ijcrr
Vol 04 issue 16
Category: Research
Received on:15/06/12
Revised on:30/06/12
Accepted on:11/07/12

ASSESSMENT OF IMPAIRED GLUCOSE TOLERANCE IN NON DIABETIC ADULT PATIENTS WITH CHRONIC PERIODONTITIS AS A RISK FACTOR FOR DIABETES MELLITUS

B.Aruna, Vanaja K Naik, C S Anand Mohan, D Mythireyi

Dept of Periodontics, SRM Dental College, SRM University, Chennai

E-mail of Corresponding Author: bbaallaa 2002 @yahoo.co.in

ABSTRACT

Background: Periodontitis is more prevalent in diabetic patients which can worsen diabetes. Periodontal disease alters the glycemic status in diabetic patients. In non diabetic adults periodontitis results in impaired glucose tolerance which is a prediabetic state and they are at a higher risk of developing diabetes. Aim: To examine the association between periodontitis and impaired glucose tolerance (IGT) using oral glucose tolerance test in adult non diabetes patients. Materials and methods: A total of 50 healthy non diabetic subjects were recruited into the study from Dept of Periodontics, SRM Dental College & Hospital, Ramapuram Chennai, India. The study population comprised of 25 control group without periodontitis and 25 study group with periodontitis. Clinical periodontal parameters such as probing depth, attachment loss, gingival index and body mass index was assessed for all patients. Metabolic status was determined by 2 hour oral glucose tolerance test. The relationship between mean probing depth, mean attachment loss, gingival index with impaired glucose tolerance were analysed.
Results: The proportion of subjects with IGT increased significantly in the subjects with higher GI, Mean PD, Mean CAL ($P<0.0001$). Discussion: In this cross sectional analysis, periodontal pockets, clinical attachment levels, gingival index were significantly associated with IGT. Periodontal pathogens in deep pockets, and periodontal inflammation causes the release of pro inflammatory cytokines mainly TNF-α which causes insulin sensitivity. The results of the study were consistent with reports of Loesche et al 2000, Saito et al 2006,Nibali et al 2007, Ryan et al 2009. Conclusion: Deep pockets, clinical attachment loss, gingival index were significantly associated with IGT, suggesting that periodontitis is associated with elevated blood glucose levels in adults without diabetes and may increase one's risk for Type 2 diabetes.

INTRODUCTION

Periodontal disease is an infectious disease caused by small group of predominantly anaerobic Gram negative microorganisms. Progression and extent of periodontitis are modulated by bacterial virulence, and host immune response. Several risk factors play an important role in development of periodontitis like age, specific bacteria, tobacco use, genetic factors, pre existing disease which influence host response mechanism[1]. Certain systemic disorders and conditions alter host tissue physiology, which may impair host barrier, integrity and host defense to periodontal infection resulting in most destructive disease.

In1900, William Hunter a British physician gave focal infection theory, which implied that there was a nidus of infection, somewhere in the body such as periodontitis which would affect distant site and organs through blood stream. Recent evidence also suggests that periodontal infection can adversely affect systemic health, with manifestation such as Coronary heart disease, Stroke, Diabetes, Premature labour, Low birth weight delivery, respiratory disease etc[2]. Among the various hormonal disease, Diabetes mellitus is an extremely important disease from periodontal stand point, as periodontitis is seen in all diabetic patients, especially in patients with poor glycemic control. The increased prevalance and severity of Periodontitis commonly seen in patients with diabetes especially with poor metabolic control led to the designation of periodontitis as the 6th complication of Diabetes mellitus[3].

It was estimated that the global burden of Type 2 diabetes mellitus (T2DM) for 2010 would be 285 million people (2010) which is projected to increase to 438 million in 2030; a 65 % increase (Snehalatha and Ramachnadaran 2009). Similarly, for India this increase is estimated to be 58% from 51 million people in 2010 to 87 million in 2030 (Snehalatha and Ramachnadaran 2009).[4]

Periodontitis is more prevalant in diabetic patients and worsens diabetes. Also periodontitis results in impaired glucose tolerance which is a prediabetic state[2]. Subjects in this category are at higher risk of developing diabetes[5]. Any chronic subclinical inflammation plays an intermediary role in pathogenesis of Type 2 diabetes (Festa 2000)[6]. Periodontal disease is a very common chronic subclinical inflammation in which there is an increase in CRP, IL-6,TNF alpha which are significant risk indicators of Type 2 diabetes.[7] These inflammatory mediators generated interfere with action of insulin receptors thereby decreasing insulin sensitivity (or) causes insulin resistance. TNF alpha causes insulin resistance by phosphorylating the serine residue of insulin receptor substrate -1 and inhibiting tyrosine phosphorylation of insulin substrate-1 which is essential for insulin signal transduction. By this mechanism TNF-alpha blocks insulin receptors and inhibits glucose transport and insulin action and causes insulin resistance in turn causing hyperglycemia and hyperinsulinemia.[8,9]

Periodontal disease is seen in Diabetic patients, in turn periodontal disease also alters the glycemic status. Also studies have indicated that treating periodontitis in diabetic patients has a beneficial effect on glucose control.[10,11] At present, studies have shown the relationship between the periodontal disease and glycemic control.[12,13,14,15,16,17,18,19,20] Saito et al[3] found that alveolar bone loss was associated with impaired glucose tolerance in Japanese men without diabetes. Similarly Nibali et al[15] found slightly higher nonfasting glucose levels in periodontitis cases compared to healthy controls. These studies suggest that periodontitis may affect glucose metabolism in healthy non diabetic adults however not much studies were done in Indian subjects.

The purpose of the current study was to examine the association between periodontitis and Impaired Glucose Tolerance(IGT) using Oral Glucose Tolerance Test(OGTT) in adult non diabetic patients cross sectionally. The hypothesis of this study is that patients with periodontitis have impaired glucose tolerance than healthy patients as periodontitis leads to insulin resistance which alters glycemic status.

AIMS AND OBJECTIVES

- To examine the association between periodontitis and impaired Glucose tolerance in adult non diabetic patients.
- To examine the association between impaired glucose tolerance with various parameters

like age, sex, smoking, Body mass index, Probing depth, Clinical attachment level and gingival index

MATERIALS AND METHODS

Fifty subjects were screened and selected from Department of Periodontics, SRM Dental College and Hospital, Ramapuram, Chennai, India. The study population were comprised of 25 study subjects diagnosed with chronic periodontitis (15 male, 10 female age 25-60 years, mean age 40.6+10.3) and 25 control subjects without periodontitis , (13 male ,12 female age 25-60 years, mean age 39.2+8.5)

All the participants were above 25 years of age had not been diagnosed with diabetes, no history of long term antibiotic use in the past 6 months , had no other systemic complications and were not obese. Study group (group I) comprised of patients with generalized chronic periodontitis with at least 30%of sites had probing depth more than $\geq$ 5mm, and radiographic evidence of bone loss. Control group (group II) comprised of Healthy subjects who had Gingivitis and with no signs of periodontitis(who had probing depth not more than 3mm, no radiographic bone loss). Informed consent was obtained from all participants.

Clinical parameters:

Clinical periodontal parameters were recorded on a full mouth basis including probing depth(PD), Attachment Loss(AL), and Gingival Index(GI). Probing depth and Attachment loss were determined at 6 sites per tooth and mean PD and mean CAL were calculated. Subjects were divided into 3 categories with respect to PD and CAL as Normal <1, Mild 1-3, Moderate 3-5, Severe >5. Gingival index was determined at 4 sites per tooth (Mesiobuccal, Mid buccal, Distobuccal and lingual) on a full mouth basis. Subjects were categorized into 3 groups in relation to GI Good 0.1-0.9, Fair 1.0-1.9, Poor 2-3.

Measure of obesity:

Body mass index was measured and divided into 3 categories as Normal 18-23, Preobese 25-30, Obese above 30, and all obese patients were excluded.

Metabolic parameters:

Metabolic status was determined by a 2 hour oral GTT. Blood samples were collected from antecubital vein the morning after an overnight fast and plasma glucose levels were recorded at 0 hour, ½ hour, 1 hour, 2 hour after consumption of 75 g of glucose mixed in water. However Fasting plasma glucose and 2 hour post challenge glucose was adopted as cut off values. The criteria for diagnosis of Diabetes was based on World Health Organisation criteria for diagnosis of diabetes[7,5] (Table 1).

Statistical analysis:

Chi-square test with Yates, Fisher exact test and student independent t – test, Mann – Whitney U test was used to compare different variables between study group and control group and also for comparison of mean values between IGT and non IGT in study group.

RESULTS

When the study group and control group were compared statistically significant difference was seen in relation to smoking habit, IGT, BMI, CAL, PD, and GI. There was increase in BMI, CAL, PD, GI in study group compared to control group. Among the study population none of them had IGT and no smokers in control group .Among the study group (n=25), 6 subjects were identified with IGT and 18 subjects had NIGT. Among these 6 subjects who had IGT 50%(3) had moderate CAL and 50% (3) had severe CAL, and 100%(6) had increased Probing depth (PD) and 100% had poor GI and only one was a smoker (16.7%). When NIGT and IGT were compared in study

group statistically significant difference was seen with GI, CAL, PD, where as no significant difference was seen with age, BMI, smoking and gender.

DISCUSSION

Type 2 Diabetes mellitus has long been known to be risk factor for periodontitis. Successful periodontal treatment appears to have beneficial role in the metabolic control in Type 2 Diabetes indicating that Type 2 Diabetes influences the pathophysiology of periodontal disease which in turn influences the disease status of Type 2 Diabetes in reciprocal fashion. Relationship between diabetes mellitus and periodontal disease in which the diabetic condition exacerbates periodontal disease and reduces the effect on periodontal treatment has been known for many years.

Saito et al 2004[7] reported a relation between a deep pockets and IGT in which deep pockets were closely associated with the past deterioration of glucose tolerance from NGT to IGT rather than IGT condition on the examination day, suggesting that deep pockets are a risk factor for glucose tolerance. This implies that periodontitis reversibly affects host glucose metabolism. Since both Type 2 Diabetes and periodontal disease takes a long time to develop and to manifest in middle aged people, IGT caused by obesity may be a true risk factor for periodontitis.

Obesity is the strongest risk factor for Type 2 Diabetes mellitus which is in turn a risk factor for periodontal disease. In this study obese patients were excluded to see whether periodontitis could associate directly with IGT independant of obesity.

In this cross sectional analysis, periodontal pockets and clinical attachment level which indicates the degree of tissue destruction and gingival index, indicator of periodontal inflammation were significantly associated with IGT. Since worsening of diabetic condition is associated with detoriating periodontal tissue a cross sectional relationship between deep pockets and diabetes was presumed. Our results support the hypothesis that deep pockets not only increases the risk of diabetes mellitus but also increases the risk of IGT.

In this study deeper pockets were associated with IGT. Generally pocket depth is directly related to subgingival bacteria. In periodontium LPS continuously produced by Gram negative bacteria such as P.ginivalis which triggers the action of TNF alpa - a pro inflammatory cytokine, which in turn causes Insulin resistance. The area of the interface where the subgingival bacteria can interact with gingival tissue is estimated to be as much as $72cm^2$ in patients with severe periodontitis and deep pockets, and this results in an enormous burden of Gram negative bacteria [16](Page et al). Periodontal treatment to remove the bacteria, appears to reduce circulating TNFα levels (Iwamato et al 2001).TNF α induced from the periodontal pathogen may increase insulin resistance which may lead to increase risk of CVD

A deep pocket usually means exisiting periodontal inflammation where as severe attachment loss usually represents a history of periodontal destruction and denotes past disease activity. Clinical attachment loss was found to be statistically significant with IGT.

Gingival index, indicator of periodontal inflammation was also significant associated with impaired glucose tolerance. The probable reason may be any chronic inflammation causes release of inflammatory mediators mainly TNF alpha causing insulin sensitivity. Though obesity was excluded body mass index of pre obese, normal patients were not significantly associated with impaired glucose test.

Smoking history was not associated with IGT, because there were low proportion of smokers in study group. The results of study were consistent

with the reports of Losche et al 2000[17], Saito et al 2006[13], Nibali et al 2007[15], Ryan E Wolff et al 2009[12], that collectively suggests that periodontitis is associated with elevated blood glucose levels in adults who have not been diagnosed with diabetes.

Loseche et al showed elevated fasting blood glucose levels in periodontits patients when compared with healthy patients. Saito et al 2006[13] found that degree of alveolar bone loss is significantly associated with IGT. Ryan et al[12] found elevated glucose related haemoglobin in patient with periodontitis.

Our results were not consistent with the studies by Saito et al 2004[7], Saito et al 2005[21]. Saito et al 2004[7] reported that deep periodontal pockets were significantly associated with IGT were as severe attachment loss were not associated with IGT. Saito et al 2005[21] found that deep periodontal pockets were not associated with IGT.

Whether deep periodontal pockets is the cause or result of IGT could not be determined as this was a cross sectional study and only a limited number of subjects were examined. However further longitudinal studies with review and follow up of IGT patients and a large sample size could help to clarify whether periodontal disease is indeed a risk for diabetes mellitus.

CONCLUSION

As periodontal disease is significantly associated with IGT, all subjects having deep pockets, clinical attachment loss and poor gingival index can be screened for IGT who are at a risk for diabetes mellitus at a future date. As diabetes is associated with significant morbidity and mortality it is reasonable to propose that the dental office can be a health care location actively involved in screening for IGT in patients with severe periodontitis.

ACKNOWLEDGEMENT

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. Authors also wish to acknowledge Dr Devapriya M.D.S., for her support and help during the study. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

REFERENCES

1. Brain L.Mealey . Influence of periodontal infections on systemic health. Periodontology 2000, Volume.21, 1999, 197-209.
2. Page RC, Offenbacher.S, Schroeder HE, Seymour GJ. Advances in the pathogenesis of Periodontitis. Summary of Development of clinical Implications, Future Directions. Perio 2000; 1999: 21.
3. Loe.H. Periodontal Disease. 6th complication of Diabetes mellitus; Diabetes Care 1993. 16(suppl);329-334.
4. Snehalatha and Ramachandran 2009, Insight into the mechanism of primary prevention of type 2 diabetes , Improvement in Insulin sensitivity and beta cell function, "Genetic and epigenetic basis of complex diseases", Conference in centre for cellular and molecular biology, Dec 2009
5. The Committee of the Japan Diabetes Society on the diagnostic criteria of diabetes . Report of the Committee on the Classification and diagnostic criteria of diabetes mellitus. Diabetes Research and Clinical Practice 55 (2002) 65-85.
6. Andreas Festa, Relph d'agostino.Jr, George Howard, Leena Mykkanen, Russell P.Tracy, Steven M. Haffner. Chronic Subclinical inflammation as Part of the Insulin

Resistance Syndrome. Circulation. 2000; 102: 42-47.
7. T.Saito, Y.Shimazaki, Y.Kiyohara, I.Kato, M.Kubo, M.lida et al. The Severity of Periodontal Disease is Associated with the Development of Glucose Intolerance in Non-diabetics: The Hisayama Study. J Dent Res 83(6): 485-490,2004.
8. Hannah Kanety, Revital Feinstein, Moshe Z.Papa, Rina Hemi and Avraham Karasik. Tumor Necrosis Factor alpha-induced Phosphorylation of Insulin Receptor Substrate-1 (IRS-1).J. Biol. Chem. 270, 23780-23784.
9. Mealey BL, Campo GL. Diabetes Mellitus and Periodontal Disease. Perio 2000; 2007; 44: 127-153.
10. Koromantzos PA, Makrilakis K, Dereka X, Katmilambras N, Vrotsos IA, Madianos PN. A Randomized, controlled trial on the effect of non-surgical periodontal therapy in patients with type 2 diabetes. Part I: effect on periodontal status and glycaemic control. J Clin Periodontol 2011; 38: 142-147.
11. Sara G.Grossi. Treatment of Periodontal Disease and Control of Diabetes: An Assessment of the Evidence and Need for Future Research. Ann Periodontol 2001; 6: 138-145.
12. Ryan E.Wolff, Larry F.Wolff,and Bryan S.Michalowicz. A Pilot Study of Glycosylated Hemoglobin Levels in Periodontitis Cases and Healthy Controls. J Periodontol 2009;80:1057-1061.
13. T.Saito, M.Murakami, Y.Shimazaki, S.Matsumoto, and Y.Yamashita . The Extent of Alveolar Bone Loss Is Associated with Impaired Glucose Tolerance in Japanese Men. J Periodontol 2006; 77:392-397.
14. Benguigui C, Bongard V, Ruidavets J-B, Chamontin B, Sixou M, Ferrieres J et al. Metabolic Syndrome, insulin resistance, and periodontitis: a cross-sectional study in a middle-aged French population. J Clin Perodontol 2010; 37: 601-608.
15. Nibali L, D'Aiuto F, Griffiths G, Patel K, Suvan J, Tonetti Ms. Severe periodontitis is associated with systemic inflammation and a dysmetabolic status: a case-control study. J Clin Perodontol 2007; 34: 931-937.
16. Ryan T Demmer, David R.Jacobs, Moise Desvarieux. Periodontal Disease and Incident Type 2 Diabetes. Diabetes Care, Volume 31, Number 7,July 2008.
17. Losche W, Karapetow F, Pohl A, Pohl c, Kocher T. Plasma lipid and glucose levels in patients with destructive periodontal disease. J Clin periodontal 2000: 27: 537-541.
18. National Health and Nutrition Examination Survey 1999-2002. Prevalence of Diabetes and Impaired Fasting Glucose in adults in the U.S. Population. Diabetes care, Volume 29, number 6, June 2006.
19. Ira B.Lamster , Evanthia Lalla. Periodontal Disease and Diabetes Mellitus: Discussion, Conclusions, and Recommendations. Ann Periodontol; Volume 6: Number 1; December 2001.
20. Han D-H, Lim S-Y, Sun B-C, Paek D, Kim H-D. The association of metabolic syndrome with periodontal disease is confoundednby age and smoking in a Korean population: the Shiwha-Banwol Environmental Health Study. J Clin Periodontol 2010; 37: 609-616.
21. Saito T, Shimazaki Y, Kiyohara Y . Relationship between Obesity, glucose tolerance and periodontal disease in Japanese Women. The Hisayama Study. J Perio Res; 2005; 40: 346-353.

Table 1: World Health Organisation criteria for diagnosis of Diabetes mellitius

	NGT	DIABETES	IMPAIRED GLUCOSE
FASTING	< 110mg/dl	126mg/dl	110 -125mg/dl
POST LOAD GLUCOSE	<140mg/dl	200 mg/dl	140 -199mg/dl

Table 2: Comparison of mean values between study and control group

Variable	Group	Mean + S.D	P- value
BMI	Study group	24.4+2.4	<0.0001*
	Control group	22.2+1.8	
GI	Study group	1.84+0.41	<0.0001**
	Control group	0.37+0.09	
Mean PD	Study group	3.45 ± 1.01	<0.0001**
	Control group	0.67 ± 0.07	
Mean CAL	Study group	3.64 ± 1.03	<0.0001**
	Control group	0.67 ± 0.07	

*Students independent t-test was used to calculate the p- value

** Mann – Whitney U-test was used to calculate the p-value

Table 3: Comparison of mean values between IGT & Non IGT group

variable	Group	Mean +S D	P- value
GI	Non IGT group	1.66+0.27	<0.0001**
	IGT group	2.38+0.26	
Mean PD	Non IGT group	3.00+ 0.58	<0.0001**
	IGT group	4.80 + 0.79	
Mean CAL	Non IGT group	3.19 ± 0.58	<0.0001**
	IGT group	5.00 ± 0.86	

** Mann – Whitney U-test was used to calculate the p-value

Fig 1: Mean age of study group & control group

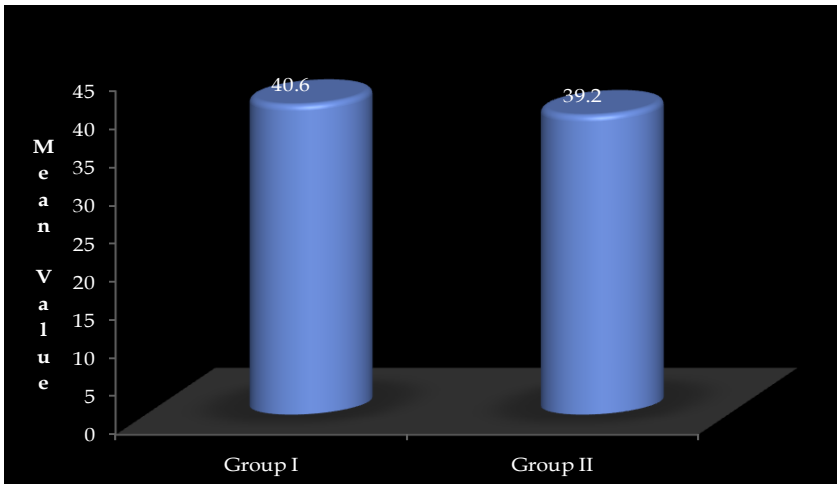

Fig 2: Mean values of GI between NIGT &IGT

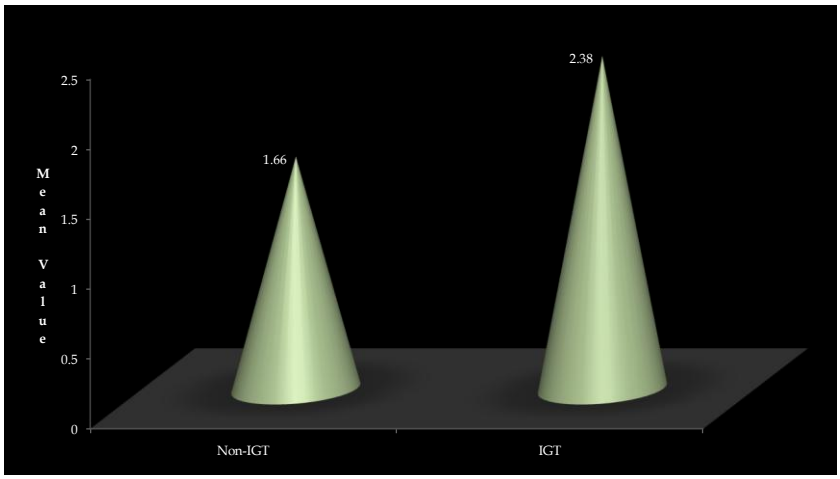

Fig 3: Mean values of probing depth between NIGT & IGT

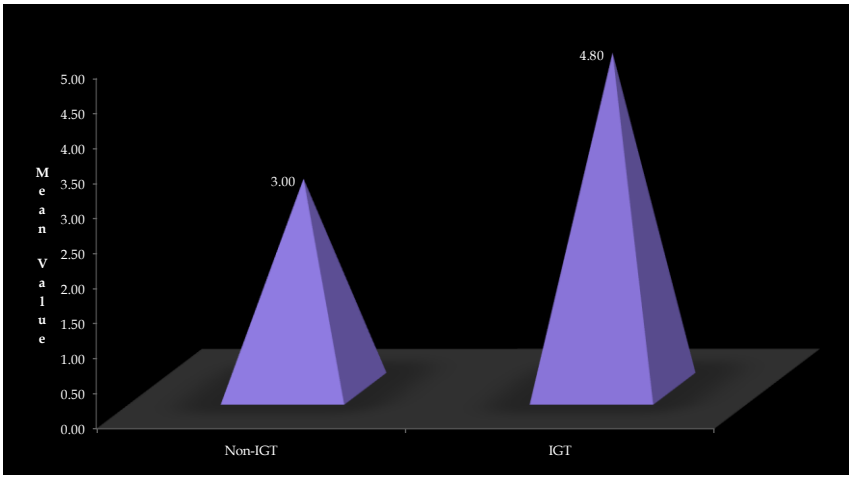

Fig 4: Mean values of mean CAL between NIGT & IGT