ISSN 0973-2063 (online) 0973-8894 (print)

Bioinformation 22(10): 6825-6829 (2026)

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BIOINFORMATION
Discovery at the interface of physical and biological sciences

BIOMEDICAL INFORMATICS

www.bioinformation.net

Volume 22(10)

Research Article

Received October 1, 2026; Revised October 31, 2026; Accepted October 31, 2026, Published October 31, 2026

DOI: 10.6026/973206300226825

SJIF 2026 (Scientific Journal Impact Factor for 2026) = 8.478
2022 Impact Factor (2023 Clarivate Inc. release) is 1.9

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Edited by Vini Mehta
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Citation: Mahajan *et al*. Bioinformation 22(10): 6825-6829 (2026)

Chairside gingival crevicular blood glucose estimation for diabetes screening

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ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 22(10): 6825-6829 (2026)
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Abstract:
Diabetes mellitus is frequently underdiagnosed, highlighting the need for accessible and minimally invasive screening approaches in dental settings. Therefore, it is of interest to evaluate the reliability of gingival crevicular blood glucose (GCBG) as a chairside screening method by comparing its measurements with finger capillary blood glucose (FCBG) in patients with periodontitis. GCBG showed a strong correlation with FCBG measurements, supporting its potential utility for diabetes screening. These findings advance knowledge by highlighting GCBG assessment as a simple, minimally invasive approach for early identification of diabetes in dental practice.

Keywords: Diabetes screening, gingival crevicular blood (GCB), periodontitis, chairside diagnosis, glucose monitoring

Background:
Diabetes mellitus represents a group of metabolic disorders with far-reaching systemic consequences **[1].** It has affected 529 million adults worldwide in 2021 **[2]**. India reported 77 million cases in 2019-a number projected to surge to 134 million by 2045 **[3].** Nevertheless, a significant proportion of cases remain undiagnosed due to the asymptomatic nature of early-stage diabetes and lack of early healthcare access, leading to unchecked progression and severe systemic complications **[4].** Recognized as its sixth complication, periodontitis complicates disease management **[5–7].** This bidirectional interplay between periodontitis and diabetes, positions dental clinics as strategic venues for diabetes screening, particularly since periodontal inflammation often produces detectable gingival bleeding during routine probing-a procedure far less invasive than traditional finger-prick blood sampling. Advances in glucometer technology enable the development of minimally invasive glucose monitoring techniques **[8].** Therefore, it is of interest to evaluate the potential of gingival crevicular blood (GCB) as a viable alternative to conventional capillary blood sampling.

Materials and Methodology:
Study design:
This cross-sectional diagnostic study was conducted in the Outpatient Department of Periodontics after obtaining ethical clearance from the Institutional Research and Ethics Committee. Min no: CDC/ ERC/2023/23

Study population:
A total of 50 participants aged 20–60 years were enrolled, comprising 35 previously diagnosed diabetic patients and 15 individuals suspected of having diabetes based on clinical signs (*e.g.,* polydipsia, polyuria, unexplained weight loss) and oral manifestations (*e.g.,* severe periodontitis, gingival inflammation). All participants provided written informed consent prior to their inclusion for the study.

Inclusion criteria:
[1] Patients included in the study were within the age group of 20-60 years.
[2] Both males and females were a part of the study.
[3] The patients had moderate to severe periodontal diseases with visible signs of gingival inflammation.

Exclusion criteria:
[1] Pregnant or lactating females were not a part of the study.
[2] Patients with any blood disorder, gout or dialysis that could cause an abnormal alteration in hematocrit were excluded.
[3] Patient requiring any antibiotic pre-medication or on medications that can interfere with the normal clotting of the blood were not a part of the study.

Sample size estimation:
The calculation was performed a priori using G*Power software (version 3.1.9.7). The test was designed for a bivariate normal model correlation analysis. Based on previous pioneering and comparable studies in the literature **[9, 10]**, a large, anticipated effect size (correlation coefficient, ρ) of 0.80 was expected. The parameters for the calculation were set as follows:
[1] Type I error rate (α): 0.05 (two-tailed)
[2] Desired power (1 - β): 0.90 (90%)
[3] Anticipated correlation coefficient (ρ): 0.80

With these parameters, the minimum required sample size was determined to be n = 37. To account for potential technical challenges in sample collection (*e.g.,* insufficient bleeding, contamination) and to strengthen the robustness of the Bland-Altman agreement analysis, the sample size was increased. Therefore, a final sample of n = 50 participants was enrolled. This appropriate sample size provides a buffer against potential data exclusions and increases the precision of our estimates for both the correlation and the limits of agreement, ensuring the findings are reliable and generalizable.

Sample sites:
After assessing the periodontal status of each tooth, an appropriate site for blood collection from gingival crevice was chosen. Sites were probed using Michigan O periodontal probe with William markings. Sites with evident gingival bleeding were chosen for sample collection. Maxillary anterior and premolars were preferred because of ease of accessibility.

Suppurative sites that may alter GCF composition and lead to inaccurate results were avoided.

Sample collection:
Standardised kit – Abbott Freestyle Optium Neo H glucometer and test strips were used for screening of the patients. This is a blood glucose monitoring system designed for hospital use. Finger capillary blood sample - Blood sample for the capillary blood glucose levels was taken from the patient's soft tissue of the index finger from the non - dominant hand. The sample site was disinfected using a spirit swab and the finger was punctured using a sterile disposable lancet. The strip was then placed in the glucometer and the blood drop was collected using the reagent strip of the glucometer. The reading was noted on the Performa sheet. GCF sample - After the selection of the site, complete isolation was maintained with gauze piece, cotton rolls and high-volume saliva ejectors. Necessary precautions were taken to avoid contamination of GCF samples from adjacent sites. Any local deposits impeding the free flow of blood are removed, prior to taking the sample. The interdental papilla was probed using the periodontal probe and the gingival crevice of chosen site was observed for bleeding point. The reagent strip is placed in the glucometer. Then, the top part of reagent strip mounted on the glucometer was carefully placed in the gingival sulcus without making any contact with the adjacent gingiva and sample was collected from the bleeding site. Strip was held onto the bleeding point till the monitor showed blood glucose levels on the screen in mg/dl and recording was noted on the Performa sheet.

Results:
A total of 50 patients; 37 males and 13 females were a part of the study. These consisted of 35 previously known cases of diabetes mellitus. 15 patients were suspected to have diabetes after a general physical and oral examination and correlating their clinical signs and symptoms. **Table 1** presents the age-wise distribution of the study participants (n=50), stratified by gender and age groups. The data reveals that the majority of participants were middle-aged to older adults, with the largest proportions in the 40-49- and 60-69-year age groups (28% each). Male participants significantly outnumbered females (74% vs 26%), with this gender distribution remaining consistent across all age categories. Notably, there was minimal representation from younger adults (20-29 years: 2%) and the elderly (≥70 years: 2%). The tables summarize the agreement and correlation between Random Blood Sugar (RBS) and Gingival Crevicular Blood Sugar (GCBS) measurements. **Table 2** presents the Bland-Altman analysis, revealing a mean difference of 7.32 ± 20.45 mg/dl between RBS and GCBS, with 95% of differences falling within ±40.08 mg/dl (limits of agreement: -32.76 to 47.40 mg/dl). This indicates clinically acceptable variability. **Table 3** shows a near-perfect correlation ($r = 0.98$, $p < 0.001$) confirming that GCBS closely mirrors RBS values.

Table 1: Age Distribution of participants (n=50)

Age Group (Years)	Male (n=37)	Female (n=13)	Total (N=50)
20–29	1	0	1 (2%)
30–39	6	1	7 (14%)
40–49	10	4	14 (28%)
50–59	9	4	13 (26%)
60–69	10	4	14 (28%)
≥70	1	0	1 (2%)
Total	37	13	50 (100%)

Table 2: Agreement between random blood sugar (RBS) and gingival crevicular blood sugar (GCBS) measurements

	RBS, GCBS (N = 50)
Minimum difference	-56
Maximum difference	56
Mean difference ± SD*	7.32 ± 20.45
95% CI of lower limit**	1.12, 13.52
95% CI of upper limit	13.52, 1.12
Coefficient 95% of agreement	40.08
Limits 95% of agreement	-32.76, 47.40

** Standard Deviation; **: Confidence Interval*

Table 3: Correlation analysis

Measurement Pair	Pearson's r(P-value)
RBS vs. GCBS	0.98 (P < 0.001)

Discussion:
The high prevalence of undiagnosed diabetes globally, estimated at 44.7%, 239.7 million of affected individuals who are unaware of this condition **[9]**, In India, the undiagnosed cases are estimated to be 25% of the affected individuals **[10].** This underscores the urgent need for accessible screening methods. Traditional diagnostic approaches (*e.g.,* fasting blood glucose, post prandial blood sugar, HbA1c) face limitations due to patient non-compliance attributing to protocols involving fasting and the necessity for follow-up visits. These create barriers to early detection of diabetes mellitus. Implementation of improved tools and strategies for diabetes surveillance, especially to detect undiagnosed diabetes mellitus cases is the need of the hour. Our findings demonstrate that gingival crevicular blood glucose (GCBG) measurement offers a viable solution, providing immediate, painless results during routine dental visits without requiring additional medical appointments. The concept of chairside diabetes screening using gingival blood was first pioneered by Stein and Nebbia **[11]**, who manually transferred blood onto test strips-a technique prone to contamination and variability. Subsequent innovations, such as Tsutsui *et al.* used curette to collect the sample **[12]** and Parker *et al.* pipette method for sample collection **[8],** addressed some limitations but remained technically cumbersome. Advances in glucometer technology have been pivotal: while early devices required large blood volumes (10–15 µL) **[13],** modern systems like the Abbott Freestyle Optium Neo H (used here) enable accurate measurements with minimal sample volume (0.6 µL) and rapid results (5 seconds). Our study validates this streamlined approach, showing near-perfect correlation between GCBG and finger-prick blood glucose (FCBG) ($r = 0.98$, $p < 0.001$), consistent with previous studies **[14-17].** The strong agreement between GCBG and FCBG (mean difference: 7.32 ± 20.45 mg/dL) supports the reliability of gingival blood for

screening. Dentists play a vital role in detecting undiagnosed diabetes cases by utilizing oral manifestations, assessing risk factors during medical history and periodontal examinations and performing chair side glucose testing. This approach and the known linkage between periodontitis and diabetes mellitus; utilizes the high frequency of dental visits to identify at-risk individuals and refer them for further medical evaluation. Notably, our integrated assessment-combining periodontal findings (*e.g.,* bleeding on probing, pocket depth) with GCBG levels-identified 15 previously undiagnosed prediabetic or diabetic patients. This aligns with evidence that periodontitis severity correlates with glycemic dyscontrol **[6–8]**, reinforcing the dentist's role in early diabetes detection. It is a technique sensitive procedure. Collecting GCBS could be technically challenging and the quality of sample may vary. In a systematic review done in 2024, it was concluded that "gingival blood could be useful to identify patients with undiagnosed diabetes when necessary amount of uncontaminated blood is taken as a sample **[18].** In our study, we have elicited a standardized technique for collection of the gingival crevicular blood glucose sample. Comparison of gingival crevicular blood glucose estimation with other non-invasive technologies for diabetes screening there are a few other technologies developed for non-invasive estimation of blood glucose. Raman spectroscopy **[19]** this is an optical technique that involves incorporation of LASERs to excite glucose molecules in tissues. The amount of light scattered is used to determine glucose concentrations without needing a blood sample. Though Raman spectroscopy offers a non-contact measurement, it requires complex technology with high equipment costs and is not readily available to be integrated to routine out-patient departments. GCBG estimation, a chair side procedure involving only a periodontal probe and glucometer, which can be used for diabetic screening for all patients reporting to the outpatient department has economic benefit. The clinical utility of Raman spectroscopy is limited due to the extended calibration period involved which may last for several weeks for data analysis. Optoacoustic microscopy **[20]** uses ultrasound waves to detect glucose in different layers of skin and tissues of living beings. These waves can be detected by sensors to infer glucose concentrations. However, the sensitive equipment, high equipment cost and unavailability for routine outpatient department limit its use. Artificial Intelligence-powered devices **[21]** some devices use artificial intelligence to interpret image data captured by LASERs and cameras from a patient's finger to predict glucose levels. However, reliability and applicability to larger population might be an area of continued research. Procuring such technique sensitive devices are not financially viable and do not address the larger population. Also, there use for detecting undiagnosed diabetic cases is also questionable. Salivary Glucose can be used for glucose estimation. Saliva- a blood substitute fluid has been used as a chair side method for diabetes screening. However, the results have shown low reliability. A recent study **[22]** showed the Pearson correlation coefficient value of 0.824 of Salivary glucose with FCBG. Our study has shown GCBG estimation to have reliability and strong correlation of 0.98 with FCBG levels. While our results are promising, confirming GCBG as painless and reasonably priced in-office diabetes screening method **[23]**. However, further multicenter studies with larger cohorts are needed to standardize GCBG protocols across diverse populations. Additionally, cost-benefit analyses could assess the feasibility of implementing this screening in resource-limited settings.

Conclusion:

GCBG is a reliable, minimally invasive method for diabetes screening using modern glucometers. Detection of previously undiagnosed cases highlights the potential of dental clinics as strategic venues and the role of dentists, particularly for high-risk individuals with periodontitis, for early diabetes mellitus detection. Elimination of painful finger pricks enhances patient compliance in this approach but offering immediate results, facilitating timely referral and intervention. Future studies should explore standardized protocols for wider implementation of this promising screening strategy.

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