REVIEW ARTICLE

Gingival Crevicular Blood Glucose Detection: Screening for Diabetes in the Dental OPD

Quratulain Saeed, Sarwat Memon, Mervyn Hosein
Ziauddin College of Dentistry, Karachi, Pakistan.

ABSTRACT

The key to successful management of any disease is its timely screening and diagnosis. Undetected and uncontrolled diabetes increases the chances of oral diseases, especially periodontitis. Chronic periodontitis and diabetes are two mutually related pathologies and are known to aggravate each other's pathological effect. Since diabetes acts as an important risk factor for periodontal inflammation, it is essential to screen blood glucose levels to detect diabetes in patients presenting with chronic periodontitis. Periodontal inflammation produces ample gingival bleeding (gingival crevicular blood: GCB) during examination by the periodontal probe, which could be utilized to evaluate blood glucose levels and glycemic control at the dental office. Early screening and diagnosis of diabetes intervenes in the long-term complications of both the diseases and helps in better disease management. The objective of this review was to highlight the reliability and acceptability of different techniques using gingival crevicular blood for evaluation of blood glucose levels along with their advantages and limitations. By this literature review, we analysed over 60 studies published regarding the use of gingival crevicular blood for screening diabetes in periodontitis patients. The data was gathered via Google scholar and Medline using the keywords "Periodontitis, Inflammation, Glycemic control, Diabetes, Gingival crevicular blood" from the years 1993-2019.

Keywords: Periodontitis; Inflammation; Glycemic Control; Diabetes; Gingival Crevicular Blood.

Corresponding Author:
Dr. Quratulain Saeed
Ziauddin College of Dentistry,
Ziauddin University, Karachi, Pakistan.
Email: ainysaeed.aidm@gmail.com
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INTRODUCTION

Oral cavity acts a window to general systemic health of a person providing an overview of the health status of an individual[1]. Oral pathologies such as gingivitis, periodontitis and dental caries can give a clue to detect many undiagnosed systemic diseases and a bidirectional relationship exists between some oral and systemic diseases like periodontal disease and diabetes mellitus[2].

Diabetes mellitus is characterised by increased blood glucose levels due to impaired insulin secretion, action or both[3]. Diabetes mellitus has been expanding rapidly around the world, both in developed and developing countries, having a prevalence of 11% in Pakistan[4]. The number of diabetics is anticipated to rise above 10 million in Pakistan by the next decade[5].

Diabetes has been known to affect all the systems of the body including oral health[6]. Early management of diabetes and control of blood glucose levels helps in preventing long-term complications, which include impaired wound healing, diabetic retinopathy, diabetic neuropathy, atherosclerosis, diabetic nephropathy and oral infections[7]. There are different oral presentations of diabetes that can be distinguished amid a standard dental examination, which may caution the dental practitioner to undiscovered asymptomatic diabetes. The poorer the glycemic control, the more apparent the oral appearances of diabetes mellitus are to the clinician [8-10].

Gingival crevicular blood (GCB) is extravagated

blood produced by the gingival crevice because of periodontal inflammation. For periodontal evaluation, a probe is gently inserted into the gingival crevice to check the periodontal pocket depth[11-12]. This diagnostic procedure delivers adequate amount of blood that can be used to assess blood glucose levels [13-15].

DISCUSSION

Diabetes has its detrimental effects on all the bodily organs, including oral cavity. Some of the major oral presentations of diabetes (Table 1) are mentioned along with their pathogenesis.

Table 1: Oral manifestations of diabetes.

Oral Manifestations of Diabetes Mellitus	Mechanism of Pathogenesis
Periodontitis	Production of Advanced glycation end substances and increase in pro-inflammatory cytokines due to hyperglycaemia[16] Defective collagen synthesis[17] Defective polymorphonuclear cell function[17] Decreased repair and regeneration of periodontal tissue[18]
Dental Caries	Low salivary flow rate[19,20] Increased salivary glucose[19]
Oral Candidiasis	Immune dysfunction Increased salivary glucose Change in the oral micro flora[21]
Oral Lichen Planus	Linked to diabetes through Immune dysfunction[22]
Burning Mouth Syndrome	Peripheral neuropathy secondary to diabetes[23]
Xerostomia	Peripheral neuropathy effecting salivary gland function[19] Side effect of drugs used in the treatment of diabetes[24]
Impaired Wound Healing	Defective cross linking of collagen Vascular and immune dysfunction[25]

Timely diagnosis of diabetes aids in improving general and oral health by enhancing patient's awareness and motivation. Early diagnosis and treatment of both the diseases decreases the likelihood of continuing complications and promote periodontal and overall well-being[26]. Therefore, there is a need to open doors for diabetes screening and early recognition at a dental setup. In light of the substantial number of patients who look for dental treatment every year, a dental visit may present an astounding chance for screening of blood glucose in periodontal patients presenting with gingival bleeding[27]. The purpose of this review is to highlight the techniques through which gingival crevicular blood could be used to diagnose diabetes in patients with periodontitis along with the advantages and disadvantages of each technique.

Sample Taking

Teeth having noticeable indications of periodontal inflammation are chosen to measure glucose levels by gingival crevicular blood[28]. As salivary and plaque contamination can alter the blood glucose readings, selected teeth are isolated with cotton gauze or rolls before taking the GCB sample[29]. The periodontal probe is inserted into the gingival crevice to assess the periodontal status. In case of gingival bleeding, the glucometer stick is used to collect blood from the bleeding site[30]. The blood glucose reading is shown by the glucometer in about 5 seconds.

Another technique of GCB collection involves using micropipettes for collection of GCB from the gingival crevice and transferring it to a glucometer strip with the help of fillers[26, 31]. Pesce also used micropipettes to collect GCB from the bleeding gingival site and the GCB sample was transferred to Whatman's filter papers and refrigerated until further analysis[32]. Specialized blood collecting cards were used in a study carried out by Strauss et al. in 2012 to collect a GCB sample for determining glycaemia control of patients having gingival bleeding[29].

Gingival Crevicular Blood HbA1c Test for Glucose Assessment

Glycated haemoglobin (HbA1c) in blood gives a history of a patient's average blood glucose levels of past 3 months, which is the anticipated half-life of erythrocytes. The HbA1c is presently suggested as a gold standard for diabetes testing and control[33]. A cut off value of ≥ 6.5% has been suggested by ADA

for diagnosis of diabetes by HbA1c test[34]. Juan et al. in 2015 analysed HbA1c levels through GCB and FSB in patients with periodontitis and the optimum level of GCB HbA1c to diagnose diabetes was determined to be 5.7% with 100% sensitivity and 95% specificity[35]. In another study by Strauss et al. in 2012, GCB was used to assess HbA1c levels with the help of special blood collection cards in 120 periodontal patients. The study supported the use of GCB for HbA1c testing at a criterion value of 6.3% [29].

Determining HbA1c Values from GCB by High Pressure Liquid Chromatography (HPLC)

High Pressure Liquid Chromatography (HPLC) is a form of liquid chromatography that measures components dissolved in a solution. A study by Pesce was done in 2015, in which gingival crevicular blood was collected and HbA1c was measured by high pressure liquid chromatography technique. Positive correlation was observed between HbA1c levels of GCB and FSB samples. Linearity, carry over and stability of gingival crevicular HbA1c was evaluated as compared to finger stick blood HbA1c. The study validates the use of HPLC technique for HbA1c testing through gingival crevicular blood. This is the only study in which HPLC method has been used for gingival crevicular blood HbA1C testing[32]. Some of the benefits of utilizing HbA1c for diabetes testing include less variation in results according to the biological site of testing and no prerequisite that the patient be fasting. HbA1c shows the glycemic control of the patient over the period of 3 months, which makes the test more reliable for diagnosing diabetes. There is minimum effect of short-term sickness and stress on the HbA1c results and the test shows greater pre-analytical constancy[3]. The drawbacks of this testing procedure include its high cost and the time required to get the test results as the patient cannot get the results on the same visit. This test also shows variation in results according to red blood cell count and turnover rates. Furthermore, probing has to be repeated in case of insufficient blood available for the analysis[35]. According to a study by Greenberg et al., patients visiting a dentist prefer chair-side screening methods as compared to laboratory procedures as they yield immediate results and are cost-effective[36]. As HPLC is a complex procedure, there is unavailability of staff trained to perform the test in most of the dental setups, which adds to the limitations of this procedure[37].

GCB Glucose Screening via Glucometers

Glucometers are portable glucose self-monitoring devices, utilized by diabetics for observing their glucose levels at home with the help of a small drop of blood[30]. Glucose estimation through gingival crevicular blood is conceivable with the utilization of these glucometers due to the low amount of blood (2-4micro litres) needed to perform investigation[27]. Modern day glucometers have been reported to be fairly accurate and easy to use for blood glucose monitoring. The accuracy has been reported to get better in the glucometers manufactured in the last two decades[38].

Strauss et al. carried out a study to evaluate the utilization of GCB for measuring blood glucose by a glucometer and checked the similarity of the results with Finger stick blood glucose readings in 2 groups of patients divided according to the extent of gingival bleeding and periodontal pocket depth. The study reported that GCB was suitable for measuring blood glucose by glucometers in patients with periodontitis with sufficient bleeding on probing[29].

In 2016, Parihar et al. performed a randomized clinical trial including diabetic and non-diabetic patients. GCB glucose readings were compared to finger stick blood glucose and intravenous blood glucose readings and positive correlation was found[39]. Khader et al. in Jordan also reported strong positive correlation between GCB and FSB glucose values. The study supported the use of GCB for blood glucose assessment[40]. Another study by Sibyl et al. reported that 88% sensitivity and 100% specificity of GCB testing as compared to finger capillary blood[41]. In Germany, Beikler et al. conducted a study involving both diabetic and non-diabetic patients with moderate to severe periodontal inflammation and found that the technique is reliable, can be conveniently performed by dental practitioners and is well tolerated by patients[42].

Whereas a study conducted by Kandwal and Batra reported that, there was significant difference in mean between glucose readings of both the samples. The study was carried out on 150 patients with pre-diagnosed diabetes and periodontal inflammation[43]. Muller and Behbehani also failed to prove the utilization of GCB for blood glucose assessment and observed difference between GCB and finger stick blood glucose values[30]. The potential advantages of this technique are as follows:

1. A Non-invasive Approach

Bleeding from gingiva is a primary indication of periodontal disease. As a diagnostic protocol, dental practitioners routinely probe the gingival crevice to check for periodontal pockets. Gingival inflammation causes bleeding during routine diagnostic procedures. Gingival crevicular blood glucose testing may be utilized as a non-invasive and less painful measure to assess blood glucose values in periodontitis patients visiting dental practitioners[28,44]. Gingival crevicular bleeding that occurs during periodontal probing could be sufficient for blood glucose screening, as minimum amount of blood is required by glucose self-monitoring devices to produce results[45]. Majority of modern-day glucometers require a low amount of blood (2-6 micro-litres) to produce readings as compared to conventionally used lab procedures

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that require much larger amount of blood. Therefore, utilizing GCB for measuring blood glucose is less invasive than a finger prick with a sharp lancet and is more convenient to the periodontal patients as compared to routinely used procedures. The procedure is less painful as compared to finger prick and venepuncture as it does not produce any sensitivity or discomfort at the blood collection site[44].

2. Patient's and Provider's Acceptance

Approval by patients and dental health care providers is necessary for the application of a chair-side screening method for blood glucose assessment at a dental setup. Majority of patients appreciate the screening of systemic diseases, including diabetes by a dental practitioner[46]. According to a study 83% of patients attending a dental practice, accept chair-side blood glucose testing as a useful method to screen diabetes[47]. Rosedale and Strauss reported that the patients visiting a dental clinic for periodontal treatment as well as the dental health care providers approved GCB over finger stick blood for screening diabetes, as the method was more convenient and tolerable for the patients[48]. The method is less time consuming at it provides chair-side monitoring of blood glucose during routine periodontal examination. Studies carried out by Kotha et al. and Greenberg et al. also suggested that the periodontal patients preferred gingival crevicular blood glucose screening as a less intrusive method over conventional blood glucose assessment approaches[37,49].

3. Cost-Effectiveness

Screening for undiagnosed pre-diabetes and diabetes may prove to be a successful approach to reduce the cost of further treatment as early diagnosis may prevent both oral and systemic complications of diabetes[46,50]. In a study, Nasseh et al. reported that screening for systemic diseases including diabetes at a dental visit could save up to 327 dollars per year per person[51]. Sampling via gingival crevicular blood is convenient and cost effective in periodontal patients as sufficient amount of blood is obtained during routine periodontal probing due to inflammation and no additional blood sampling procedure are required. Furthermore, the patients can be informed about the test result instantaneously as the glucose self-monitoring device shows results within five seconds[52]. Therefore, it reduces the patient's expenses of repeated visits.

Possible Limitations

Insufficient amount of gingival crevicular blood to successfully carry out the test and difficulty of gingival crevicular blood sample isolation from saliva, Gingival crevicular fluid, food debris and inflammatory exudates, are some of the factors that may restrict the utilization of GCB for assessing blood glucose levels amid routine periodontal examination[40]. The flowchart summarizes (Figure 1) the diabetes screening techniques via GCB along with their advantages and limitations.

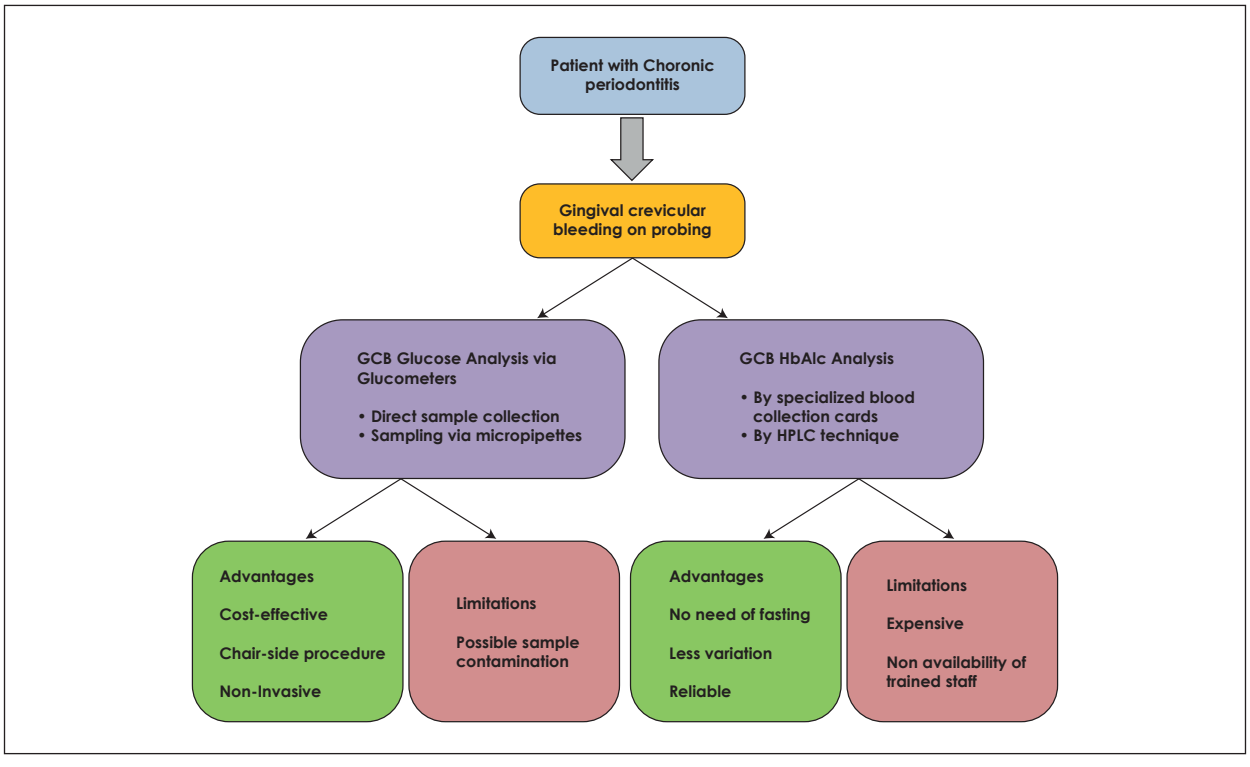

Figure 1: Summary of the techniques used for screening diabetes via gingival crevicular blood (GCB) in patients with periodontitis.

CONCLUSION

Through this literature review, a dental visit can serve as a good opportunity for blood glucose screening via gingival crevicular blood. However, there is a need to carry out more studies with larger sample size to determine the accuracy, reliability and reproducibility of this screening method. The dental professionals should be trained to conduct chair-side blood glucose analysis of patients with periodontal inflammation. Early screening and detection will help in avoiding complications of both diabetes and periodontitis, as they are two mutually related diseases.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

AUTHOR'S CONTRIBUTION

QS conceived the idea, reviewed the literature and drafted the manuscript. SM reviewed the manuscript. MH further reviewed and approved the manuscript.

REFERENCES

1. Kane SF. The effects of oral health on systemic health. Gen Dent. 2017;65(6):30-34.
2. O' Reilly PG, Claffey NM. A history of oral sepsis as a cause of disease. J Periodontol. 2000;23:13-18.
3. Am Diab Assoc. Diagnosis and classification of diabetes mellitus. J Diab Care. 2014;37(1):S81-S90.
4. Shera AS, Basit A, Fawwad A, Hakeem R, Ahmedani MY. Pakistan national diabetes survey: Prevalence of glucose intolerance and associated factors in the Punjab province of Pakistan. Prim Care Diabetes. 2010;4(2):79-83.
5. Bahadar H, Mostafalou S, Abdollahi M. Growing burden of diabetes in Pakistan and the possible role of arsenic and pesticides. J Diabetes Metab Disord. 2014;13:117-124.
6. Albert DA, Ward A, Allweiss P, Graves DT. Diabetes and oral disease: implications for health professionals. Ann N Y Acad Sci. 2012;1255:1-15.
7. Graves DT, Kayal RA. Diabetic complications and dysregulated innate immunity. Front Biosci. 2008;13: 1227-1239.
8. Tanwir F, Tariq A. Effect of glycemic control on periodontal status. J Coll Physicians Surg Pak. 2012; 22(6):371-374.
9. Punthakee Z, Goldenberg R, Katz P. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. Can J Diabetes. 2018;42(1): s10-s15.
10. Boyd R, Leigh B, Stuart P. Capillary versus venous bedside blood glucose estimations. Emerg Med J. 2005;22:177-179.
11. Somannavar S, Ganesan A, Deepa M, Datta M. Random capillary blood glucose cut points for diabetes and pre-diabetes derived from community-based opportunistic screening in India. J Diab Care. 2009;32 (4):641-643.
12. Singh VP, Bali A, Singh AN, Jaggi AS. Advanced glycation end products and diabetic complications. Korean J Physiol Pharmacol. 2014;18(1):1-14.
13. Somannavar S, Ganesan A, Deepa M, Datta M. Random capillary blood glucose cut points for diabetes and pre-diabetes derived from community-based opportunistic screening in India. J Diab Care. 2009;32 (4):641-643.
14. Armitage GC. Diagnosis of periodontal diseases. J Periodontol. 2003;74(8):1237-1247.
15. Darling-Fisher CS, Kanjirath PP, Peters MC, Borgnakke WS. Oral health: an untapped resource in managing glycemic control in diabetes and promoting overall health. J Nurse Pract. 2015;11(9):889-896.
16. Parker RC, Rapley JW, Isley W, Spencer P, Killoy WJ. Gingival crevicular blood for assessment of blood glucose in diabetic patients. J Periodontol. 1993;64(7):666-672.
17. Banerjee S, Ganguly R, Pal T. Gingival crevicular blood: A noninvasive pathway to determine blood glucose level in periodontal patients.Indian J Dent Sci. 2017;9(4):220-224
18. Ryan ME, Camu O, Kamer A. The influence of diabetes on the periodontal tissues. J Am Dent Assoc. 2003;134(1):34S-40S.
19. Pacios S, Kang J, Galicia J, Gluck K. Diabetes aggravates periodontitis by limiting repair through enhanced inflammation. FASEB J. 2012;26(4): 1423-1430.
20. Hoseini A, Mirzapour A, Bijani A. Salivary flow rate and xerostomia in patients with type I and II diabetes mellitus. Electron Physician. 2017;9(9):5244-5249.
21. Javed M, Shahid SM, Ali-ul-Qader S, Azhar A. Dental caries in diabetes mellitus: role of salivary flow rate and minerals. J Diabet Complications. 2011;25(3):183-186.
22. Bhuyan L, Hassan S, Dash KC. Candida species diversity in oral cavity of type 2 diabetic patients and their in vitro antifungal susceptibility. Contemp Clin Dent. 2018;9(1):s83-s88.
23. Petrou-Amerikanou C, Markopolous AK, Belazi M, Karamitsos D, Papanayotou P. Prevalence of oral lichen planus in diabetes mellitus according to the type of diabetes. J Oral Dis. 1998;4(1):37-40.
24. Moore PA, Guggenheimer J, Orchard T. Burning mouth syndrome and peripheral neuropathy in patients with type 1 diabetes mellitus. J Diabetes Complications. 2007;21(6):397-402.
25. Indurkar MS, Maurya AS, Indurkar S. Oral Manifestations of diabetes. Clin Diabetes. 2016;34(1):54-57.
26. Ahmed AS, Antonsen EL. Immune and vascular

dysfunction in diabetic wound healing. J wound care. 2016;25(7):35-46.
27. Kaur H, Singh B, Sharma A. Assessment of blood glucose using gingival crevicular blood in diabetic and non-diabetic patients: A chair side method. J Clin Diag Res. 2013;7(12):3066-3069.
28. Estrich CG, Araujo MWB, Lipman RD. Prediabetes and diabetes screening in dental care settings: NHANES 2013 to 2016. JDR Clin Trans Res. 2019;4 (1):76-85.
29. Strauss SM, Tuthill J, Singh G, Rindskopf D, Maggiore JA, Schoor R. Novel intra-oral diabetes screening approach in periodontal patients: Results of a pilot study. J Periodontol. 2012;83(6):699-706.
30. Muller HP, Behbehani E. Screening of elevated glucose levels in gingival crevice blood using a novel, sensitive self-monitoring device. Med Princ Pract. 2004;13(6):361-365.
31. Feroz M, Hegde S, Kashyap R. Utility of gingival crevicular blood for assessment of blood glucose in individuals with diabetes mellitus and evidence of periodontitis. J Dent Med Sci. 2014;13(1):24-27.
32. Pesce MA. Measurement of HbA1c in gingival crevicular blood using a high pressure liquid chromatography procedure. Lab Med. 2015;46(4):290-298.
33. Sherwani SI, Khan HA, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomark Insights. 2016;11:95-104.
34. Gillett MJ. International expert committee report on the role of the A1C assay in the diagnosis of diabetes. Clin Biochem Rev. 2009;30(4):197-200.
35. Juan WU, Xuan Z, Wei-bin S, Yue L, Liang-yuan L. HemoglobinA1c in gingival crevicular blood screening for diabetes. J Oral Sci. 2017;33(8):856-859.
36. Greenberg BL, Kantor ML, Jiang SS, Glick M. Patients' attitudes toward screening for medical conditions in a dental setting. J Public Health Dent. 2012;72(1):28-35
37. Bonora E, Tuomilehto J. The pros and cons of diagnosing diabetes with A1C. J Diab Care. 2011; 34(2):S184-S90.
38. Heinemann L, Volkar L, Freckmann G. Accuracy in blood glucose measurement: What will a tightening of requirements yield? J Diabetes Sci Technol. 2012;6(2):435-443.
39. Parihar S, Tripathi R, Parihar AV, Samadi FM, Chandra A, Bhavsar N. Estimation of gingival crevicular blood glucose level for the screening of diabetes mellitus: a simple yet reliable method. J Oral Biol Craniofac Res. 2016;6(3):198-203.
40. Khader YS, Al-Zu'bi BN, Judeh A, Rayyan M. Screening for type 2 diabetes mellitus using gingival crevicular blood. Int J Dent Hyg. 2006;4(4):179-182.
41. Sibyl S, Bennadi D, Kshetrimayum N, Manjunath M. Correlations between gingival crevicular blood glucose and capillary blood glucose: A preliminary report. J Lab Physicians. 2017;9(4):260-263.
42. Beikler T, Kuczek A, Petersilka G, Flemming TF. In-dental-office screening for diabetes mellitus using gingival crevicular blood. J Clin Periodontol. 2002;29 (3):216-218.
43. Kandwal A, Batra M. Gingival crevicular blood as a screening tool for diabetic patient: A randomized clinical trial. Ann Dent Spec. 2014;2(1):6-8.
44. Shetty N, Shankarpillai R, Mathur LK, Manohar B, Mathur A, Jain M. Gingival crevicular blood: As a non-invasive screening tool for diabetes mellitus in dental clinics. J Indian Soc Periodontol. 2013;17 (4): 472-477.
45. Debnath P, Govila V, Sharma M, Sainy A, Pandey S. Glucometric assessment of gingival crevicular blood in diabetic and non-diabetic patients: A randomized clinical trial. J Oral Biol Craniofac Res. 2015;5(1):2-6.
46. Creanor S, Millward BA, Demaine A, Price L, Smith W, Brown N. Patients' attitudes towards screening for diabetes and other medical conditions in the dental setting. Br Dent J. 2014;216(1):1-5.
47. Barasch A, Safford MM, Qvist V, Palmore R, Gesko D, Gilbert GH. Random blood glucose testing in dental practice. J Am Dent Assoc. 2012;143 (3):262-269.
48. Rosedale MT, Strauss SM. Diabetes Screening at the Periodontal Visit: Patient and provider experiences with two screening approaches. Int J Dent Hyg. 2012;10(4):250-258.
49. Kotha M, Kripal K, Reddy SS, Kumar PA. Type II Diabetes screening at the periodontal visit: patients experience with two screening methods- a descriptive study. EC Dent Sci. 2017;9(3):84-93.
50. Lamster IB, Kunzel C, Lalla E. Diabetes mellitus and oral health care- time for the next step. J Am Dent Assoc. 2012;143(3):208-210.
51. Nasseh K, Greenberg B, Vujicic M, Glick M. The effect of chairside chronic disease screenings by oral health professionals on health care costs. Am J Public Health. 2014;104(4):744-750.
52. Rajesh KS, Irshana R, Kumar MS, Hegde S. Effectiveness of glucometer in screening diabetes mellitus using gingival crevicular blood. Contemp Clin Dent. 2016;7(2):182-185.