

ORIGINAL RESEARCH

Unlocking the diagnostic value of GCF: Sclerostin as a biomarker in Periodontitis and Diabetes Mellitus – A Cross-sectional observational study

Pallavi K. Nanaiah¹ | A M Savita² | Ashwin Prabhu³ | Archana R Naik⁴ | Koduru Sravani⁵

¹Reader, Department of Periodontics,
Dayananda Sagar College of Dental Sciences,
Bangalore, India

²Prof & Head, Department of Periodontics,
Dayananda Sagar College of Dental Sciences,
Bangalore, India

³Professor, Department of Periodontics,
Dayananda Sagar College of Dental Sciences,
Bangalore, India

⁴Professor, Department of Periodontics,
Dayananda Sagar College of Dental Sciences,
Bangalore, India

⁵Senior Lecturer, Department of Periodontics,
Dayananda Sagar College of Dental Sciences,
Bangalore, India

Correspondence

Dr. Pallavi Nanaiah K, Dayananda Sagar
College of Dental Sciences, Bangalore.
Email: pallavinanaiah@dscds.edu.in

Abstract

Background: Sclerostin, a critical regulator of bone metabolism, has emerged as a potential biomarker in the pathogenesis of periodontal disease. Its elevated expression in individuals with type 2 diabetes mellitus (T2DM) underscores the need to explore local versus systemic detection methods for better diagnostic accuracy. **Aim:** This cross-sectional study aimed to assess and compare sclerostin levels in gingival crevicular fluid (GCF), saliva, and serum among chronic periodontitis patients with and without T2DM, to determine the most sensitive medium for early diagnosis. **Materials and Methods:** Thirty-six individuals aged 30–60 years were enrolled and stratified into three groups: healthy (Group 1), chronic periodontitis (Group 2), and chronic periodontitis with T2DM (Group 3). Clinical periodontal parameters were recorded, followed by collection of GCF, saliva, and serum samples. Sclerostin concentrations were quantified using ELISA, and statistical analyses were performed using ANOVA and Pearson's correlation. **Results:** Significantly higher sclerostin levels were observed in GCF compared to saliva and serum across all groups. Group 3 exhibited the highest mean GCF sclerostin levels (40.19 ± 5.87 ng/mL), followed by Group 2 (29.11 ± 4.36 ng/mL) and Group 1 (25.75 ± 4.92 ng/mL), with $p < 0.001$. GCF demonstrated greater diagnostic specificity in identifying disease progression, particularly in diabetic patients. **Conclusion:** GCF serves as a superior medium for detecting sclerostin, reflecting site-specific periodontal pathology and offering valuable clinical utility for early intervention in periodontitis, especially among high-risk diabetic individuals.

KEYWORDS

Sclerostin, Gingival Crevicular Fluid, Chronic Periodontitis, Diabetes Mellitus, Biomarkers, ELISA, Diagnostic Sensitivity, Periodontal Disease

1 | INTRODUCTION

Chronic periodontitis is characterized by dysregulated host-microbial homeostasis within the subgingival environment, contributing to periodontal tissue destruction. Notably, alterations in signaling proteins such as sclerostin (SOST) and WNT5a have been observed in the gingival tissues of periodontitis patients when compared to healthy controls¹. The oral microbiome, a dynamic and intricate community, undergoes significant compositional shifts during disease progression,

disrupting the equilibrium of host immune responses and initiating connective tissue breakdown². The growing field of osteoimmunology highlights the interplay between immune modulators and bone cells in periodontal and endodontic pathology, elucidating bone resorption pathways³. Bone remodeling relies on the balanced interaction between osteoblasts and osteoclasts, which becomes disrupted in periodontitis⁴. This remodeling is critically regulated by the RANK/RANKL/OPG axis, a triad central to osteoclastogenesis and overall bone metabolism^{5,6,7}. Concurrently, the Wnt signaling pathways modulate bone cell differentiation; while canonical Wnt/ β -catenin signaling supports osteoblast proliferation, non-canonical WNT5a activates osteoclast differentiation and propagates inflammation^{8,9}. Sclerostin, a Wnt antagonist encoded by the SOST gene and secreted by osteocytes, inhibits Wnt/ β -catenin

signaling, contributing to bone loss in diseases like van Buchem disease and periodontitis¹⁰. The inhibition of sclerostin enhances bone mass and healing in osteoporotic models, underscoring its potential as a therapeutic target^{11,12,??}. WNT5a further contributes to inflammatory osteolysis through its pro-osteoclastogenic signaling, supported by experimental models in arthritis, cancer, and periodontal lesions^{??,??,??}. Moreover, genetic susceptibility to periodontitis is under active investigation, highlighting loci associated with disease risk[?]. Proinflammatory cytokines such as IL-1 and TNF- α significantly contribute to tissue destruction in periodontitis, and their inhibition reduces bone loss in experimental models^{??}. TNF- α has also been shown to upregulate sclerostin expression under estrogen-deficient conditions, implying a link between inflammation and bone turnover[?]. Given the prevalence of periodontitis, early identification of reliable biomarkers remains imperative[?]. Host-derived biomarkers in gingival crevicular fluid (GCF), such as cytokines and enzymes, reflect tissue catabolism and serve as potential diagnostic tools^{??,??}. Improvements in GCF collection methodologies and sampling protocols have enhanced the reproducibility and sensitivity of biomarker assessments^{??,??}. Wnt inhibitors including sclerostin and DKK1 have been detected in GCF of periodontitis patients, implicating their role in localized bone remodeling[?]. Quantitative analyses of sclerostin, OPG, and RANKL in GCF correlate with disease severity and support their clinical significance[?]. Additionally, microbial shifts in periodontal disease modulate Wnt-related gene expression^{??}, while systemic factors such as age, gender, obesity, and diabetes further influence biomarker levels and disease risk^{??,??}. This study aims to evaluate and correlate sclerostin and RANKL/OPG signaling molecules in gingival crevicular fluid of chronic periodontitis patients and periodontally healthy individuals, while considering host and systemic modifying factors that may influence local biomarker expression. Scope of the Study: Despite growing recognition of sclerostin's role in periodontal pathogenesis and systemic bone turnover, comparative studies evaluating its levels across GCF, saliva, and serum in chronic periodontitis patients with and without T2DM are scarce. This cross-sectional investigation aims to quantify sclerostin concentrations in these biological fluids and examine interrelationships, with a focus on determining the diagnostic utility of GCF in detecting early and progressive bone changes. The study will explore whether GCF more accurately reflects local sclerostin expression compared to systemic media, especially in high-risk diabetic populations, thereby supporting biomarker-driven approaches in periodontal diagnosis and management.

2 | METHODOLOGY

This cross-sectional study was conducted on patients attending the Department of Periodontics, Dayananda Sagar College of Dental Sciences, with the objective of evaluating the diagnostic potential of gingival crevicular fluid (GCF) as a reliable medium for the detection of sclerostin (SOST) levels in chronic periodontitis patients, with and without type 2 diabetes mellitus. A total of 36 subjects aged between 30 to 60 years

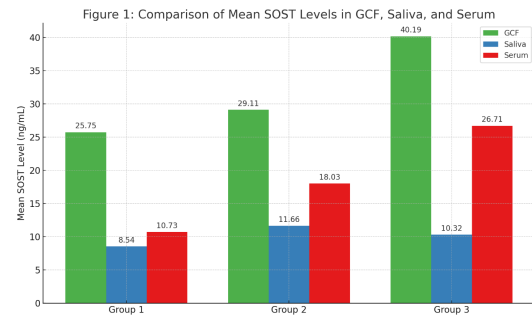


FIGURE 1 SOST distribution across biological fluids indicates that GCF exhibits the most significant diagnostic sensitivity in both periodontitis and diabetic-periodontitis groups.

were selected and categorized into three groups, each comprising 12 individuals. Group 1 included systemically and periodontally healthy individuals with probing depth ≤ 3 mm, no attachment loss, and a gingival index score less than 1. Group 2 consisted of patients diagnosed with chronic periodontitis as per the American Academy of Periodontology (AAP) 1999 classification, while Group 3 included patients with chronic periodontitis and a confirmed diagnosis of type 2 diabetes mellitus. Subjects were excluded from the study if they presented with systemic diseases other than type 2 diabetes, had received periodontal treatment in the past six months, or had a history of antibiotic or anti-inflammatory drug use within the same duration. Additional exclusion criteria included pregnancy or lactation, history of radiation or immunosuppressive therapy, and lifestyle factors such as smoking, alcohol consumption, or substance abuse. Written and verbal informed consent was obtained from all participants prior to inclusion. Clinical periodontal examination was performed by a single calibrated examiner to maintain consistency and included the recording of Plaque Index (PI) as per Silness and L  e (1964), Gingival Index (GI) as per L  e and Silness (1963), probing pocket depth (PPD), and clinical attachment level (CAL) using a UNC-15 periodontal probe (Hu-Friedy). These assessments were carried out one day prior to sample collection. On the following day, three types of biological samples—gingival crevicular fluid, unstimulated saliva, and venous blood—were collected from each subject under standardized protocols. For saliva collection, participants were instructed not to consume food, beverages, or perform oral hygiene procedures for at least 30 minutes beforehand. Around 4 mL of unstimulated saliva was collected in sterile containers via the passive drooling method. GCF samples were collected from the most inflamed or deepest periodontal site using a microcapillary pipette (Sigma Aldrich, St. Louis, USA) placed at the sulcus entrance (extrasulcular method), ensuring a standardized 3 μ L volume. Contaminated samples were discarded and recollected. Blood samples were drawn under aseptic precautions and serum was separated by centrifugation. All collected samples were transferred into sterile vials containing phosphate-buffered saline (PBS) and 0.5% bovine serum albumin (BSA) and stored at -80°C until biochemical evaluation. The concentration of sclerostin in the samples was measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit. The

TABLE 1 Intergroup Comparison of Clinical Parameters and Sclerostin Levels (Group 1: Healthy, Group 2: Chronic Periodontitis, Group 3: Chronic Periodontitis + T2DM)

Parameter	Group	N	Mean	SD	P value	Pairwise Comparisons
Plaque Index (PI)	G1	12	0.4392	0.27520	<0.001*	G1 vs G2: <0.001*; G1 vs G3: <0.001*; G2 vs G3: 0.089
Gingival Index (GI)	G1	12	0.2658	0.12376	<0.001*	G1 vs G2: <0.001*; G1 vs G3: <0.001*; G2 vs G3: <0.001*
Probing Depth (PD, mm)	G1	12	1.6983	0.32646	<0.001*	G1 vs G2: <0.001*; G1 vs G3: <0.001*; G2 vs G3: <0.001*
Clinical Attachment Loss (CAL, mm)	G1	12	1.5725	0.34641	<0.001*	G1 vs G2: <0.001*; G1 vs G3: <0.001*; G2 vs G3: 0.004
SOST GCF (ng/mL)	G1	12	25.7525	4.92054	<0.001*	G1 vs G2: 0.285; G1 vs G3: <0.001*; G2 vs G3: <0.001*
SOST Saliva (ng/mL)	G1	12	8.5442	2.91043	0.014*	G1 vs G2: 0.015*; G1 vs G3: 0.224; G2 vs G3: 0.419
SOST Serum (ng/mL)	G1	12	10.7250	0.93104	<0.001*	G1 vs G2: <0.001*; G1 vs G3: <0.001*; G2 vs G3: <0.001*

TABLE 2 Summary of Diagnostic Relevance of SOST Levels by Group and Fluid

Group	Fluid Type with Highest SOST	Diagnostic Potential
Healthy (Group 1)	GCF	Distinct difference from saliva/serum
Periodontitis (Group 2)	GCF	Moderate elevation; high specificity
Periodontitis + Diabetes (Group 3)	GCF	Highest levels; strongest diagnostic marker

mean optical densities of standard duplicates were used to generate a standard curve, and the concentrations of the unknown clinical samples were calculated based on the regression equation derived from the curve ($y = mx + c$). Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 19. Normality of the data was assessed using Kolmogorov–Smirnov and Shapiro–Wilk tests. Intergroup comparisons of clinical and biochemical parameters were performed using one-way analysis of variance (ANOVA), followed by post hoc Tukey’s test for pairwise comparisons. Correlations between SOST levels in GCF, saliva, and serum were evaluated using Pearson’s correlation coefficient. A p-value less than 0.05 was considered statistically significant.

3 | RESULTS AND OBSERVATION

To investigate the diagnostic relevance of sclerostin (SOST) levels in gingival crevicular fluid (GCF), saliva, and serum across varying periodontal conditions, we measured periodontal clinical parameters and sclerostin concentrations in 36 subjects grouped into three categories: healthy controls (Group 1), chronic periodontitis (Group 2), and chronic periodontitis with Type II diabetes (Group 3). The results demonstrated significant differences in clinical scores and sclerostin levels across groups. GCF consistently exhibited higher sclerostin levels, suggesting superior diagnostic potential. to summarize these findings, and provides a visual comparison of SOST levels in different fluids.

4 | DISCUSSION

The present study reinforces the diagnostic superiority of gingival crevicular fluid (GCF) over saliva and serum for detecting sclerostin levels among systemically healthy individuals, chronic periodontitis patients, and those with chronic periodontitis complicated by type II diabetes mellitus. A statistically significant escalation in clinical periodontal indices—Plaque Index (PI), Gingival Index (GI), Probing Depth

(PD), and Clinical Attachment Level (CAL)—from Group 1 to Group 3 ($p < 0.001$) delineates a clear gradient of periodontal deterioration. These findings are in agreement with the documented exacerbation of periodontal inflammation in diabetic patients due to impaired immune regulation and vascular dysfunction⁷. Sclerostin, a glycoprotein chiefly secreted by osteocytes, antagonizes the Wnt/ β -catenin signaling pathway by binding to LRP5/6, thereby inhibiting osteoblast differentiation and promoting bone resorption^{10,12}. The substantially elevated GCF-sclerostin levels in Group 3 (mean = 40.19 ± 5.87 ng/mL) echo the findings of Chatzopoulos et al. (2019), who reported significantly higher gingival crevicular sclerostin concentrations in chronic periodontitis patients compared to healthy controls.¹ This further emphasized the pathological relevance of sclerostin in disrupting periodontal bone homeostasis via Wnt signaling modulation, as increased gingival levels of sclerostin in chronic periodontitis patients have been shown to antagonize the Wnt/ β -catenin pathway, impairing osteoblast function and favoring bone resorption¹². Intra-group comparisons revealed that GCF consistently harbored the highest sclerostin concentrations across all groups, with saliva and serum demonstrating relatively diminished levels. These inter-fluid differences validate the local specificity of GCF in reflecting periodontal bone dynamics, as supported by Napimoga et al.² and Balli et al.², who demonstrated the differential presence of Wnt pathway antagonists and bone-related biomarkers like sclerostin, osteoprotegerin, and RANKL in periodontitis. The absence of a significant difference between saliva and serum sclerostin in Group 1 ($p = 0.293$) likely indicates that systemic alterations in bone turnover are minimal in periodontally and systemically healthy individuals. In contrast, the pronounced differences among diabetic subjects in Groups 2 and 3 may reflect systemic bone remodeling dysregulation, consistent with observations made by Schulte et al.² and Preshaw et al.², who highlighted the roles of pro-inflammatory Wnt5a and metabolic disturbances in the context of diabetes and periodontal disease. Moreover, the elevated serum sclerostin in diabetic-periodontitis subjects underscores the interplay between systemic bone metabolism and local periodontal inflammation. However, the limited diagnostic precision of serum due to its systemic dilution and multifactorial influences has been previously noted by Balli et al.² and Buduneli & Kinane². Biomarker fidelity is pivotal in translational periodontology. Our data emphasize GCF as a site-specific, minimally invasive, and dynamic matrix for biomolecular monitoring—an assertion aligned with the biomarker framework outlined by Buduneli

TABLE 3 Intragroup Comparison of Mean Sclerostin Levels in GCF, Saliva, and Serum

Group	Fluid Type	Sample (n)	Mean SOST (ng/mL)	SD	P value	Pairwise Comparison	P value
Group 1	GCF	12	25.7525	4.92054	<0.001*	GCF vs Saliva	<0.001*
	Saliva	12	8.5442	2.91043		GCF vs Serum	<0.001*
	Serum	12	10.7250	0.93104		Saliva vs Serum	0.293
Group 2	GCF	12	29.1092	4.36388	<0.001*	GCF vs Saliva	<0.001*
	Saliva	12	11.6567	2.23352		GCF vs Serum	<0.001*
	Serum	12	18.0308	1.38171		Saliva vs Serum	<0.001*
Group 3	GCF	12	40.1933	5.87962	<0.001*	GCF vs Saliva	<0.001*
	Saliva	12	10.3175	2.15119		GCF vs Serum	<0.001*
	Serum	12	26.7067	1.59478		Saliva vs Serum	<0.001*

and Kinane² and supported by the periodontal biomarker insights reviewed by Uitto et al.³. In summation, this study affirms the diagnostic and prognostic potential of GCF-sclerostin quantification, especially in the context of chronic periodontitis with systemic comorbidities like type II diabetes. This approach advances precision diagnostics and supports the paradigm shift toward personalized periodontal care, as envisioned by Preshaw et al.⁴ and Balli et al.⁵.

5 | CONCLUSION

Gingival crevicular fluid (GCF) shows higher sensitivity and specificity in detecting sclerostin levels compared to saliva and serum. Elevated GCF sclerostin levels correlate with increased periodontal destruction, especially in diabetic individuals. GCF-based sclerostin assessment can aid in early diagnosis, risk stratification, and monitoring of periodontal disease progression in clinical settings.

6 | LIMITATION

The small sample size and cross-sectional design limit the generalizability and causal interpretation of the findings.

7 | FUTURE PERSPECTIVE

Longitudinal studies with larger samples and GCF-based point-of-care diagnostics are warranted.

8 | ETHICAL CLEARANCE & CONSENT

Ethical approval was obtained, and informed written consent was taken from all participants prior to data collection.

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