaque were observed. The assessment had confirmed a diagnosis of periodontitis, characterized by progressive clinical attachment loss and bone loss, accompanied by periodontal pocket formation and gingival recession respectively.

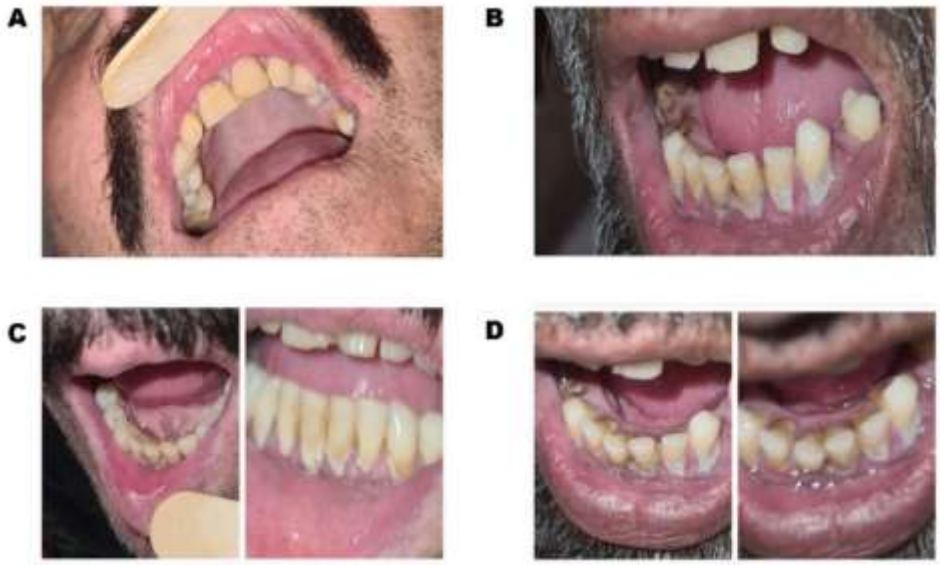

Fig 1. (A) A 45-year-old male patient presented with a chief complaint of gingival bleeding and pain, (B)Clinical examination revealed periodontal pockets, average depth of 4-5mm, (C) Intraoral view showed a poor level of oral hygiene, with significant accumulation of dental calculus and plaque on labial surface

of lower incisors, (D) Progressive clinical attachment loss (CAL) and alveolar bone damage accompanied by periodontal pockets and gingival recession.

Sample Collection

In the morning, between 8:00am and 11:00am, a sample of saliva was collected. Before the examination, participants were instructed not to eat, drink, or brush their teeth in the morning. settling into a comfortable sitting position on a dental chair with their heads lightly forward and their eyes open, each person took a seat and gargled with tap water. After that, participants were required to expectorate all of their saliva into a small, sterile cup for five minutes using the drooling technique. Next, 2 to 5 ml of an unstimulated saliva sample were placed into a polypropylene tube. The obtained saliva samples were transferred to the lab within 30 minutes, where they underwent a 15-minute centrifugation at 4000 rpm. Subsequently, they were frozen at -80°C until analysis and transferred into Eppendorf tubes.

IL-6 Estimation

Using a commercially available ELISA kit, the concentrations of salivary IL-6 were measured. The manufacturer's instructions were followed when performing the assay. In short, the kit was based on the sandwich ELISA method, and the steps were as follows: standards and sample were applied to the IL-6 antibody microplate that had already been coated, and it was then incubated for one hour at 37 degrees centigrade before being buffer-washed. A detection antibody conjugated with HRP was applied to the cleaned plate. Following a wash to remove the unbound antibody, the wells were filled with chromogen substrate, which caused the conjugate to gradually form a blue-colored complex. The final product turned yellow as stop solution was added, halting the color development. The amount of IL-6 present, which was determined in a microplate reader at 450 nm, is proportionate to the intensity of color generated. The amount of IL-6 contained in each sample was then calculated using the optical density that was obtained. The kit had a detection range of 1.5 pg to 48 pg/ml at least. The findings were given in partograms per milliliter of saliva.

RESULTS

The study was conducted on 20 enrolled cases of moderate and severe Periodontitis from January 2024 to February 2024. All the results are shown and discussed in the following section in form of tables and charts along with descriptions.

Mean Age

The age of the patients suffering from Periodontitis ranged from 30 to 60 years with the mean age of 45.90 with standard deviation of ±7.999.

Age Distribution of IL6 Marker In Periodontitis

The age group 30 to 45 appears to have a relatively higher percentage of patients compared to other groups. The mean age of this group was 39±6.999. This suggests that middle-aged individuals in this range might be more prone to the periodontal issues documented in the dataset. The IL6 before treatment for this group was 36.07pg/ml which dropped to 31.01pg/ml after treatment as shown in Table 2. The give Figure 2 of pie chart is representing the distribution of patients in two age groups, blue segment illustrating patients of age group 30-45 years (11 patients, the greater proportion), while the green segment is representing patients of age group 46-60 years (9 patients, the minor proportion). These results emphasized that slightly more patients in the study were from the younger age group such as 30-45 years.

Table 2. Age Wise Distribution of 20 Cases of Periodontitis Patients

No of patients in each group	Age range	Mean age	Mean Pre IL6pg/ml	Mean Post IL6pg/ml
11	30-45	39	36.07pg/ml	31.01pg/ml
9	46-60	51	39.38pg/ml	33.32pg/ml

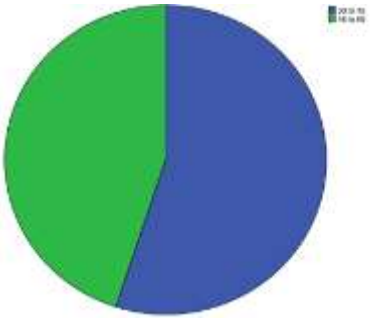

Fig 2. Age distribution of IL6 marker in periodontitis, presenting 11 cases in age group of 30-45 years (mean age 39 years) and 9 cases in age group of 46-60 years (mean age 51 years).

Distribution of Periodontal Pocket Probing Depth among Patients

Among the distribution of probing depth in this study, out of 20 cases the 5mm probing depth (65.0%) was the most common among patients, indicating that a moderate level of periodontal pocket depth is prevalent in this group. The IL6 before intervention for this group was 37.13pg/ml ± 3.407 after treatment which dropped to 32.07pg/ml ± 2.209.

The 6mm depth (20.0%), representing more severe periodontal involvement, also has a significant representation, showing that many patients were dealing with more advanced periodontal disease. The IL6 before intervention for this group was 40.54pg/ml ± 1.561 after treatment which dropped to 34.82pg/ml ± 0.547.

The 4mm depth (10.0%), which typically indicates milder periodontal issues, was less frequent. This could suggest that patients in this study might be seeking care when the condition has progressed to more severe stages. The IL6 before intervention for this group was 32.94pg/ml ± 1.364 after treatment which dropped to 24.73pg/ml ± 0.367.

The 5mm probing depth category (13patients) shows the most significant difference between pre and post IL6 levels. This indicates that probing depth at 5mm correlates strongly with treatment improvement as illustrated in Table 3. The given Fig 3, of a bar chart is illustrating the distribution of probing depths among 20 periodontitis patients, with a higher proportion of 13 patients presenting a probing depth of 5 mm, 5 patients with 6mm and 2 patients with 4mm respectively. The mean levels of IL-6 were observed to be raised with greater probing depth such as 32.94 pg/ml at 4 mm to 40.54 pg/ml at 6 mm pre-treatment. Following intervention, IL-6 levels were decrease significantly across all probing depths, with the highest reduction significantly distinguished in deeper pockets ($p < 0.0001$), indicating that inflammatory load had a correlation with probing depth and had responded to the given treatment.

Table 3. Illustrating the mean levels of IL-6 (±SD) before and after treatment at different probing depths with significant post-treatment reductions

Probing Depth	Pre mean IL6pg/ml)	SD	Post mean IL6(pg/ml)	SD	P value
4mm	32.94	±1.364	24.73	± 0.367	0.0072
5mm	37.13	±3.407	32.07	± 2.209	< 0.0001
6mm	40.54	± 1.561	34.82	± 0.547	< 0.0001

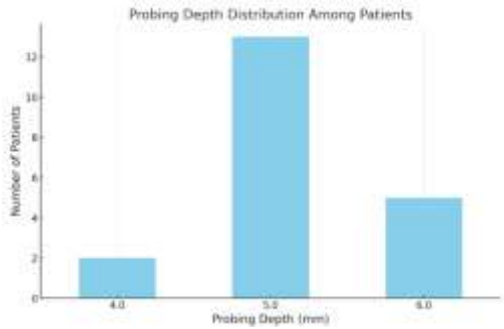

Fig 3. Bar chart, illustrating the distribution of probing depths among periodontitis patients, with highest frequency at 5 mm, followed by 6 mm and 4 mm respectively.

Distribution of Periodontal Stages among Patients

Among the distribution of periodontal stages in this study, out of 20 cases the moderate stage was the most common among patients, although both groups saw significant improvements, the moderate group demonstrated a larger average reduction in IL-6 levels. Patients in both the moderate and severe periodontal stages experienced a reduction in IL-6 levels after treatment. For the moderate group, the mean IL-6 level decreased from 36.24pg/ml ±3.89 to 30.59pg/ml ± 3.74 and for the severe group, it dropped from 39.17pg/ml ±1.31 to 33.82pg/ml ±1.31. These reductions indicate a positive effect of the treatment on reducing systemic inflammation, as measured by IL-6 levels as shown in Table 4. The bar chart as shown in Figure 4, is illustrating the distribution of periodontal stages among selected patients, with expected 11 cases in moderate stage and 9 cases of periodontitis in the severe stage. The accompanying Table 4, presented the mean levels of IL-6 (±SD) for these groups, where advanced baseline IL-6 levels were observed in severe cases (39.17 ± 1.31 pg/ml) compared to moderate cases (36.24 ± 3.89 pg/ml). Post-treatment values had shown a significant reduction in both groups such as the IL-6 levels decreased to 30.59 ± 3.74 pg/ml in the moderate stage and 33.82 ± 1.31 pg/ml in the severe stage ($p < 0.001$). Together, the bar chart Fig 4 and Table 4 had been demonstrated that IL-6 expression had a correlation with periodontal disease severity and significantly declined after therapy.

Table 4. Periodontal stages and mean IL-6 levels (±SD) before and after treatment in moderate and severe periodontitis, demonstrating higher IL-6 levels observed in severe cases and both groups showed significant post-treatment reductions

Periodontal Stage	Mean PreIL6pg/ml	SD	Mean Post IL6pg/ml	SD	P_value
Moderate	36.24	±3.89	30.59	±3.74	0.00049
Severe	39.17	±1.31	33.82	±1.31	0.00039

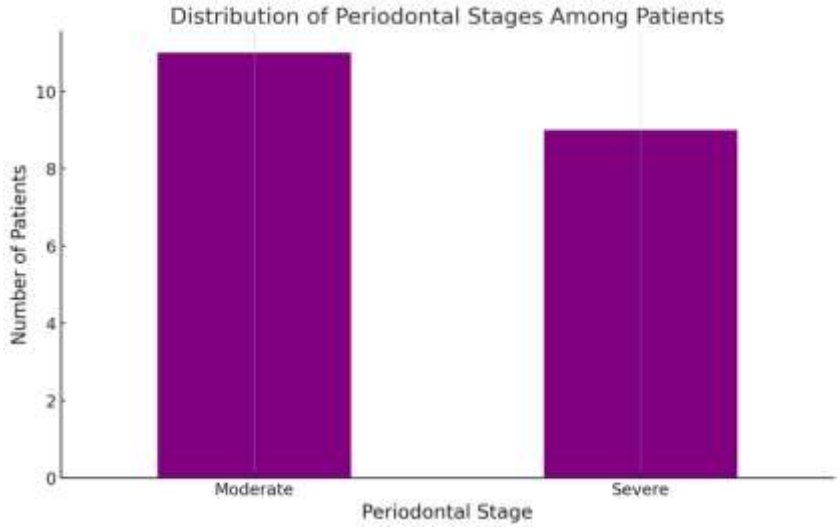

Fig 4. A Bar chart showing Periodontal stages distribution among patients, with 11 cases in the moderate stage and 9 cases in the severe stages of periodontitis.

Oral Health Distribution

A majority of patients fall under the Poor (75%) oral health category, indicating that many patients were experiencing significant oral health issues that were not severe enough to be classified as Very Poor, but are still concerning. The Very Poor (15.0%) category also has a noticeable percentage, suggesting that some patients were in critical need of periodontal and oral health intervention. The Fair (10.0%) category, with a smaller percentage, indicates that only a few patients maintain a relatively better oral health status compared to the others as shown in table 5. The Table 5 is presenting the mean levels of IL-6 (±SD) in these groups, where patients with fair oral health exhibited the lowest baseline IL-6 levels (36.23 ± 4.024 pg/ml), those with poor oral health showed moderately higher levels (37.43 ± 3.63 pg/ml), and with very poor oral health had demonstrated the highest levels (40.64 ± 0.415 pg/ml). Furthermore, following

the given treatment, a significant reduction in the levels of IL-6 had been observed across all categories, with the greatest reduction in patients with fair oral health ($p = 0.004$), followed by poor ($p < 0.0001$) and very poor groups ($p = 0.0007$). The pie chart, given in Figure 5 is illustrating the distribution of patients according to oral health status, showing categories of fair, poor, and very poor oral health. These observations are providing strong evidence that poorer oral health status is associated with elevated IL-6 expression, and therapeutic interventions resulted in significant reductions across all groups of periodontitis.

Table 5. Oral health status groups, Mean baseline and post-treatment levels of IL-6 (±Standard Deviation) showing lowest baseline IL-6 levels in 'Fair' health group, highest in the 'Very Poor' health group and a significant reduction in IL-6 levels observed following treatment across all groups.

	Oral health status	Mean Pre IL6(pg/ml)	SD	Mean Post IL6(pg/ml)	SD	P value
0	Fair	36.23	±4.024	28.67	±5.302	0.004
1	Poor	37.43	±3.63	32.35	±2.64	< 0.0001
2	Very poor	40.64	±0.415	34.79	±0.277	0.0007

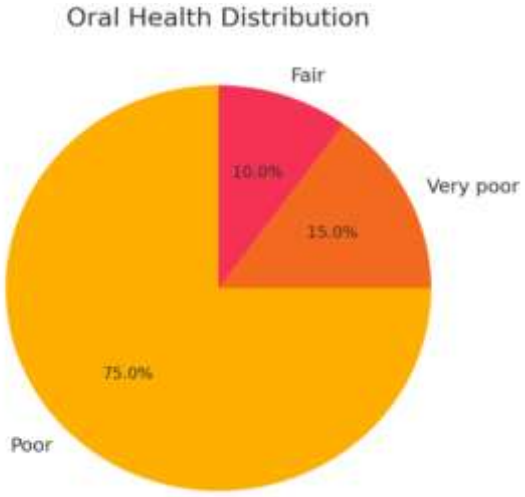

Fig 5. Pie chart of oral health distribution among patients, illustrating that the majority of patients are categorized as having 'Poor' oral health, followed by 'Fair' and 'Very Poor' health

The predominance of poor oral health indicates widespread oral hygiene challenges in the patient population. The few patients with "Fair" oral health suggest some variation, but overall, there's a strong need for enhanced oral health interventions.

Comparison of Pre and Post IL-6 Levels

The IL-6 levels, a marker for inflammation, were generally lower after treatment compared to before. The average IL-6 level before the intervention/treatment across all patients was 37.563pg/ml ±3.56. After the intervention/treatment across all patient theIL6 level decrease to 32.0495pg/ml ±3.29**.** The decrease in the mean IL-6 levels from 37.563 ±3.56 pg./ml (Pre-treatment) to 32.0495 ±3.29pg/ml (post-treatment) suggests that there might have been a positive effect of the treatment/intervention on reducing IL-6 levels among the patients as shown in Table 6. The graph shown in Figure 6 is demonstrating the comparison of pre- and post-treatment IL-6 levels among respondents such as A-T. The blue line in the graph is representing the levels of IL-6 before intervention whereas the red line is highlighting the IL-6 levels after treatment. It has been concluded that for almost all respondents, the post treatment levels of IL-6 were consistently lower than the observed pre-treatment values. The observed average IL-6 level before treatment was as 37.563 pg/ml ± 3.56, while after treatment, it has reduced to 32.0495 pg/ml ± 3.29. The significant reduction in mean IL-6 levels suggested that the treatment/intervention most likely had a positive impact on lowering inflammation as indicated by reduced IL-6 levels.

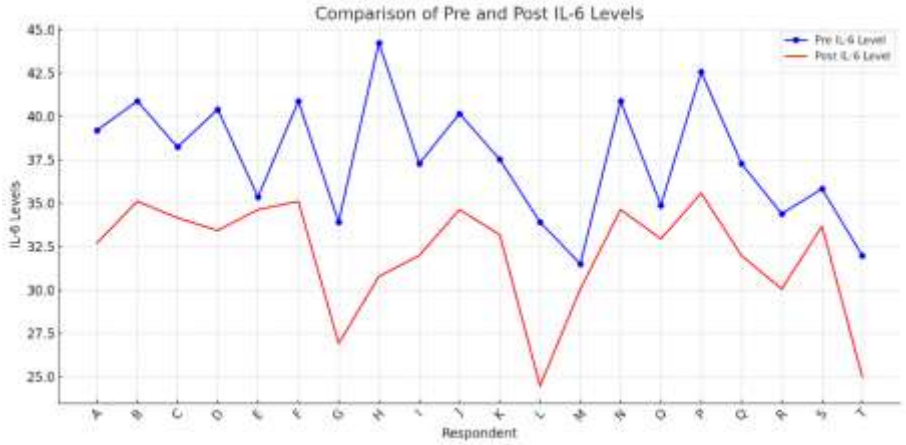

Fig 6. Illustration of comparison of pre- and post-treatment levels of IL-6 among respondents (A–T), blue line (pre-treatment) levels remained consistently higher than the red line (post-treatment) levels, and this downward trend demonstrated the positive impact of treatment in reducing IL-6 levels.

The reduction in IL-6 levels post-treatment suggests that the interventions were effective in reducing inflammation among the patients. This was a positive outcome, indicating that the treatment likely helped in managing the periodontal disease by reducing inflammatory markers.

Table 6. Showing the comparison of mean IL-6 levels (pg/ml) before and after treatment in 20 patients, mean IL-6 level decreased significantly from 37.56 ± 3.56 pg/ml (pre-treatment) to 32.05 ± 3.29 pg/ml (post-treatment) with a p-value of >0.0001, indicating that the treatment had a significant effect on lowering IL-6 levels.

No of patients	Mean pre IL6pg/ml	SD	Mean post IL6pg/ml	SD	P value
20	37.56	± 3.56	32.05	±3.29	> 0.0001

DISCUSSION

The current study had assessed the effect on IL-6 levels after periodontal therapy, among patients with moderate and severe periodontitis, with estimated mean applicant age of 38.2 ± 4.1 years. The distribution of age reveal that the majority of the participants were in the age group of 30-45years, further more suggesting that the individuals in middle age are more likely susceptible to the periodontitis. The results also revealed that on analysis of probing depth, individuals with 5mm pockets presented the largest group and this group was estimated to exhibit the most significant reduction in the levels of IL-6 following the therapeutic approach suggesting a strong correlation between periodontal probing depth and the inflammatory process. Further more it was also demonstrated that the IL-6 levels and expression was significantly high in severe stages of periodontitis as compared to moderate stages, however both these groups showed a significant post treatment reduction and suggesting the effectiveness of therapy in controlling inflammation. Moreover, distribution of oral health status of the selected patients, demonstrated that patients with poorer oral health presented with higher IL-6 baseline levels, yet all categories showed significant improvements after intervention. Hence, the overall comparison of pre- and post-treatment IL-6 levels demonstrated that a clear downward trend was observed, with mean IL-6 concentrations decreasing significantly. Overall, these results supported the hypothesis that periodontal treatment can positively influence inflammatory markers and have a significant role in management of systemic inflammation in periodontitis.

The findings of this study demonstrated that the valuable intervention had significantly reduced IL-6 levels in patients with periodontal disease, indicating a crucial decrease in the intensity of inflammatory response. The mean levels of IL-6 had declined from 37.56 pg/mL to the level 32.05 pg/mL post treatment and significantly suggested by a highly critical paired t-test results of $t = 8.57$, $p = 5.94\times10^{-8}$). Values of ANOVA such that $F = 6.03$, $p = 0.024$ and Regression analysis $R^2 = 0.251$, coefficient = 3.23 had confirmed that the levels of IL-6 correlate with the severity of disease, and higher levels of IL-6 had been

observed post-treatment in severe periodontitis cases. Individuals with advanced and severe form of periodontitis showed intense inflammatory responses and necessitated personalized treatment approaches. Apparently, the proposed doxycycline-coated bioactive glass chewing gum offers a novel and sustained release mechanism to reduce the Cytokine IL-6 levels and probing depths efficiently. Unlike traditional methods such as systematic antibiotics and mouth rinses, the current approach will ensure prolonged drug contact at the site of disease and enhancing anti-inflammatory effects with minimum side effects.

Previous studies supported the efficacy of localized doxycycline delivery. For instance, Savita et al. reported that the use of 1% chitosan nanoparticle gel with adjunct to SRP (scaling and root planning) reduced probing depth and improved CAL (clinical attachment loss), however its antimicrobial effects will be short lived compared to chewing gum approach(Savita, Sunil, Tejashwini, & Pallavi Nanaiah, 2021). Similarly, it also has been demonstrated that sub-antimicrobial dose doxycycline (SDD) reduced the levels of MMP-8, MMP-9 and IL-6 reported by Dong-Hoon Choi et al., however limitations included inconsistent efficacy in severe cases and systemic side effects(Cho, Song, Choi, & Gwon, 2020). Nano-doxycline gel provided prolonged and long-lasting anti-inflammatory effects that the traditional doxycline, yet the professional application remained a barrier as demonstrated by Madi et al(Patel, Sharma, & Mehta, 2018). Additionally, Zuhal et al., showed that curcumin gel reduced the levels of IL-6 and increased IL-10, however its temporary staining and limited antimicrobial potency restricted its clinical utility(Ay et al., 2020).

Hence the chewing gum approach promises to overcome these limitations of conventional drug delivery systems by merging bioactive glass sustained release, mechanical biofilm disruption and enhanced salivation improving patient compliance and therapeutic outcomes. The currently proposed intervention designed to inhibit MMPs and collagen degradation, as doxycline are known to suppress the effects of matrix metalloproteinases and preserves the integrity of periodontal tissue reported by Kinane et al., 2024(Kinane, Lappin, & Culshaw, 2024). Tylutka et al., 2024 suggested that it also had the potential to modulate the inflammatory process systematically as reduced levels of IL-6 lowers systematic inflammation risks in cases such as cardiovascular diseases and diabetes(Tylutka, Walas, & Zembron-Lacny, 2024). It had been emphasized that IL-6 and TNF-α levels were reduced by probiotic-loaded hydrogels, restoring microbial balance and offered a synergistic approach to reduce inflammatory response(Teymouri, Pourhajibagher, & Bahador, 2025).

Furthermore, the chewing gum has the tendency to enhance drug retention, ensuring prolonged drug contact at the site of inflammation in the oral cavity and periodontal pockets as compared to oral gels and rinses suggested by Wang et al., 2024(Ding, Zhu, Zhang, & Wang, 2024). Additionally, Roe et al., 2024 suggested that its noninvasive nature and self-administered characteristics have the potential to improve patient adherence and compliance by integrating effortlessly into duality routine(Roe, 2024). Hence this approach will illustrate promising, long-term studies needed to assess optimal dosing, its association with other inflammatory markers e.g. TNF- α, IL-1β and comparative efficacy against other localized strategies such as microneedles and nanospheres. Huimin Li et al. established a dissolvable microneedle in 2023 for delivery of minocycline and accomplishing deep periodontal penetration also a sustained release, though scalability remains a challenge in this experiment(Li et al., 2025).

In conclusion, the current doxycycline-coated bioactive glass chewing gum claimed to emerge as a superior adjunctive treatment for periodontitis, presenting sustained release of drug, enhanced compliance, and dual biochemical-mechanical benefits.

CONCLUSION

The chewing Gum containing Doxycycline loaded Bioactive Glass has considerably decreased the level of IL-6 in Periodontitis patients. The reduction in IL-6 levels post-treatment were effective in reducing inflammation among the patients. This is a positive outcome, indicating that the treatment likely helped in managing the periodontal disease by reducing inflammatory markers. The reported doxycycline-coated bioactive glass chewing gum is established as a superior adjunctive therapy for periodontitis and offers a sustained drug release, improved patient compliance, and possess dual mechanical-biochemical benefits. The potential to reduce both localized and systemic inflammation and advancing precision periodontal care will be

validated against alternatives such as microneedles by further research in future.

Limitations and Recommendations

Sample size of the current study was small, so it is suggested to carry out further studies with greater number of sample size. Other significant inflammatory biomarkers associated with periodontitis and the role of bioactive glass in terms of remineralization has not been studied. Since only male patients were considered in this study, hence the results might not be applicable to female patients. Hence the future recommendations are to study further inflammatory biomarkers, include female patients and study the effects of bioactive glass o remineralization.

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