

Clinical Resolution of Periodontitis Among Diabetic Patients under-Medical-Dental Coordinated Care: A Preliminary Study in Kuantan

Munirah Yaacob¹, Tin Myo Han^{1,2}, Razida Ismail³, Sorayah Sidek⁴, Padmini Hari⁵, Mohd Aznan Md Aris⁶, Iskandar Firzada Osman⁶, Mahendran Thuraiappah⁷, Fa'iza Abdulla², Than Tun Sein⁸, Roslan Bin Saub⁹

1. Kulliyah of Dentistry, International Islamic University, Kuantan, Malaysia.
2. Family Medicine Department, Kulliyah of Medicine, IIUM, Kuantan.
3. Periodontal Specialists' clinics, Klinik Kesihatan Paya Besar, Kuantan.
4. Periodontal Specialists' clinic, Klinik Kesihatan Presinct 18, Putrajaya
5. Periodontal Specialist, Faculty of Dentistry MAHSA University, KL.
6. Family Medicine Specialist, Klinik Kesihatan Jaya Gading, Kuantan, Pahang.
7. Primary Care Department, Faculty of Medicine, MAHSA University, KL.
8. Anthropology Department, Yangon University, Myanmar.
9. Department of Community Oral Health & Clinical Prevention, Faculty of Dentistry, University Malaya, Kuala Lumpur.

Abstract

The literature had reported the clinical resolution of periodontitis (CRP) in type-2 diabetic patients (T2DM-P) following non-surgical periodontal treatment (NSPT). However, the changes in glycemic control status during NSPT have not been presented clearly. Hence, this study was aimed to evaluate the CRP of T2DM-P under medical- and dental-coordinated care (M-DCC).

A 6-month follow-up quasi-experimental study was conducted on 20 T2DM-P patients who underwent M-DCC in Kuantan. M-DCC, which included the standard diabetic care was administered by medical professionals at three health clinics, while NSPT by two periodontal specialists at their respective clinics. The target glycemic control achievement (TGCA), HbA1c \leq 6.5% – was assessed at 0 and 6 months post-NSPT. Clinical resolution of PD was measured in terms of the following parameters: (1) full mouth bleeding score (FMBS); (2) clinical attachment level (CAL) (mm); (3) probing pocket depth (PPD) (mm); as well as (4) PPDs of $<$ 4 mm, \geq 4 mm, and \geq 6 mm at 0, 3, and 6 months post-NSPT respectively. Paired simple t-tests and ANOVA “F” tests were performed to interpret the clinical resolution of periodontitis as well as its relationship with TGCA.

Of fifteen (25%) uncontrolled T2DM-P patients, two (10%) patients achieved the TGCA (HbA1c \leq 6.5%) at 6 months after the completion of NSPT and M-DCC. However, no significant reductions in the overall mean HbA1c values were noted. In spite of that, there were significant differences in the CRP and all periodontal parameters at baseline and 6-month follow-up. Nevertheless, there were no significant changes in the mean CAL ($p > 0.05$).

NSPT, under M-DCC, gave rise to significant changes in the periodontal health of diabetic patients 6 months post-treatment. The effects of NSPT on HbA1c level were inconclusive. (WC:251).

Clinical article (J Int Dent Med Res 2020; 13(1): 283-289)

Keywords: Clinical resolution of periodontitis, Periodontal therapy, Target HbA1c, Type-2 diabetes, Periodontitis.

Received date: 10 October 2019

Accept date: 18 November 2019

Introduction

Periodontitis is a common, chronic, multifactorial infectious disease that affects the

*Corresponding author:

Munirah Yaacob
Kulliyah of Dentistry, International Islamic University,
Kuantan, Malaysia.
E-mail: mun_ira@iium.edu.my

periodontal attachment apparatus (i.e. the ligaments attached to a tooth, which include gingival tissues and bone). This infection is activated and sustained by an aberrant host immune-inflammatory response to bacteria in the subgingival biofilm. It is characterized by alveolar bone loss, abscess formation, tooth mobility, and eventual tooth loss.

It is widely known that periodontitis is the sixth complication of uncontrolled diabetes

mellitus¹. Since the mid-nineties, more and more scientific evidences have established the bidirectional relationship between diabetes and periodontal disease^{2,3}. Evidently, severe forms of periodontitis correlate with patients with diabetes mellitus co-morbidity⁴. It has been proposed that an inflamed periodontium can exaggerate the secretion of pro-inflammatory cytokines which reduce glycemic control and subsequently give rise to insulin resistance as well as increased risk of other diabetic complications⁵. Periodontitis has also been reported to be a useful risk indicator for pre-diabetes screening⁶. Furthermore, many randomized controlled trials (RCTs) and interventional studies have reported the clinical resolution of periodontitis (CRP) of type-2 diabetic patients with periodontitis (T2DM-P) after receiving non-surgical periodontal treatment (NSPT)⁷⁻¹⁰. However, most studies have been conducted on DM patients who visited dental offices for their oral health problems. Besides, the studies have mostly emphasized on CRP rather than the provision of treatment for glycemic control during periodontal therapies.

Realizing the importance of blood glucose control as a part of periodontitis treatment, systematic medical-dental coordinated care (M-DCC) was established at selected clinics in Kuantan, Pahang, Malaysia during a pilot project. Under the M-DCC, the T2DM-P patients were referred from medical clinics to dental clinics for non-surgical periodontal treatment by periodontal specialists. Concurrently, medical professionals provided these patients with glycemic control measures. Thus, this study was aimed to evaluate the CRP of T2DM-P in terms of FMBS, PPD, and CAL.

Materials and methods

Design

This was a quasi-experimental trial with a follow-up duration of 6 months, whereby the DM patients with periodontitis were subjected to medical-dental coordinated care (M-DCC). The M-DCC was established in Kuantan, Malaysia, by a medical-dental collaborated research team which comprised four family medicine specialists (FMS), four periodontal specialists, two medical public health specialists, and one dental public health specialist. The M-DCC included glycemic control and periodontal treatment (PT); the former was provided by four FMS, four medical officers, and four DM nurses at three public

primary care clinics (PPCCs), while the latter by two PD specialists and 4 dental nurses at two PD specialist clinics.

The process of M-DCC included an initial active screening for PD in the DM patients at the medical clinics. In this step, the Malay version of a self-reported questionnaire (SRQs-MM) was administered on the patients by the medical staff. Basic periodontal examination (BPE) was conducted by the periodontal specialists after the DM patients with periodontitis were referred to the PD specialists' clinics by the medical professionals. The purposes of M-DCC is to (i) encourage the patients to comply with their regular DM care for glycemic control and PT; (ii) provide standard DM care in accordance with 2015 clinical practices guidelines for DM in Malaysia; as well as (iii) provide NSPT in accordance with the updated 2012 national clinical practice guidelines for the management of chronic periodontitis⁽¹¹⁾; (iv) counsel the patients on the common risk factors of DM and PD (such as oral hygiene practices, smoking, exercise, and nutrition); as well as (v) exchange information on PD status and glycemic control status between the medical and dental professionals.

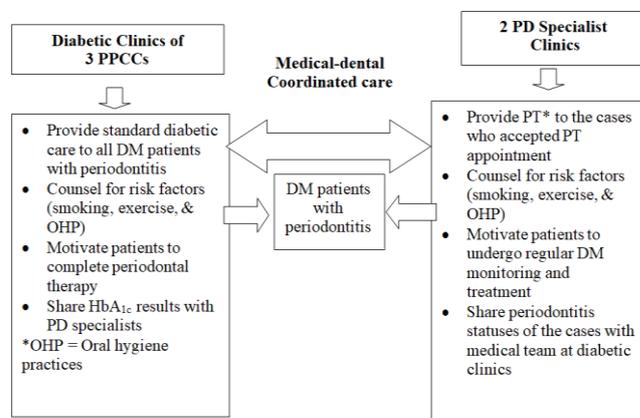


Figure 1. Provision of medical-dental coordinated care to DM patients with periodontitis at diabetic clinics of three PPCCs and two PD specialist clinics.

NSPT protocol, which was provided by the PD specialists to the T2DM-P, included oral hygiene education, full-mouth periodontal assessments, standard periodontal treatment, full-mouth root surface debridement (RSD), irrigation with 0.2% chlorhexidine (CHX), as well as prescription of chlorhexidine 0.12% mouthwash (twice a day for two weeks post-

treatment) and antibiotics (which were indicated for patients with recurrent abscesses). The standardization of the periodontal treatment protocol was done by the two PD specialists in the study. Post M-DCC, CRP in T2DM-P was measured via full mouth periodontal reassessments 3 and 6 months after the baseline measurements. The parameters of interest were FMBS, PPD, and CAL. Figure 1 summarizes the procedure of M-DCC provision.

Sample size estimation and sampling methods

A total of 123 T2DM-P from the diabetic clinics of three PPCC were recruited for the M-DCC study in accordance with the calculated sample size ($N = 124$). Although 42% (52/123) patients agreed to undergo PT for their periodontitis, only 37 visited the two PD specialist clinics, and only 20 completed the NSPT (including full periodontal reassessments) at 3 and 6 months. Data on the progress of periodontal disease of the controls (i.e. those who did not undergo NSPT) remained incomplete as they dropped out and hence, comparisons with the completed cases could not be made.

DM patients who met the inclusion and exclusion criteria were invited to participate in this study. The inclusion criteria were (i) Malaysians who were aged between 18 and 65 years, residents of Kuantan, and active DM treatment-seekers (oral antidiabetics, insulin, as well as both oral antidiabetic and insulin users) for at least one year; (ii) patients who had at least 12 teeth, as well as (iii) those who were willing to seek PT. The exclusion criteria were (i) DM patients with other known medical diseases (tuberculosis, diseases of the immunocompromised, and thyroid disorders), other dental diseases, and severe periodontitis which required surgical interventions; as well as (ii) patients who could not adhere to the study protocol. The eligible DM patients were screened for PD by the periodontal specialists using the SRQs-MM and BPE to identify the patients' periodontal health status.

HbA1c Assessment

The HbA1c results of the patients were assessed 0 and 6 months after NSPT at their respective diabetic clinics. The target glycemic control achievement (TGCA) of the patients who were under the M-DCC were classified into two groups – controlled ($HbA1c \leq 6.5\%$) and uncontrolled ($HbA1c > 6.5\%$). Patients with

glycemic control changes before and after periodontal therapy were categorized into four groups: (i) controlled before and after PT, (ii) uncontrolled before and after PT, (iii) controlled before and uncontrolled after PT, as well as (iv) uncontrolled before and controlled after PT. The HbA1c differences before and after PT were also computed and classified into three groups: (i) reducing HbA1c (negative difference), (ii) increasing HbA1c (positive difference), as well as no change (zero difference).

Periodontal Disease Assessment

Periodontal status was evaluated in terms of extent (number of affected sites) and severity of clinical parameters based on the classification system by the American Academy of Periodontology¹². The periodontal clinical parameters that were used to measure CRP were (i) probing pocket depth (PPD), which was measured from the free gingival margin to the bottom of the sulcus¹³; (ii) clinical attachment level (CAL), which was measured from the cemento-enamel junction to the bottom of the sulcus¹³; (iii) recession (REC), which was measured from the free gingival margin to the exposed cement-enamel junction¹³; as well as (iv) full-mouth bleeding-on-probing score (FMBS), which was measured as the percentage of sites that bled upon probing¹³. All measurements were recorded at six sites per tooth (mesio-buccal, disto-buccal, midfacial, mesio-lingual, disto-lingual, and mid-lingual) using a calibrated periodontal probe UNC-15 (University of North Carolina; Hu-Friedy, Chicago, IL). The reporting was done according to the consensus recommended by Holtfreter B et al 2015¹⁴.

Statistical Data Analysis

Cross-analysis, paired t-test, ANOVA "F" test, and correlation matrices were used to inferentially analyze the improvement in CRP. Specifically, the PPDs at 3 and 6 months were analyzed against TGCA differences before and after NSPT. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 16 software.

Results

The demographic details and clinical backgrounds of the 20 T2DM-P who completed NSPT (including those during the 3- and 6-month follow-ups) and had HbA1c of ≤ 6.5 are presented here. The HbA1c differences (before

and after NSPT), CRP details (in terms of FMBS, PPD, and CAL gain), as well as TGCA-CRP relationship are also presented.

Demographic Details, Clinical Backgrounds

In the study, 65% (13/20) of the patients were from the diabetic clinic of Klinik Kesehatan (KK) Paya Besar. 80% (16/20) of them underwent NSPT at the PD specialist clinics of KK Paya Besar. The majority of patients were Malays (90%), males (70%) aged 40 - 60 years (80%) had DM for less than 5 years (60%) and taking oral hypoglycemic agents (70%) (Table 1).

Target Glycemic Control Achievement Before and After NSPT

At baseline, 75% (15/20) of the patients had HbA_{1c} of $\geq 6.5\%$. After completing NSPT, 50% (10/20) achieved the target glycemic control (HbA_{1c} $\leq 6.5\%$). However, when the pre- and post-NSPT changes in TGCA were analyzed, 50% (10/20) did not achieve their target glycemic control at both points in time, with some 10% (2/20) having their statuses changed uncontrolled status (HbA_{1c} $\geq 6.5\%$) to controlled (HbA_{1c} $\leq 6.5\%$). No significant change was observed in the mean and SD of the post-PT percentage difference in HbA_{1c} when all patients were included in the analysis (Table 2).

Progress of Clinical Resolution of Periodontal Disease

CRP was measured in terms of comparisons of the mean PPD, FMBS, and CAL of the patients at 0, 3, and 6 months post-NSPT. There were significant improvements in periodontal disease parameters post-NSPT for PPD, PPD (< 4 mm), PPD (≥ 4 mm), PPD (≥ 6 mm) and FMBS ($p < 0.05$). These results are presented in Table 3.

Relationship between Clinical Resolution of Periodontitis post-NSPT and Changes in Target Glycemic Control Achievement under M-DCC

When the relationship between CRP and pre-/ post-NSPT changes in TGCA were analyzed, the average improvements of PPD (mm) and CAL (mm) were found to be significant in patients who achieved the target glycemic control before and/ or after NSPT (Table 4). Table 4 shows the periodontal parameters of the glycemia-controlled and -uncontrolled patients at 0, 3, and 6 months post-NSPT with respect to their TGCA statuses. The F value for FMBS was low but the converse was true for PPD and CAL, which showed that the variances were high. Table 5 shows the correlations of HbA_{1c} with the

parameters of periodontal disease before and 6 months after NSPT. The Pearson correlation coefficient for HbA_{1c} vs mean PPD was 0.44 and that for HbA_{1c} vs mean CAL was 0.46. Hence, there were moderate correlations between the changes in HbA_{1c} as well as (i) mean changes in PPD and (ii) mean CAL ($p \leq 0.05$). No significant correlations were noted between HbA_{1c} as well as (i) FMBS, (ii) PPD < 4 mm, and (iii) PPD ≥ 4 mm. However, a significant moderate correlation was observed between mean CAL and mean PPD ($r = -0.47$). Additionally, strong negative correlations were noted between mean PPD < 4 mm and PPD ≥ 4 mm ($r = -0.99$) as well as between PPD < 4 mm and PPD ≥ 6 mm ($r = -0.72$).

Discussion

In this study, a group of DM patients with chronic periodontitis have been selected and treated by full-mouth RSD to determine the presence of clinical differences in their CRP and TGCA following PT under M-DCC. The result did reveal statistically significant improvements in the periodontal health parameters post-NSPT. However, the reduction of mean HbA_{1c} value was insignificant at 6 months.

Reductions in PPD, as well as modest CAL gain and FMBS were obtained during the 6-month follow up, which showed the effectiveness of the RSD adopted by this study. These were in accordance with previous report^{8,15,16}, which have observed improvements in the periodontal parameters of DM patients' 1-year post-NSPT. Reductions in CRP have also been reported in many recent clinical trials even though there was an inverse effect of CRP on HbA_{1c}^{17,18}. Our study has noted that over time, all subjects had CRP reductions that were independent of their glycemic control. Upon review of the glycemic control, the initial mean HbA_{1c} level was $7.97 \pm 1.99\%$. According to Ternoven and Karjalainen (1997), the influence of diabetes on periodontal tissue health could be more significant if diabetic control (HbA_{1c}) was constantly $> 10\%$ (such a value could also increase the vulnerability to other diabetic complications)¹⁹. Thus, in order to verify the effectiveness of NSPT in the periodontal health of T2DM-P, it might have been better to recruit T2DM-P (without other comorbidities) who had HbA_{1c} of $> 10\%$ at baseline while controlling for other confounders.

Many researches have considered the degree of glycemic control to be an important determinant of severe periodontitis owing to its negative effects on the treatment outcomes in light of exaggerated host inflammatory responses, deficient healing, and reduced resistance²⁰⁻²³.

Even though the reduction in mean HbA_{1c} was not statistically significant, two subjects (10%) who initially presented with uncontrolled diabetes had a TGCA of < 6.5% following PT. While the mean reduction in HbA_{1c} in this research was small (0.18%; 95% CI: -0.84 -- 0.48), it was still within the ranges reported in many prior studies^{6,24,25}. The small reduction could have been related to variations in the HbA_{1c} levels between the subjects during initial treatment; the same point has been raised by Mizuno (2017)¹⁷. However, the said improvement should be interpreted with caution, as the number of subjects in this preliminary study was small. PT which was aimed at reducing the microbial bio-burden in the oral cavity and inflammation within the periodontium might eventually result in the reduction of serum markers and mediators of systemic inflammation, subsequently increasing insulin sensitivity and improving glycemic control²⁶. The importance of HbA_{1c} reduction is related with the likely reduction in the risk of diabetic complications, with the lowest risk occurring in those with HbA_{1c} values within the normal range (< 6.0%)²⁷.

Under hospital-based medical-dental collaborative care, a similar study in Japan has reported a larger reduction of HbA_{1c} value - 2.5% in 50% of the subjects following completion of NSPT²⁸. Evidently, this value was much higher than that those of many meta-analyses since 2010^{6,24,25,29}. However, they mentioned that the concomitant initiation of diabetic medications at the beginning of periodontal treatment played a major role in HbA_{1c} reduction. Conversely, some studies have reported that PT alone might not be sufficient for improving glycemic control. Accordingly, they have suggested that other factors were involved in the control of diabetes^{30,31}, examples of which included changes in the subjects diets, BMI, and physical activities. Despite close monitoring of adherence to anti-diabetic medications and NSPT under M-DCC, three subjects had worsening glycemic statuses (from controlled to uncontrolled), thus suggesting that self-management behaviors do have some role in glycemic control.

In this study, none of the subjects had indications for antibiotics. However, pocket irrigation with 0.12% chlorhexidine digluconate post-RSD has been performed in all subjects as per our protocol. Nevertheless, systematic reviews on subgingival irrigation in the treatment of periodontitis were inconclusive owing to the lack of standardizations in the research methodologies³². We have performed subgingival irrigation in view of the high risk of infection in the T2DM-P patients. Evidently, the conventional therapy was administered on more than 50% of the subjects of this study as some of them did not manage to undergo one-stage-full-mouth-RSD in view of discomfort and the time-consuming nature of the procedure. Previous researches did not reveal significant differences in the CRP when conventional therapy was administered on DM and non-DM subjects^{31,33}. In spite of that, some authors have recommended that one-stage-full-mouth approach be done to improve the CRP in DM patients, in accordance with Rodrigues et al. (2003) and Schara et al. (2006)^{34,35}. This approach was believed to help to minimize the risk of cross-infections and reinfections at the treated areas in subjects who were highly susceptible infections (e.g. diabetics)³⁴. Some authors have suggested the use of low level laser therapy (LLL) as an adjunct to NSPT. They have reported improved clinical parameters and decreased level of HbA_{1c} and high-sensitivity C-reactive protein³⁶.

It can be postulated that the optimization of diabetic care coordination under the M-DCC protocol – which included close monitoring of the subjects' TGCA and other metabolic parameters –, in addition to NSPT, continuous reinforcement of OHI, as well as and advised to comply to treatment-compliance advice by both physicians; the physician and dentists in that achieved during this study were can be associated with improved the positives CRP. Likewise, a Japanese study conducted earlier in 2013 that adopted a collaborative clinical pathway program to treat ten T2DM-P patients has reported; positive glycemic control with significant improvements in of PPD and FMBS²⁸. A qualitative research has revealed that DM patients perceived the existence of a divide between the medical and dental professions, which had a potentially negatively impact on diabetic care³⁷. Hence, the M-DCC can facilitate patient-physician-dentist communications, shared decision-making, and

understanding of patient healthcare needs for the successful management of T2DM-P with its inherent complexity and frequent multi-morbidities^{38,28}.

For future studies, we would like to propose the adoption of common patient- management forms that include the patients' treatment details for diabetes and periodontal disease treatment details, review schedules, etc. These should, be shared online for access by health care providers and patients in order to reduce the study dropouts from the study. In addition, as per within our subjective observations, diabetic subjects who were under M-DCC better engaged with dental treatment following receipt of advice from their physicians. Moreover, the physicians who participated in this study had a deeper understanding of the bidirectional effects of T2DM-P and the significance of periodontal management in the patients' general well being.

Conclusions

This study has shown that effective NSPT under M-DCC gave rise to significant improvements in the clinical periodontal health parameters of diabetic patients after 6 months. Improvements in TGCA have been noted in two patients. However, the effectiveness of NSPT in lowering HbA_{1c} was inconclusive, presumably due to the small sample size and absence of control groups. Nevertheless, periodontal treatment should be included in the measures for preventing and managing diabetes.

Acknowledgements

We thank the Ministry of Health Malaysia, KK Paya Besar, KK Jaya Gading and KK Kurnia community clinic for their support in this study.

The study was supported by grants from the International Islamic University of Malaysia (IIUM) Endowment Type B (IREC-308), MAHSA University, Malaysia (RP 70-10/14) and Research Initiative grant (RIGS 16-330-0494).

Declaration of Interest

The authors report no conflict of interest.

References

1. Loe H. Periodontal Disease: The sixth complication of diabetes mellitus. *Diabetes Care*. 1993;16:329-334.

2. Southerland JH, Taylow GW, Offenbacher S. Diabetes and Periodontal Infection: Making the Connection. *Clinical Diabetes*. 2005;23(4):171-178.
3. Winning L, Linden GJ. Periodontitis and Systemic Disease: Association or Causality? *Current Oral Health Rep*. 2017;4:1-7.
4. Harsas NA, Lessang R, Soeroso Y, Putri GA. Periodontal Status Differences between Chronic Periodontitis Patient with and Without Type 2 Diabetes Mellitus. *Journal of International Dental and Medical Research*: 2019; 12 (1):175-180
5. Ohlrich EJ, Cullinan MP, Leichter JW. Diabetes, periodontitis and the subgingival microbiota. *Journal of Oral microbiology*. 2010;2(1):5818.
6. Teeuw WJ, Gerdes VEA, Loos BG. Effect of Periodontal Treatment on Glycemic Control of Diabetic Patients, A systematic review and meta-analysis. *Diabetes Care*. 2010;33(2):421-427.
7. Tsoigny-Tsague NF, Lontchi-Yimagou E, Nana EARN, et al. Effects of nonsurgical periodontal treatment on glycated haemoglobin on type 2 diabetes patients (PARODIA 1 study): a randomized controlled trial in a sub-Saharan Africa population. *BMC Oral Health*. 2018;18(1):28.
8. Hayashi J, Hasegawa A, Hayashi K, et al. Effects of periodontal treatment on the medical status of patients with type 2 diabetes mellitus: a pilot study. *BMC Oral Health*. 2017;17(1):77.
9. Raman RPC, Taiyeb Ali TB, Chan SP, Chinna K, Vaithilingam RD. Effect of nonsurgical periodontal therapy verses oral hygiene instruction on Type 2 diabetes subjects with chronic periodontitis: a randomised clinical trial. *BMC Oral Health*. 2014;14(1):79.
10. Kiran M, Arpak N, Ünsal E, Erdoğan MF. The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. *J Clin Periodontol*. 2005;32(3):225-72.
11. Ministry of Health Malaysia. Clinical practice guideline: Management of Chronic Periodontitis. Oral Health Division. 2012.
12. Armitage GC. Development of classification system for periodontal disease and conditions. *Ann Periodontol*. 1999;4(1):1-6.
13. Spolsky V. The epidemiology of gingival and periodontal disease. In: Carranza FA, ed. *Glickman's Clinical Periodontology*. 7th ed. Philadelphia, PA: W.B.Saunders Co; 1990.
14. Holtfreter B, Albandar JM, Dietrich T, et al. Standards for reporting chronic periodontitis prevalence and severity in epidemiologic studies: Proposed standards from the Joint EU/USA Periodontal Epidemiology Working Group. *J Clin Periodontol*. 2015;42(5):407-12.
15. Miller LS, Manwell MA, Newbold D, et al. The Relationship Between Reduction in Periodontal Inflammation and Diabetes Control: A Report of 9 Cases. *J Periodontol*. 1992;63(10):843-848.
16. Seppala B, Ainamo J. A site by site follow-up study on the effect of controlled versus poorly controlled insulin-dependent diabetes mellitus. *J Clin Periodontol*. 1994;21(3):161-165.
17. Mizuno H, Ekuni D, Maruyama T, et al. The effects of non-surgical periodontal treatment on glycemic control, oxidative stress balance and quality of life in patients with type 2 diabetes: A randomized clinical trial. *PLoS one*. 2017;12(11):e0188171.
18. Goel K, Pradhan S, Bhattarai MD. Effects of nonsurgical periodontal therapy in patients with moderately controlled type 2 diabetes mellitus and chronic periodontitis in Nepalese population. *Clinical, Cosmetic and Investigational Dentistry*. 2017;9:73-80.
19. Tervonen T, Karjalainen K. Periodontal disease related to diabetic status. A Pilot study of the response to periodontal therapy in type 1 diabetes. *J Clin Periodontol*. 1997;24:505-510.
20. Lalla E, Lamster IB, Feit M, et al. Blockade of RAGE suppresses periodontitis-associated bone loss in diabetic mice. *J Clin Invest*. 2000;105(8):1117-1124.

21. Grossi SG. Treatment of Periodontal Disease and Control of Diabetes: An Assessment of the Evidence and Need for Future Research. *Ann Periodontol.* 2001;6(1):138-145.
22. Mealey BL, Ocampo GL. Diabetes mellitus and periodontal disease. *Periodontol 2000.* 2007;44(1):127-153.
23. Martijn J. L. Verhulst, Bruno G. Loos, Victor E. A. Gerdes, Wijnand J. Teeuw. Evaluating All potential oral complication of Diabetes Mellitus. *Front Endocrinol (Lausanne)* 2019; 10: 56. doi: 10.3389/fendo.2019.00056
24. Preshaw PM. Diabetes and periodontal disease. *Int Dent J.* 2008;58(S4):S237-S243.
25. Teshome A, Yitayeh A. The effect of periodontal therapy on glycemic control and fasting plasma glucose level in type 2 diabetic patients: systematic review and meta-analysis. *BMC Oral health.* 2017;17(1):31.
26. D'Aiuto F, Parkar M, Andreou G, et al. Periodontitis and systemic inflammation: control of the local infection is associated with a reduction in serum inflammatory markers. *J Dent Res.* 2004;83(2):156-160.
27. Stratton IM, Adler AI, Neil HAW, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BM Jour.* 2000;321:405-412.
28. Ota M, Seshima F, Okubo N, et al. A Collaborative Approach to Care for Patients with Periodontitis and Diabetes. *Bull Tokyo Dent Coll.* 2013;54(1):51-57.
29. Li Q, Hao S, Fang J, Xie J, Kong XH, Yang JX. Effect of non-surgical periodontal treatment on glycemic control of patients with diabetes: a meta-analysis of randomized controlled trials. *Trials.* 2015;16(1):291.
30. Christgau M, Palitzsch KD, Schmalz G, Kreiner U, Frenzel S. Healing response to non-surgical periodontal therapy in patients with diabetes mellitus: clinical, microbiological, and immunologic results. *J Clin Periodontol.* 1998;25(2):112-124.
31. Rodrigues DC, Taba Jr M, Novaes Jr AB, Souza SL, Grisi MF. Effect of Non-Surgical Periodontal Therapy on Glycemic Control in Patients with Type 2 Diabetes Mellitus. *J Periodontol.* 2003;74(9):1361-1367.
32. Nagarakanti S, Gunupati S, Chava VK, Reddy BVR. Effectiveness of Subgingival Irrigation as an Adjunct to Scaling and Root Planing in the Treatment of Chronic Periodontitis: A Systematic Review. *J Clin Diagn Res.* 2015;9(7):ZE06-ZE09.
33. Faria-Almeida R, Navarro A, Bascones A. Clinical and Metabolic Changes After Conventional Treatment of Type 2 Diabetic Patients With Chronic Periodontitis. *J Periodontol.* 2006;77(4):591-598.
34. Rodrigues DC, Effect of Non-surgical periodontal therapy on glycemic controls in patients with Type-2 Diabetes Mellitus. *J Periodontol.* 2003;74:1361-1367
35. Schara R, Medvescek M, Skaleric U. Periodontal disease and diabetes metabolic control: a full-mouth disinfection approach. *J Int Acad Periodontol.* 2006;8(2):61-6.
36. Bunjaku V, Popovska M, Grcev A, Mrasori S, Kameri A, Sllamniku Z, Dragidella F. Non-surgical Periodontal Treatment and Low Level Laser Therapy (LLLT) Outcomes for Patients Suffering from Type 2 Diabetes Mellitus, Obesity and Chronic Periodontitis. *Journal of International Dental and Medical Research* 2017; 10 (2):214-221
37. Bisset SM, Stone KM, Rapley T, Preshaw PM. An exploratory qualitative interview study about collaboration between medicine and dentistry in relation to diabetes management. *BMJ Open.* 2013;3(2):e002192.
38. Hummel J, Gandara BK. Health Information Exchange and Care Coordination of Diabetic Patients Between Medicine and Dentistry. *Diabetes spectrum.* 2011;24(2):205-210.