

1. Date of posting of results summaries

We will input this on the day of posting the results.*

2. Date of the first journal publication of results

16th April 2025.

3. URL hyperlink(s) related to results and publications

<https://pmc.ncbi.nlm.nih.gov/articles/PMC12025252/> (For the first publication)

4. Baseline Characteristics: Data collected at the beginning of a clinical study for all participants and for each arm or comparison group. These data include demographics, such as age and sex, and study-specific measures.

Table 1. Sociodemographic characteristics according to glycemic status. (N= 88)

	Normoglycemic	Prediabetes	Diabetes	p-Value
	N (%)	N (%)	N (%)	(Fisher's Exact Test)
Mean age (SD)	50.5 (13.7)	54.7 (13.2)	60.9 (12.3)	0.017 *
Gender				
Male	6 (54.5)	19 (59.4)	21 (46.7)	0.539
Female	5 (45.5)	13 (40.6)	24 (53.3)	
Highest level of education				
Primary	1 (9.1)	1 (3.1)	2 (4.4)	0.444
Secondary	1 (9.1)	12 (37.5)	12 (26.7)	
Tertiary	9 (81.8)	19 (59.4)	31 (68.9)	
Ethnicity				
Yoruba	7 (63.6)	17 (53.1)	24 (53.3)	0.908
Igbo	3 (27.3)	8 (25)	11 (24.4)	
Others	1 (9.1)	7 (21.9)	10 (22.2)	
Religion				
Christianity	8 (72.7)	28 (87.5)	36 (80)	0.495
Islam	3 (27.3)	4 (12.5)	9 (20)	

* Statistical significance. SD: Standard Deviation.

Table 2: Sociodemographic characteristics of the participants (N=77)

	Diabetes N (%)	Prediabetes N (%)	Both N (%)	p value
Mean Age (SD)	60.91(12.31)	54.66(13.19)	58.31(12.97)	0.036*
Sex				
Male	21(46.67)	19(59.38)	40(51.95)	0.356
Female	24(53.33)	13(40.63)	37(48.05)	
Highest level of Education				
Less than Tertiary	14(31.11)	13(40.63)	27(35.06)	0.470
Tertiary and above	31(68.89)	19(59.38)	50(64.94)	
Ethnicity				
Yoruba	24(53.33)	17(53.13)	41(53.25)	0.998
Igbo	11(24.44)	8(25.00)	19(24.68)	
Others	10(22.22)	7(21.88)	17(22.08)	
Hypertension Status				
Normal	2(4.44)	3(9.38)	5(6.49)	0.031*
Elevated	12(26.67)	2(6.25)	14(18.18)	
Stage 1	10(22.22)	15(46.88)	25(32.47)	
Stage 2	21(46.67)	12(37.50)	33(42.86)	
BMI Status				
Normal	10(23.26)	12(40.00)	22(30.14)	0.280
Overweight	18(41.86)	11(36.67)	29(39.73)	
Obese	15(34.88)	7(23.33)	22(30.14)	
Frequency of brushing				
Once	27(60.00)	21(65.63)	48(62.34)	0.642
Twice	18(40.00)	11(34.38)	29(37.66)	

* Statistical significance. SD: Standard Deviation.

5. Participant flow:

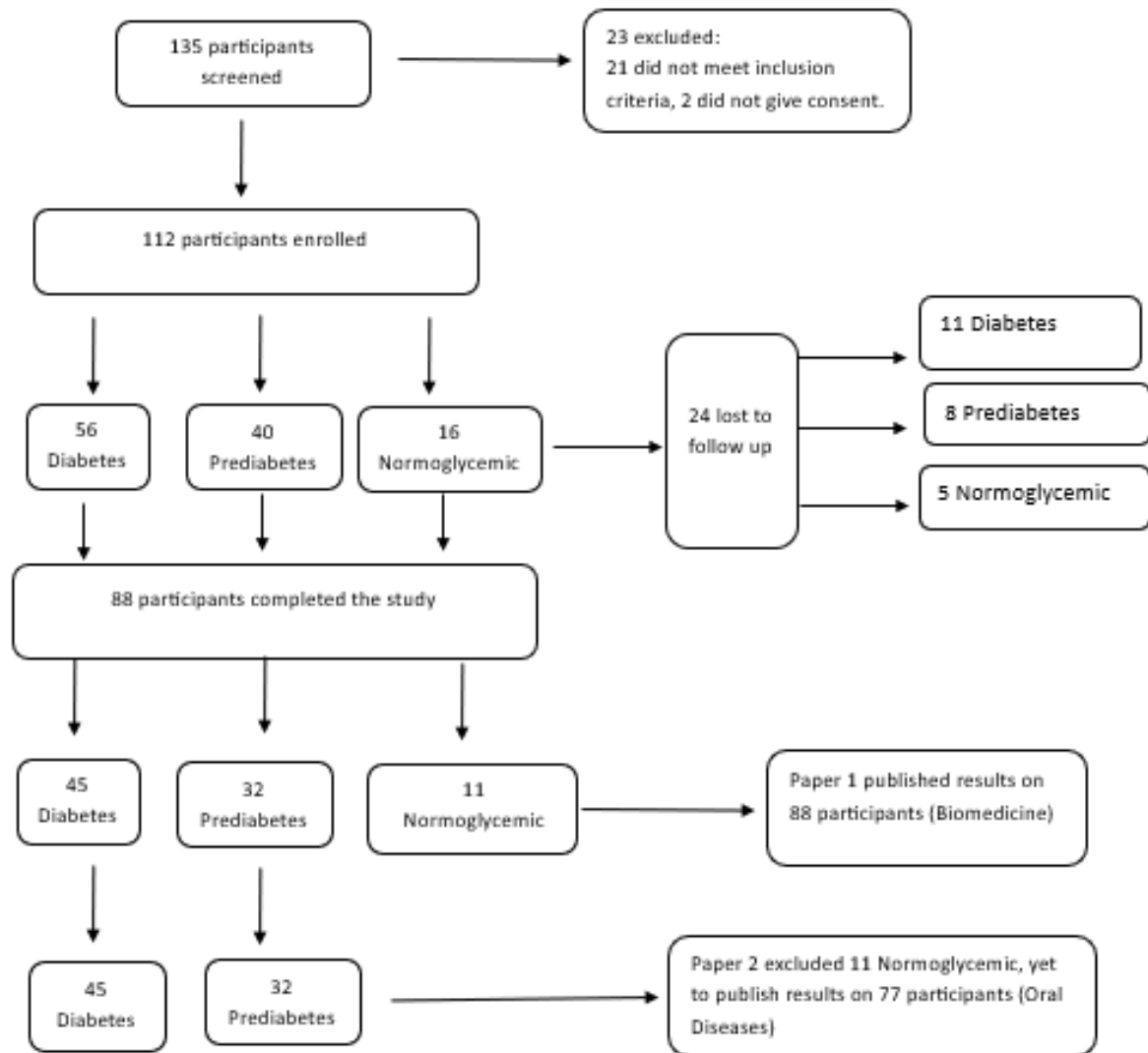


Figure 1. Flow Chart for participants' enrolment into the study.

6. Adverse events: There were no adverse effects documented during the course/immediately after this study.

7. Outcome measures:

Table 3. Pre- and post-SRP on periodontal clinical parameters in all groups (N = 88)

Variables	Time	Mean (SD)	Confidence Interval (Paired Differences)		<i>p</i> -Value
			Lower Level	Upper Level	
PPD ≥ 4 mm	Pre-SRP–Post-SRP	14.6 (16.2)			
	Pre-SRP	23.0 (19.2)	11.2	18.0	<0.001 *
	Post-SRP	8.4 (9.3)			
CAL (mm)	Pre-SRP–Post-SRP	0.2 (0.8)			
	Pre-SRP	2.2 (1.1)	–0.01	0.3	0.064
	Post-SRP	2.0 (1.1)			
OHI-S	Pre-SRP–Post-SRP	1.2 (1.2)			
	Pre-SRP	2.6 (1.2)	1.0	1.5	<0.001 *
	Post-SRP	1.4 (0.8)			
BOP (%)	Pre-SRP–Post-SRP	14.5 (16.4)			
	Pre-SRP	27.9 (16.4)	1.7	11.0	<0.001 *
	Post-SRP	13.3 (9.6)			

* Statistical significance. SD: Standard Deviation. *p*-values calculated by paired-samples *t*-test (2-sided test).

Table 4. Pre- and post- SRP aMMP-8 (ng/mL) and HbA1c (%) by periodontitis staging status. (N= 88)

Variables	Time	Mean (SD)	Confidence Interval (Paired Differences)		p-Value
			Lower Level	Upper Level	
aMMP-8 (ng/mL)	Pre-SRP–Post-SRP	10.5 (27.7)	4.6	16.4	<0.001 *
	Pre-SRP	37.4 (30.9)			
	Post-SRP	26.9 (24.9)			
	Stage II periodontitis (N = 32)				
	Pre-SRP–Post-SRP	7.2 (20.3)	−0.2	14.5	0.055
	Pre-SRP	29.3 (21.9)			
	Post-SRP	22.2 (22.1)			
	Stage III + IV periodontitis (N = 56)				
	Pre-SRP–Post-SRP	12.4 (31.2)	4.0	20.8	0.004*
	Pre-SRP	42.0 (34.4)			
	Post-SRP	29.6 (26.2)			
	All groups (N = 88)				
HbA1c (%)	Pre-SRP–Post-SRP	0.4 (1.0)	0.2	0.6	0.001*
	Pre-SRP	6.9 (1.6)			
	Post-SRP	6.5 (1.2)			
	Stage II periodontitis (N = 32)				
	Pre-SRP–Post-SRP	0.3 (1.1)	−0.08	0.7	0.107
	Pre-SRP	6.8 (1.8)			
	Post-SRP	6.4 (1.2)			
	Stage III + IV periodontitis (N = 56)				
	Pre-SRP–Post-SRP	0.4 (1.0)	0.2	0.7	0.002*
	Pre-SRP	6.9 (1.5)			
	Post-SRP	6.5 (1.2)			

*Statistical significance. SD: Standard Deviation. *p*-values calculated by paired-samples *t*-test (2-sided test).

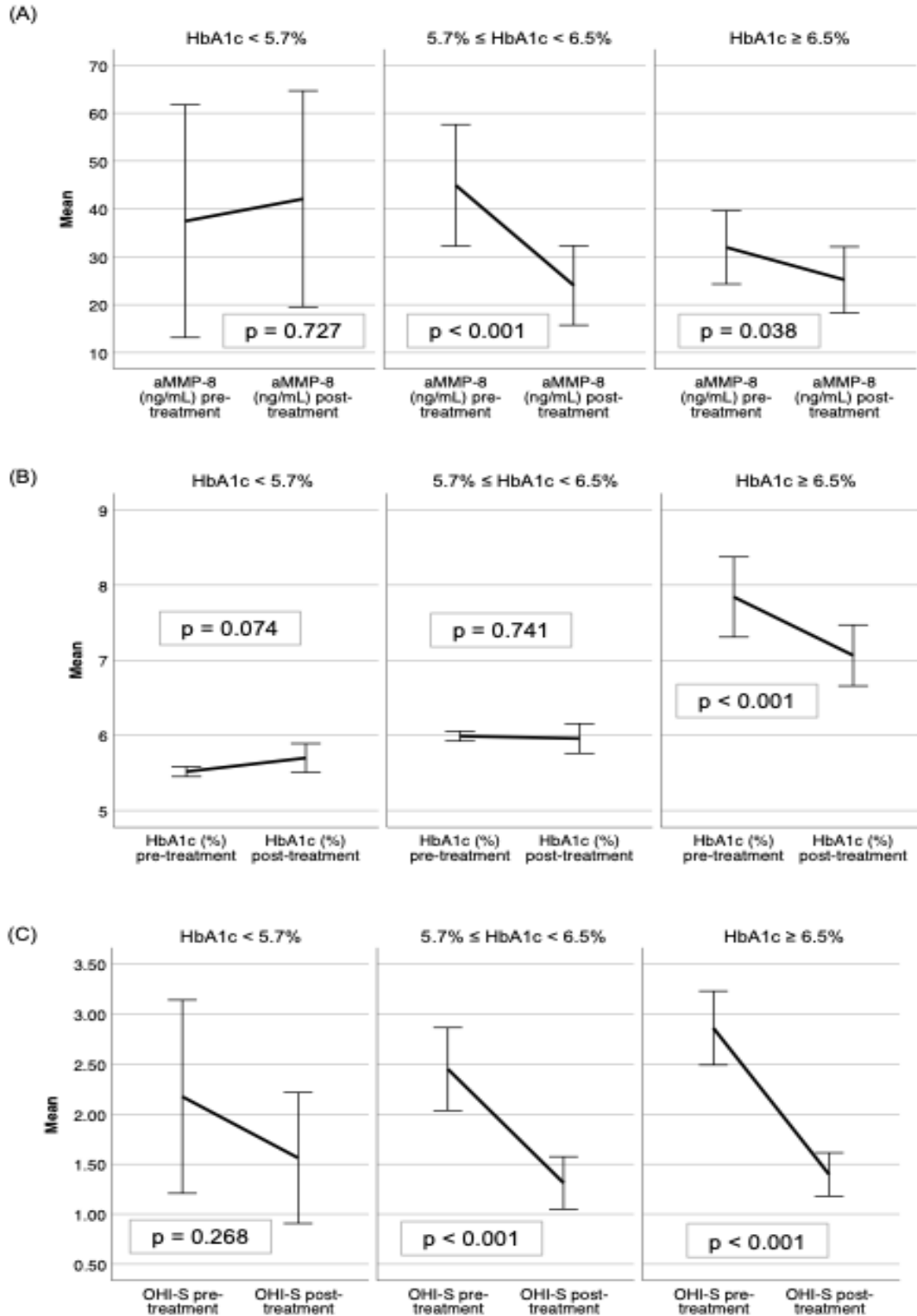


Figure 2. Pre- and post-SRP treatment effect on mean levels with 95% confidence intervals shown of (A) aMMP-8 (ng/mL), (B) HbA1c (%), and (C) OHI-S among normoglycemic ($HbA1c < 5.7\%$), prediabetes ($5.7\% \leq HbA1c < 6.5\%$) and diabetes ($HbA1c \geq 6.5\%$) groups. (N= 88)

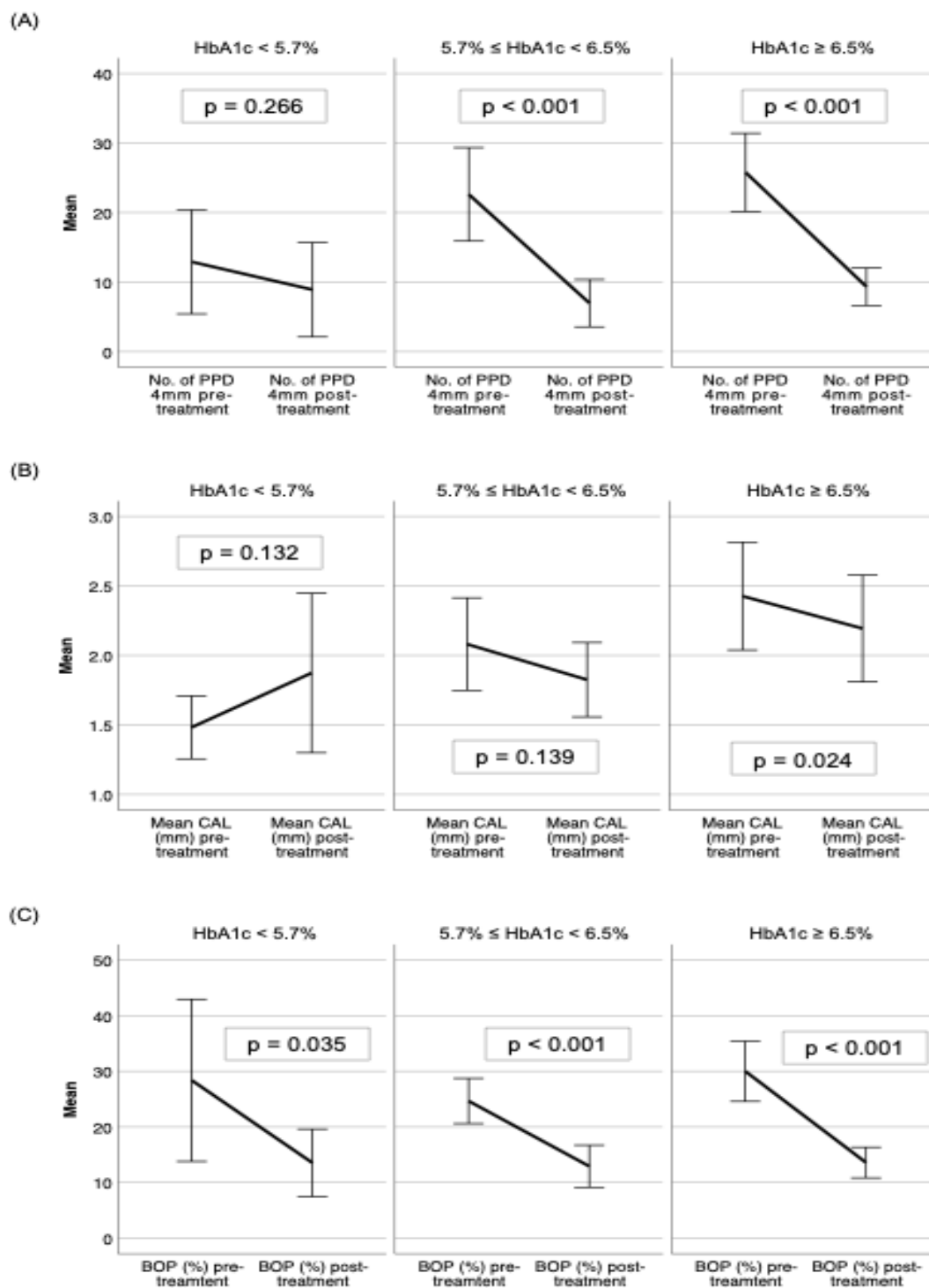


Figure 3. Pre- and post-SRP treatment effect on mean levels with 95% confidence intervals shown of (A) PPD ≥ 4 mm, (B) mean CAL, and (C) BOP (%) among normoglycemic (HbA1c < 5.7%), prediabetic (5.7% ≤ HbA1c < 6.5%), and diabetic (HbA1c ≥ 6.5%) groups. (N = 88)

Table 5. Periodontal clinical and systemic parameters pre- and post- NSPT in both groups. (N=77)

Parameter	Interval	Mean (SD)	95% Confidence interval (Paired differences)		
			Lower level	Upper level	p value
Plaque Index	Pre-NSPT–Post-NSPT (N=77)	0.29 (0.47)	0.18	0.40	<0.001*
	Pre-NSPT	0.95 (0.43)			
	Post-NSPT	0.66 (0.36)			
Gingival Index	Pre-NSPT–Post-NSPT (N=77)	0.35 (0.53)	0.23	0.47	<0.001*
	Pre-NSPT	1.17 (0.39)			
	Post-NSPT	0.83 (0.47)			
PISA scores	Pre-NSPT–Post-NSPT (N=77)	277.94 (316.94)	206.00	349.88	<0.001*
	Pre-NSPT	426.33 (347.67)			
	Post-NSPT	148.39 (138.11)			
aMMP-8 (ng/mL)	Pre-NSPT–Post-NSPT (N=77)	12.65 (24.55)	7.08	18.22	<0.001*
	Pre-NSPT	37.36 (30.37)			
	Post-NSPT	24.71 (22.87)			
HbA1c (%)	Pre-NSPT–Post-NSPT (N=77)	0.47 (1.06)	0.23	0.71	<0.001*
	Pre-NSPT	7.07 (1.64)			
	Post-NSPT	6.61 (1.22)			
hsCRP (mg/L)	Pre-NSPT–Post-NSPT (N=77)	2.46 (6.55)	0.98	3.95	0.001*
	Pre-NSPT	6.90 (8.09)			
	Post-NSPT	4.44 (4.30)			

*Statistical significance (p<0.05); SD: Standard Deviation

Effect of NSPT on Clinical and Biochemical Outcomes
(Separate Models by Glycemic Status Adjusted for Age and Sex)

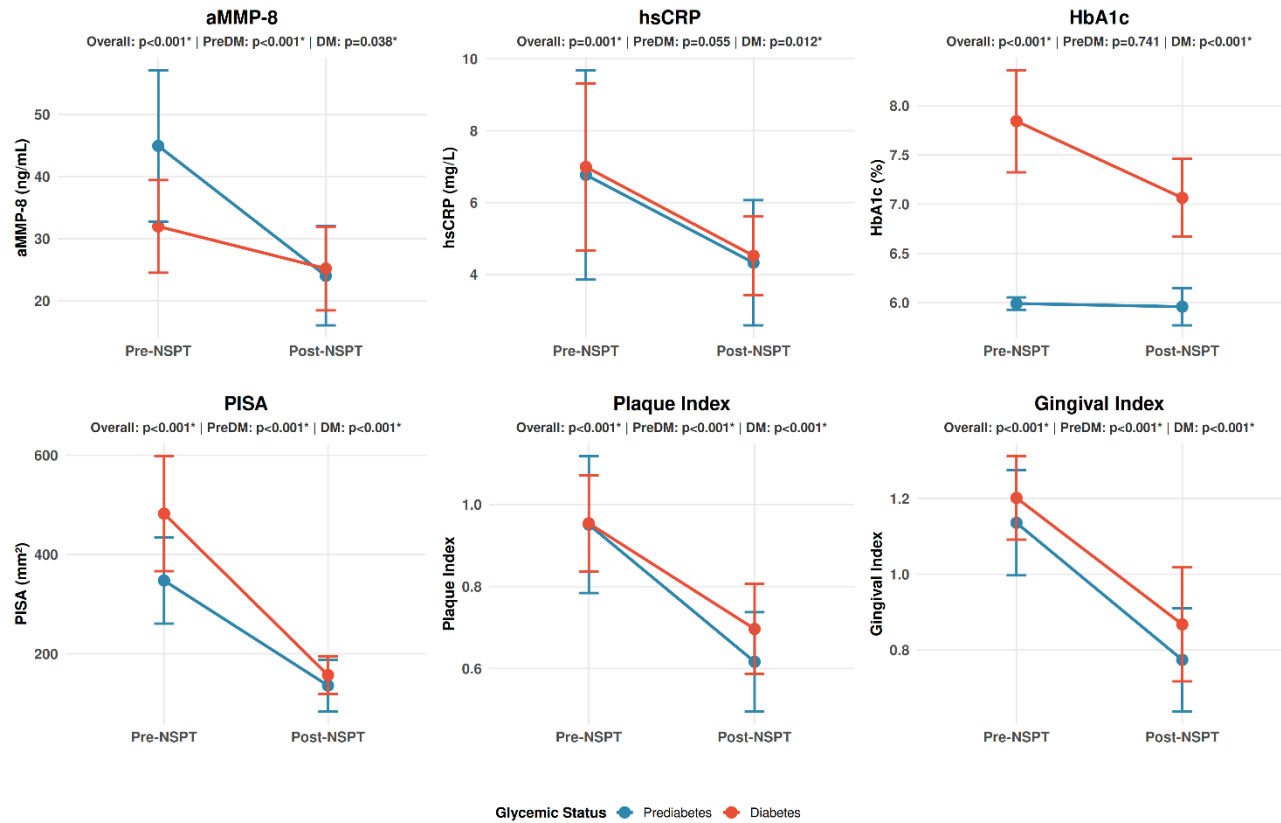


Figure 4. Effect of non-surgical periodontal therapy (NSPT) on the clinical and biochemical parameters, adjusted for glycemic status, age and sex. *Statistical significance ($p < 0.05$). (N=77)

Table 6. Association between periodontal clinical and systemic parameters in both groups (N=77)

Variable		Change in HbA1c	Change in Plaque index	Change in Gingival index	Change in hsCRP	Change in aMMP-8	Change in PISA
Change in HbA1c	Pearson	1	-0.062	0.238**	0.251**	0.070	0.163
	Correlation						
	Sig. (2-tailed)		0.595	0.037	0.028	0.546	0.156
Change in Plaque index	Pearson	-0.062	1	0.353**	0.216	0.348**	-0.021
	Correlation						
	Sig. (2-tailed)	0.595		0.002	0.060	0.002	0.858
Change in Gingival index	Pearson	0.238**	0.353**	1	0.168	0.033	0.310
	Correlation						
	Sig. (2-tailed)	0.037	0.002		0.144	0.774	0.006
Change in hsCRP	Pearson	0.251**	0.216	0.168	1	0.192	0.072
	Correlation						
	Sig. (2-tailed)	0.028	0.060	0.144		0.095	0.535
Change in aMMP-8	Pearson	0.070	0.348**	0.033	0.192	1	0.045
	Correlation						
	Sig. (2-tailed)	0.546	0.002	0.774	0.095		0.695
Change in PISA	Pearson	0.163	-0.021	0.310	0.072	0.045	1.000
	Correlation						
	Sig. (2-tailed)	0.156	0.858	0.006	0.535	0.695	

** Significant correlation (p <0.05)

Table 7. Linear Mixed Effects Model - Treatment Effects Adjusted for Glycemic Status, Age and Sex. (N=77)

Outcome	Overall Effect (95% CI)	Overall p	Prediabetes Effect (95% CI)	Diabetes Effect (95% CI)	Interaction Effect (95% CI)	Interaction p
aMMP-8 (ng/mL)	-12.65 (-18.13, -7.17)	<0.001*	-20.91 (-29.11, -12.70)	-6.78(-13.70, 0.14)	14.13 (3.39, 24.86)	0.012*
hsCRP (mg/L)	-2.46 (-3.92, -1.00)	0.001*	-2.45 (-4.73, -0.16)	-2.47 (-4.40, -0.55)	-0.03 (-3.01, 2.96)	0.987
HbA1c (%)	-0.47 (-0.70, -0.23)	<0.001*	-0.03 (-0.38, 0.31)	-0.78 (-1.07, -0.49)	-0.75 (-1.20, -0.30)	0.002*
PISA (mm ²)	-277.94(-348.73,-207.15)	<0.001*	-211.56 (-320.34, -102.78)	-325.14 (-416.88, -233.41)	-113.58 (-255.88, 28.72)	0.122
Plaque Index	-0.29 (-0.39, -0.19)	<0.001*	-0.33 (-0.50, -0.17)	-0.26 (-0.39, -0.12)	0.08 (-0.13, 0.29)	0.478
Gingival Index	-0.35 (-0.46, -0.23)	<0.001*	-0.36 (-0.55, -0.18)	-0.33 -0.49, -0.18)	0.03 (-0.21, 0.27)	0.821

*Statistical significance (p<0.05). CI: Confidence Interval

Table 8. Sensitivity Analysis - Effect Modification by Body Mass Index (BMI). (N=77)

Outcome Variable	Normal BMI Effect	Overweight Difference (p)	Obese Difference (p)
aMMP-8 (ng/mL)	-24.45	+14.05 (0.038*)	+21.12 (0.005*)
hsCRP (mg/L)	-2.03	-0.81 (0.649)	+0.86 (0.656)
HbA1c (%)	-0.46	-0.09 (0.759)	+0.14 (0.685)
PISA (mm ²)	-287.41	-9.24 (0.918)	+78.75 (0.421)
Plaque Index	-0.49	+0.22 (0.089)	+0.41 (0.004*)
Gingival Index	-0.40	+0.04 (0.790)	+0.19 (0.258)

*Statistical significance (p<0.05).

8. URL link to protocol file(s) with version and date. This will apply when the protocol has either been published in a journal or on an institutional website.

Not applicable, as the protocol has not been published.

9. Brief summary

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia due to insulin deficiency, affecting 589 million people worldwide and costing \$1.015 trillion in medical expenses. In Nigeria, approximately 11.4 million adults have diabetes, the highest in sub-Saharan Africa. Type 2 diabetes (T2D) accounts for over 90% of cases and is the 8th leading cause of disease burden. Uncontrolled DM leads to complications, including periodontitis, the sixth complication of DM. Prediabetes also increases the risk of developing diabetes and periodontitis. Periodontitis affects approximately 1.1 billion people globally, causing tooth loss and decreased quality of life. Active matrix metalloproteinase-8 (aMMP-8) is a biomarker for diagnosing periodontitis, and the Periodontal Inflammatory Surface Area (PISA) index quantifies periodontal inflammation. This condition worsens systemic inflammation, particularly in individuals with diabetes.

Evidence suggests a two-way link: poorly controlled diabetes increases periodontal disease severity, while periodontitis worsens glycaemic control. Periodontal therapy can reduce systemic inflammation markers like high sensitivity C-reactive protein (hsCRP). Studies show that treating periodontitis in patients with diabetes leads to greater reductions in inflammatory markers. Previous research indicates that non-surgical periodontal therapy (NSPT) improves glycemic control in individuals with prediabetes and diabetes who have periodontitis. Few studies have demonstrated its effects on mouthrinse active-matrix metalloproteinase-8 (aMMP-8) level as it relates to glycemic control. Furthermore, there is limited research on the correlations between periodontal measures (PISA, aMMP-8), glycated hemoglobin (HbA1c), and hsCRP post-treatment among Nigerians. This research aims to evaluate the impact of NSPT on these parameters and their interrelationships in periodontitis patients with diabetes, prediabetes, and normoglycemia.

In this prospective interventional study, 88 Nigerian patients aged 25–78, with stage II–IV periodontitis out of 112 initial participants completed the study (45 diabetes, 32 prediabetes, 11 normoglycemia). They received non-surgical periodontal therapy (NSPT). Full-mouth clinical examinations were used to evaluate their periodontal parameters [periodontal probing depth (PPD), clinical attachment level (CAL), simplified oral hygiene index (OHI-S), and percentage bleeding on probing (BOP%)]. The treatment response on their periodontal clinical parameters, HbA1c and aMMP-8 levels using point-of-care kits was assessed before and approximately three months after full mouth disinfection (scaling and root planing). The results indicated that there were positive treatment effects on their clinical parameters, aMMP-8 and HbA1c levels in the prediabetes and diabetes groups. The aMMP-8 reduction was significant in the prediabetes and prediabetes + diabetes groups, while HbA1c decreased significantly in the diabetes and prediabetes + diabetes groups. In contrast, a non-significant increase in mean aMMP-8 levels, HbA1c, and CAL was observed in the normoglycemia group. Stage III + IV periodontitis showed significant treatment effects for aMMP-8 and HbA1c compared to stage II, regardless of glycemic status. The conclusion was that NSPT significantly improved periodontal health as well as HbA1c and aMMP-8 levels in people living with prediabetes and diabetes.

Further analysis of a subset of the population (diabetes and prediabetes groups alone), using paired t-tests, Pearson correlation, linear mixed effect models and sensitivity analysis, with the inclusion of other clinical parameters [periodontal inflamed surface area (PISA), Plaque Index (PLI)], aMMP-8, hsCRP, and HbA1c, at baseline and three months post-treatment, revealed significant improvements in all parameters for both groups. Participants with diabetes demonstrated a greater reduction in HbA1c (-0.78%) while the participants with prediabetes experienced a larger decrease in aMMP-8 (-20.91ng/mL). Obesity negatively impacted aMMP-8 and PLI responses, with no sex differences observed. In conclusion, NSPT effectively reduced systemic inflammation and improved glycemic control, indicating its utility in monitoring periodontal health and diabetes risk.