# THE IMPACT OF PERIODONTAL THERAPY ON PERIODONTAL PATIENT WITH TYPE 2 DIABETES MELLITUS.


## ABSTRACT:

Diabetes is a common disease with many oral manifestations; persistent poor glycemic control has been associated with the incidence and progression of diabetes related complications including gingivitis and periodontitis which the most common cause of tooth loss, evidence suggests that periodontitis affects glucose control in diabetes.

The periodontitis induced bacteremia will cause elevation in serum pro inflammatory cytokines leading to hyperlipidermia and ultimately causing an insulin resistance syndrome and contributing to destruction of pancreatic beta cells. Treating chronic periodontal infections is essential for managing diabetes. Aim of this literature review is to examine the effect of periodontal therapy on glycemic control in type II diabetic patients.




## INTRODUCTION:

Type 2 diabetes mellitus and obesity are the severe nutritional disorders of multyfactorial nature, which altered almost over 100 million population. ( Gursoy UK, Marakoglu, Ersan S.)Patient with diabetes have increased incidence and severity of periodontal disease not accounted for by differences in the sub gingival microbial infection poor glycemic control has been consistently associated with periodontal disease severity. Also recent evidence suggests that hyper glycemia may induce inflammatory cytokine production. (Engebretson SP, Hey-Hadavi J, Ehrhardt FJ, Hsu D, Celenti RS,Grbic JT, Lamster IB.)Deep pockets were closely related to current glucose toleranc Engebretson SP, Hey-Hadavi J, Ehrhardt FJ, Hsu D, Celenti RS,Grbic JT, Lamster IB.) Deep pockets were closely related to current glucose tolerance status and the patient with glucose

intolerance has more deep pockets. Further studies suggested that periodontitis affects glucose control in diabetes. (Saito T, Shimazaki Y, Kiyohara Y, Kato I, Kubo M,Iida M, Koga T.) . Diabetes had fewer caries and plaque, lower salivary flow rates and buffer effect, and more frequent growth of yeasts than their non-diabetic control. (Siudikiene J, Machiulskiene V, Nyvad B, Tenovuo J, Nedzelskiene I.)Periodontal disease is most common cause of tooth loss. It has insidious onset, chronic course and commonly result due to cumulative effect of dietary habits, oral hygiene methods and oral habits practiced over the years.( Shah N , Sundaram KR.)

Diabetes is a group of infections and lesions affecting the periodontal tissues that form that attachment apparatus of a tooth. (Stegeman CA.)

Laminin 5(ln-5) is involved in the afical migration of epithelial cells during the development of periodontal pockets. Low-dose doxycycline (LDD) can therapeutically modulate the host response with its non-anti microbial properties. (Emingil G, Atilla G, Sorsa T, Savolainen P, Baylas H.) Taylor GW.

In addition, evidence supports the observation that periodontal infections contribute to problems with glycemic control( Taylor GW.)

for e.g.: adults with diabetes who received ultrasonic scaling curettage in combination with systematically administrated at three months, significant reduction in mean HbA1c nearly 10% from pretreatment value.(Grossi SG, Skrepcinski FB, DeCaro) Evidence suggests that periodontitis induced bacteremia will cause elevation in serum pro inflammatory cytokines, leading to hyperlipidermia and ultimately causing an insulin resistance syndrome and contributing to destruction of pancreatic beta cells.( Iacopino AM.) Treating chronic periodontal infections is essential for managing diabetes.

**Literature REVIEW**:

Type 2 diabetes mellitus patient were 2.8 times more likely to have destructive periodontal disease( Emrich LJ, Shlossman M, Genco RJ (1991).and 4.2 times more likely to have alveolar bone loss progression.( Taylor G, Burt B, Becker M, Genco RJ,

ShlossmanM(1998a). periodontal disease has been considered to be another complication of diabetes mellitus and evidence (Lo¨ e H (1993). also support poorer glycemic control contributing to poorer periodontal health.( Ainamo J, Lahtinen A, Uitto V 1990; Unal T, Firatli E, Sivas A, Meric H, Oz H 1993; Novaes AJ, Gutierrez F, Novaes A 1996; Taylor G, Burt B, Becker M 1998b)

Recent studies illustrated the syenergistic relasionship between diabetes and periodontics.sever periodontics was associated with poor glycaemic control and exacerbated diabetes included hyperglycaemia .Although it has been ( Taylor, G. W., Burt, B. A., Becker, M. P.,

Genco, R. J., Shlossman, M., Knowler, W. C.& Pettitt, D. J. (1996) . Although it has been reported that improved metabolic control may lead to improved periodontal health,( Sastrowijoto, S. H., van der Velden, U., vanSteenbergen, T. J., Hillemans, P., Hart, A. A.,de Graff, J. & Abraham-Inpijn, L. (1990) It is still unclear whetherthe control of periodontal infection may improve the metabolic control of diabetes.The aim of the present study was to investigate the effect of improved periodontal health on metabolic control in type 2 Dm patients. It is known that infections are often accompanied by tissue insulin resistance Vki-Jarvinen, H., Sammalkorpi, K., Koivisto,V. & Nikkila, E. (1989) A recent study has demonstrated that during the acute phase of a bacterial infection, insuline resistance increased by 33% whereas during the convalesce period it increased by 28% (sammalkorpi 1989).moreover ,Grossi, S. G., Skrepcinski, F.B., DeCaro, T.,Zambon, J.J., Cummin, D. & Genco, R. J. 1996)have suggested that chronic gram-negative infections and chronic endotoxemia, such as is seen in periodontal disease could also induce insulin resistance and a worsening of metabolic control in diabetic patients.In view of these facts, it has been hypothesized that control of periodontal infections improves metabolic control of diabetes.

one study investigated several microbial treatments in type 2 diabetics.,to determine their efficacy compared to conventional non surgical therapy.(Grossi 1996) Another report examined the correlation between gingival bleeding and blood glucose levels in 9 diabetics with moderate –to – sever periopdntitis( .Miller LS, Manwell MA, Newbold D,

Reding ME, Rasheed A,Blodgett J,Kornman KS.1992) In this study ,glycated hemoglobin (HbA 1c)and glycated albumin were determined prior to periodontal therapy, and 4 and 8 weeks after therapy. Periodondal therapy consisted of 1 and 2 sessions of root planning, oral hygine instructions, doxycycline 100 mg for 14 days, and polishing at 2 weeks.A nonsignificant decrease in HbA1c from 9.44% to 9.01% was observed in the 9 subjects.Glycated albumin levels did not change after therapy 5 to 9 subjects had a consistent reduction in bleeding on probing (reduced at 4 to 8 weeks) In these 5 subjects ,HbA1c was reduced from 8.7% to 7.8%,which was statistically significant Therefore, this small , short-term pilot study suggested that controlling periodontal inflammation may improve metabolic control of diabeties. (Grossi S. G., Skrepcinski, F.B., DeCaro, T.,Zambon, J.J., Cummin, D. & Genco, R. J.1996).

Study of 85 type 2 diabeties mellitus Native Americans (Grossi S. G., Skrepcinski, F.B., DeCaro, T.,Zambon, J.J., Cummin, D. & Genco, R. J.1996). It was found that fasting blood glucose did not significantly improve after periodontal treatment, but a statically significant decrease in HbA1c was observed. This improvement was attributed to be a possible effect of doxycycline inhibition of glycation of hemoglobin. These findings were discussed in further detail in a subsequent report (grossi, S.G, Skrepcinski, included an additional 28 subjects .In the treatment group which exhibited the greatest improvement, baseline HbA1c level was 10.5% and decreased to 9.6% 3 months after periodontal treatment. However, by the 6 months examination, HbA1c levels returned to baseline, in spite of continuing improvement in periodontal probing depths and attachment levels. In this report, periodontal therapy, in addition to doxycycline,was credited for the improvement in HbA1c.

There is strong evidence to suggest that the incidence and severity of periodontics is influenced by the presence or absence of diabetes of mellitus, as well as the degree to which the disease in control by patients (. Bacic M, Plancak D, Granic M 1988 Emrich IJ, Shlossman M, Genco RJ.1991, Lalla E, Lamster IB, Schmidt AM1998, Nelson RG, Shlossman M, Budding IM,PettitDj,Saad MF, Genco Rj, Knowler Wc 1998 Novaes AB Jr, Gutierrez FG, Novaes AB.1996. Oliver RC, Tervonen T1993, Ringelberg ML, Dixon

DO, Francis AO, Plummer RW1977, Shlossman M, Knowler WC, Pettitt DJ, Genco RJ. 1990, Ternoven T, Oliver R.1993) other report indicate that the existence sever generalized periodontitis may adversely influence the control of underlying systemic disease (Grossi SG, Genco RJ. 1998 Grossi SG, Skrepcinski FB, DeCaro T, Zambon JJ, Cummins D, Genco RJ.1996, . Miller LS, Manwell MA, Newbold D, Reding ME, RasheedA, Blodgett J, Kornman K. 1992Sammalkorpi K.1989. . Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M.Kinder WC,Pettitt DJ1998, William R,Mahan C.1960, . Y ki-Jarvinen, H., Sammalkorpi, K., Koivisto,V. & Nikkila, E. (1989)). Epidemiological data indicate the growing elderly population has a far higher incidence of type 2 diabetes mellitus than do younger age groups (Gottsegen R.1990, Mealey BL 1998, Nathan DM, Dale DC, Federman DD, 1996, United States Pharmacopeia Drug Information1998).

Certain systemic disease, such as diabetes mellitus (DM), are known to increase this risk (.Grossi,S., Zambon, J,Ho,1994) Page, R. C. & Beck, J. D. (1997c). Less research attention has been paid to roll that chronic oral disease may play in systematic disease, despite the possibility that the morbidity and mortality rates of some diseases might be reduced by an improvement in periodontal health. (Beck , J. D., Garcı´a, R., Heiss, G., Vokonas, P.S. & Offenbacher, S. (1996), Offenbacher, S., Katz, V., Fertik, G. (1996) Grossi &Genco RJ,1998, Scannapieco,F.A.& ,Genco R,J,1999).Periodontitis as a chronic localized oral infection that tiggers a systematic as well as local host immune-inflammatory response and that can be a source of bacteraemia, because of the large epithelial surface with uncerated periodontal, pockets (Ebersole ,J.L.&Cappelli,D.2000). Periodontitis, especially in its severe clinical form,is currently considered to influence the pathogenisis orincrease the risk of some systematic diseases (Garsia R,Henshaw, M.&Krall,E.2001).the biological relationship between DM and periodontal disease is well documented (Mattson J. S. & Cerutis, R. (2001) ,Soskoline ,W.A. & Klinger, A.2001).Periodontal disease and DM are closely associated and are highly prevalent chronic diseases with many similarities in pathobiology. Inflammation is a critical player in the association,& its importance is just now coming to light(Mealey, B. L,& Oates,

T.W. (2006) 2006)DM,the most common human endocrinal disease,is characterized as a metabolic disorder associated with a chronic highper glycaemic state.It was first demonstrated that DM was a risk factor for periodontitis and substiquently the inverse relationship was proposed,i.e. that periodontitis may be a risk factor for diabetic decompensation, and this hypothesis has been supported by various studies (. Grossi, S.G.2001, Iacopino AM. 2001, Lalla E, Lamster IB, Stern DM, Schmidt AM2001, Taylor GW. 2001, Katz, J, Bhattacharyya, I, Farkhondeh- Kish, F, Perez, F.M, Caudle, R.M.&Heft, M. W. (2005), Takeda, M, Ojima, M, Yoshioka, H. Inaba, H, Kogo, M, Shizukuishi, s, Nomura,M.& Amano,A (2006) Lim, L.P, Tay, F.B.K, Sum, C.F.& Thai, A.C.&2007 Rea). Several recent experimental studies have addressed the mechanisms underlying the interaction in between DM and periodontitis. All reported a strong inflammatory response characterized by a large secretion of inflammation mediators, mainly pro-inflammatory cytokines, which can have both local (periodontal destruction) and systemic (impaired glycaemic control) effects( Grossi ,S.G.(2001) Iacopino ,A.2001, Lalla ,E,Lamster, I, Stern, D.& Schmidt, A.M.(2001), Nishimura ,F, Iwamoto, Y., Mineshiba, J., Shimizu, A., Soga, Y. & Murayama, Y. 2003, Genco ,R.J., Grossi, S.g., Ho, A., Nishimura, F.& Murayama, Y.2005). Various studies have been published on the effect of periodontal treatment on DM control. Although some authors found (Miller,L. S., Manwell, M,A., Newbold, D. 1992, . Grossi, S. G., Skrepcinski, F.B., DeCaro, T., Zambon, J.J., Cummin, D. & Genco, R. J. 1996, Grossi SG, Skrepcinski FB, DeCaro 1997, Iwamoto, Y., Nishimura, F., Nakagawa, M.2001, Rodrigues, D., Taba, M., Novaes, A., Souza, S. & Grisi, M. 2003, Kiran , M., Arpak, N., Unsal, E.& Erdogan, M.F.2005) that periodontal therapy may have a beneficial effect on glycaemic controlo, not allreported this improvement (seppala ,B., Seppala, M.& Ainamo, J.1993, Seppala & Ainamo ,J.1994, Aldrdge,J. P., Lester, V., Watts, T.L.P, Collins, A., Viberti, G.& Wilson, R. F. 1995, Smith,G.T., Greenbaum, C.J., Johnson, B. D. & Persson, 1996, westfelt ,e., Rylander, H., Blohme, G., Jonasson, P. & Lindhe,J.1996, Christgau, M.,Palitzsch, K-D., Schmalz, G., Kreiner,U.&Frenzel, S.1998, Hagiwara et al 2002, Jones, J. A., Miller, D. R., Wehler, C. J., Rich, S. E., Krall-Kaye, E. A., McCoy, L. C., Christiansen, C. L.,

Rothendler, J.A.& Garcia, R. I. 2007). Even now, at the beginning of 21st century, the scientific evidence remains inadequate and inconclusive. With this background, a cynical study was designed to determine whether an improvement in the periodontal status of type 2 diabetic subjects is accompanied by an improvement in their metabolic control

Microbial dental plaque is the initiator of periodontal disease. Systemic factors modify all forms of periodontitis principally through their normal effects on the normal immune and inflammatory defences. Periodontal disease has been characterized as the sixth complication of diabetes. (Loe H. 1993) .A 1995 report (Aldridge JP, Lester V, Watts TL, Collins A, Viberti G, Wilson RF. 1995) confirmed that metabolic control may be the most important factor between periodontal health and IDDM. These data support the hypothesis that diabetes and the level of metabolic control are important modifiers of periodontitis.

Data on the efficacy of periodontal care on improving glycaemic control in poorly controlled diabetes are equivocal (.. Taylor GW 1999,2001,2003,US Department of Health and Human & Services. 2000) .A two way relationship between diabetes and periodontitis has been postulated (Grossi, S.G., & Genco, R J, 1998; Iacopino, A. 2001), but supportingdata are sparse. Several studies suggest that improvements in periodontal condition will improve glycaemic control (Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A,Blodgett J,Kornman KS 1992,Taylor, G. W., Burt, B. A., Becker, M. P.,Genco, R. J., Shlossman, M., Knowler, W. C.& Pettitt, D. J 1996, Grossi SG, Skrepcinski FB, DeCaro 1997; St Iwamoto ,Y., Nishimura, F., Nakagawa, M. Sugimoto, H., Shikata, K., Makino, H., Fukuda, T., Tsuji, T., Iwamoto, M. & Murayama, Y.2001. Stewart, J.E., Wager, K.A., Friedlander, A. H. & Zadeh, H. H. 2001).

Epidemiological studies have demonstrated an association between both types of diabetes and periodontal disease (Emrich LJ, Shlossman M, Genco RJ. 1991, Moore PA, Weyant RJ, Mongelluzzo MB, Myers DE, Rossie K, Guggenheimer J, Block HM, Huber H, Orchard T.1999). However increased periodontal risk is often related to duration and adequacy of control of the diabetic state. For example, it has been noted that individuals with non-insulin-dependent diabetes mellitus have a three-fold increased risk of

developing periodontal disease theat can not otherwise be explained on the basis of age, sex or oral hygiene (Emrich LJ, Shlossman M, Genco RJ. 1991). Study (. Sastrowijoto, S. H., van der Velden, U., van Steenbergen, T. J., Hillemans, P., Hart, A. A., de Graff, J. & Abraham- Inpijn, L. 1990) that showed that individuals with poor metabolic control had increased attachment loss compared to well-controlled subjects, despite similar oral hygiene levels. It is also well documented that diabetic patients have a compromised ability to respond to bacterial infections, and it has been proposed that it is this compromised host response that in part may increase diabetics risk of periodontal disease. Interestingly, the reverse possibility that the periodontal infection may exacerbate the diabetic condition is now beginning to receive increasing attention (Grossi, S. G. & Genco, R. J. 1998) . The presence of glycated hemoglobin in the circulation and in tissues, resulting from the hyperglycemia of diabetes, is believed to be a contributing factor to the degenerative micro vascular and arterial changes that are common sequelae of diabetes. A study of the Gila river Indian community, a population having a prevalence of non-insulin-dependent diabetes mellitus of about 50%. Has recently tested the hypothesis that severe periodontitis in individuals with non-insulin-dependent diabetes mellitus increases the concentration of glycated hemoglobin. (Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M1998) The results showed that severe periodontitis at baseline was associated with increased risk of having poor glycaemic control at follow-up 2 or more years later. If periodontal disease does affect diabetic status, we would expect that treating periodontal disease would reduce the severity of diabetes. A recent systematic review of the literature by Grossi, S. G. & Genco, R. J. 1998). Concluded that the effect on diabetic status was dependent upon the treatment modality. Studies that investigate the effect of only mechanical debridement were unable to demonstrate any effect on blood glucose level or glycated hemoglobin level regardless of periodontal disease severity or degree of diabetes control Aldridge JP, Lester V, Watts TL, Collins A, Viberti G, Wilson RF, 1995, O'Neil TC 1979, Seppala B, Ainamo J. 1994). However, all three studies that added systemic antibiotics to mechanical debrident demonstrated improved metabolic control of diabetes 2. (Miller LS, Manwell MA,

Newbold D, Reding ME, Rasheed A,Blodgett J,Kornman KS 1992, O'Neil TC 1979, Williams RC Jr, Mahan CJ 1960). Results indicate that all subjects that were treated with doxycycline experienced a reduction in glycated hemoglobin (Grossi SG, Skrepcinski FB, Dcaro T, Zambon jj,Cummins D,Genco RJ1996) These results suggest that periodontal antimicribial treatment may reduce the level of glycated hemoglobin in diabetic subjects and may ultimately hold the potential to reduce diabetic sequelae.

There is an extensive body of literature that point to an emerging "two-way relationship" between diabetes/poor glycaemic control and periodontal disease. Specifically, the severity of the diabetic condition, whether insulin-dependent diabetes mellitus is related to the incidence and severity of periodontal disease (Soskolne WA, Klinger A. 2001 Taylor GW 2001,. Tsai C,Hayes C, Taylor GW 2002). Conversely, there is evidence that the severity of periondal disease may affect the level of glycaemic control in diabetic patients (Grossi SG. 2001, Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A,Blodgett J,Kornman KS, .Stewart JE, Wager KA, Friedlander AH, Zadeh HH. 2001, Taylor GW. 2001). It has been proposed that this effect may due in part to the role of the chronic bacterial load and chronic inflammation that is characteristic of periodontal disease. Products of the bacterial load and products of the inflammatory response could enter the systemic circulation, leading to an increase and the resistance to insulin. This would result in an elevated blood glucose, which in turn could react with hematogenous proteins such as haemoglobin to form glycosylated hemoglobin. Further glycation and oxidation of proteins and lipids would then lead to formation pf advanced glycation end products that could promote saquelae of diabetes such as local destructive inflammatory responses and tissue damage (Stewart JE, Wager KA, Friedlander AH, Zadeh HH 2001)

Conclusion ;

For the dental practitioner, an important area of clinical research centers on improving glycemic control (as measured by the glycosylated hemoglobin) through periodontal therapy. Studies using combinations of debrident, local irrigation, and/or systematic antibiotics on both NIDDM and IDDM patients have shown small, but in some cases significant, reductions in glycosylated hemoglobin after periodontal treatment (Grossi SG

2001, .Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A,Blodgett J,Kornman KS1992, .Stewart JE, Wager KA, Friedlander AH, Zadeh HH 2001, .Taylor GW 2001). We concluded that periodontal therapy itself improves metabolic control and reinforces that T2DM is a risk factor for periodontitis.

REFRENCES:


1. Ainamo J, Lahtinen A, Uitto V (1990). Rapid periodontal destruction in adult humans with poorly controlled diabetes.A report of 2 cases. J Clin Periodontol 17: 22–28
2. Aldridge JP, Lester V, Watts TL, Collins A, Viberti G, Wilson RF(1995). Single-blind studies of the effects of improved periodontal health on metabolic control in type 1 diabetes mellitus. J Clin Periodontol 22: 271–275.
3. Bacic M, Plancak D, Granic M. (1988) CIPTN assessment of periodontal status in diabetics. J Periodontol 59: 816–822.
4. Beck, J. D., Garcı´a, R., Heiss, G., Vokonas, P.S. & Offenbacher, S. (1996) Periodontaldisease and cardiovascular disease. Journalof Periodontology 67, 1123–1137.
5. Christgau, M., Palitzsch, K.D., Schmalz., G., Kreiner, U. & Frenzel,S. (1998) Healing response to non –surgical periodontal therapy in patient with diabetes mellitus; clinical microbiological, and immunologic results Journal of clinical Periodontology 25,112-124.
6. Ebersole, J.L. & Cappelli, D.(2000) Acute phase reactants in infections and inflammatory diseases. Periodontology 2000 23, 19-49.
7. Emrich LJ, Shlossman M, Genco RJ (1991). Periodontaldisease in non-insulin-dependent diabetes mellitus. J Periodontol62: 123–131.
8. Emrich G,Emingil G, Atilla G, Sorsa T, Savolainen P, Baylas H. Periodontal,2004;75 (10):1387- 96.

9. Engebretson SP, Hey-Hadavi J, Ehrhardt FJ, Hsu D, Celenti RS,Grbic JT, Lamster IB.Garcia, R, Henshaw, M. & Krall, E. (2001) Relationship between periodontal disease and systemic health. Periodontology 2000 25, 21-36.
10. Genco,R.J , Grossi, S.G., Ho, A., Nishimura,F.& Murayama, Y.(2005) A proposed model linking inflammation to obesity, diabetes and periodontal infections. Journal of Periodontology 76, 2075-2084.
11. Gottsegen R.(1990)Diabetes mellitus, cardiovascular diseasesand alcoholism.In: Schluger S, Yuodelis R, Page RC, JohnsonRH, ed. Periodontal diseases. 2nd edn. Philadelphia:Lea and Febiger, 273–279.
12. Grossi, S. G., Skrepcinski, F.B., DeCaro, T., Zambon, J.J., Cummin, D. & Genco, R. J.(1996) Response to Periodontal Therapy in Diabetics and Smokers. *J Periodontal* 67,1094–1102.
13. Grossi SG, Skrepcinski FB, DeCaro T al (1997). Treatmant of periodontal disease in diabetics reduces glycated heamoglobin .J Periodontal 68:713-9.
14. Grossi SG, Genco RJ.(1998) Periodontal disease and diabetes mellitus: a two-way relationship. AnnPeriodontol 3: 51–61..
15. Grossi SG. (2001) Treatment of periodontal disease and control of diabetes: an assessment of the evidence and need for future research. Ann Periodontol 6:138-145
16. Gursoy UK, (2006) Marakoglu, Ersan S. Periodontal status and cytoplasmic enzyme activities in gingival crevicular fluid of type 2 diabetic and/or obese patient with chronic periodontitis. Jan;8(1);2-5.
17. Gustke CJ.(1999)Treatment of periodontitis in the diabetic patient.A critical review.J Clin Periodontol :26:133-137.
18. Hagiwara, S., Ogaawara, Y. & Tanaka, A.(2002) Effect of non surgical periodontal therapy on dibetic metabolic control. Journal of Dental Research 81(Special issue), 206(abstract 1551).
19. Hall R. Oral medications for diabetes. Periodontal Insights 1998:5:12-13.

20. Iacopino AM(2001). Periodontitis and diabetics interrelationships:role of inflammation. Ann Periodontal. 6(1):125-37
21. Iwamoto, Y. Nishimura, F., Nakagawa, M. (2001) The effect of antimicrobial periodontal treatment on circulating TNF-@ and glycated hemoglobin level in patients with type 2 dibetes. Journal of Periodontology 72, 774-748.
22. Jones , J. A., Miller, D. R., Wehler, C. J, Rich, S.E &Krall-Kaye, E. A.&Garicia ,R.I.(2007) Does periodontal care improve glycemic control ?The department of veterans affairs dental dibetes study.Journal of Clinical Periodontology 34, 46-52.
23. Katz, J.,Bhattacharyya, I., Farkhondeh-kish, F., Perez, F. M., Caudle, R. M. & Heft, M.W.(2005) Expression of the receptor of advanced glycation end products in gingival tissue of type 2 dibetes patients with chronic periodontal disease:a study utilizing immunohistochemistry and RT-PCR. Journal of clinical Periodontology 32, 40-44.
24. Kiran ,M. Arpak, N. Unsal, E.&Erdogan,M.F.(2005) Effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. Journal of Clinical Periodontology 32, 266-272.
25. Lalla E, Lamster IB, Schmidt AM(1998). Enhanced interaction ofadvanced glycation end products with their cellular receptor RAGE: implications for the pathogenesis of accelerated periodontal disease in diabetics. Ann Periodontol **3**: 13–19.
26. Lalla E, Lamster IB, Stern DM, Schmidt AM (2001).Receptor for advance glycation end products, inflammation,and accelerated periodontal disease in diebeties:mechanisms and insight into therpatic modalities, Ann Periodontol 6:113-118.
27. Lim L.P., Tay, F.B.K., Sum, C.F.&Thai, A.C.(2007) Relationship between markers of metabolic control and inflammation on severity of periodontal disease in patient with diabetes mellitus. Journal of Clinical Periodontology 34, 118-123.
28. Lo¨ e H (1993**).** The sixth complication of diabetes mellitus. Diabetes Care 16: 476–480.

29. Mattson, J.S.& Cerutis, R. (2001) Diabetes Mellitus. A review of the literature and dental implication. Compendium of Continuing Education in Dentistry22, 757-772.
30. Mealey BL(1998). Impact of advances in diabetes care on dentaltreatment of the diabetic patient. Compendium ContinEduc Dent 19: 41–58.
31. Mealy BL & AotsT.W.(2006) Diabetes mellitus and and periodontal disease. Journal of Periodontology 77, 1289-1303.
32. Miller LS, Manwell MA, Newbold D, Reding ME, Rasheed A,Blodgett J,Kornman KS (1992).The relationship between reduction in periodontal inflammation and diabetes control :a report of 9 cases, J Periodontol 63:843-848.
33. Moore PA, Weyant RJ, Mongelluzzo MB, Myers DE, RossieK, Guggenheimer J, Block HM, Huber H, Orchard T. (1999) Type Idiabetes mellitus and oral health: assessment of periodontaldisease. J Periodontol 70: 409–417.
34. Nathan DM, Dale DC, Federman DD, ed. Diabetes mellitus.Sci Am Med 1996: 6: 1–24.
35. Nelson RG,Shlossman M, Budding IM,PettitDj,Saad MF, Genco Rj, Knowler Wc(1990) .Periodontal disease and NIDDM in Pima Indians. Diabetes Care 13: 836–840.
36. Nishimura, F., Iwatomo, Y., Mineshiba, J., Shimizu, A., Soga, Y. & Murayama, Y. (2003) Periodontal disease and diabetes mellitus; the role of tumor necrosis factor -@ in a 2 way relationship. Journal of Periodontology 74,97-102.
37. Novaes AJ, Gutierrez F, Novaes A (1996). Periodontal disease progression in type II non-insulin-dependent diabetes mellitus patients (NIDDM). Part I – Probing pocket depth and clinical attachment. Braz Dent J 7: 65–73
38. Offenbacher, S., Katz, V., Fertik, G. et al.(1996) Periodontal infection as a possible risk factor for preterm low birth weight.Journal of Periodontology 67,1103-1113.

39. Oliver RC, Tervonen T(1993). Periodontitis and tooth loss. Comparingdiabetics with the general population. J Am DentAssoc 124: 71–76.
40. O'Neil TC.(1997) Plasma female sex-hormone levels and gingivitis in pregnancy. J Periodontol 50: 279–282.
41. Page, R. C. & Beck, J. D. (1997c) Risk assessment for periodontal diseases. InternationalDental Journal 47, 61–67.
42. Ringelberg ML, Dixon DO, Francis AO, Plummer RW.(1997)Comparison of gingival health and gingival crevicular fluid flow in children with and without diabetes. J Dent Res 56: 108–111.
43. Rodrigues, D, Taba, M, Novaesd, A, Souza, S. & Grisi, M. (2003) Effect of non-surgical periodontal therapy on glycemic control in patients with type 2 diabetes mellitus. Journal of Periodontology 74, 1361-1367.
44. Sammalkorpi, K. (1989) Glucose intolerance in acute infections. *J Intern Med* 255, 15–19.
45. Sastrowijoto SH, van der Velden U, van Steenbergen TJ, Hillemans P, Hart AA, de Graaff J, Abraham-Inpijn L (1990). Improved metabolic control, clinical periodontal status and subgingival microbiology in insulin-dependent diabetes mellitus. J Clin Periodontol 17: 233–242.
46. Scannapieco, F. A. & Genco, R. J. (1999) Association of periodontal infections with atherosclerotic and pulmonary diseases. Journalof Periodontal Research 34, 340–345.
47. Seppala, B, Seppala M. &Ainamo, J. (1993) A Longitudenal study on insulin-denandent diabetes mellitus and periodontal disease. Jjournal of Clinical Periodontology 20, 161-165.
48. Seppala B, Ainamo J.(1994) A site-by-site follow-up study on theeffect of controlled versus poorly controlled insulin-dependentdiabetes mellitus. J Clin Periodontol 21: 161–165.
49. Shlossman M, Knowler WC, Pettitt DJ, Genco RJ.(1990) Type 2diabetes mellitus and periodontal disease. J Am Dent Assoc 121: 532–536

50. Shah N , Sundaram KR (2003).Impact of socio-demographics variables,oral hygiene practices and oral habits on periodontal health status of Indian elderly:acommunity –based study .Indian J Dent Res.14(4):289-97.
51. Smith, G. T, Greenbaum, C.J ,Johnson, B.D.& Person, G. R.(1996) Short- term responses to periodontal therapy in insulin-dependent diabetic patients. Journal ofperiodontology 67, 794-802.
52. Soskolne WA, Klinger (2001) A. Relationship between periodontal disease and diabetes: an overview. Ann Periodontal :6:91-98.
53. Stewart JE, Wager KA, Friedlander AH, Zadeh HH. (2001) The effect of periodal treatment on glycemic control in patients with type 2 diabetes mellitus. Clin Periodontol :28:306-310
54. Stegeman CA (2005).Oral manifestations of diabetes. Home Health Nurse. 23(4): 233-40; quiz 241.
55. Steenbergen, T. J., Hillemans, P., Hart, A. A.,de Graff, J. & Abraham-Inpijn, L. (1990) Improved metabolic control, clinical periodontal status and subgingival microbiology in insulin-dependent diabetes mellitus. Journalof Clinical Periodontology 17, 233–242.
56. William R,Mahan C. (1960) Periodontal disease and dibetes in young adults.JAMA 172:776-778.
57. Yki-Jarvien H, Sammalkorpi K, Koivisto VA, Nikkila EA(1989). Severity,duration and mechanisms of insulin resistance during acute infections. J Clin Endocrinol Metab 69:317–323.