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TITLE PAGE

TITLE OF THE ARTICLE: POTENTIAL ASSOCIATION BETWEEN PRE-DIABETIC CONDITIONS AND GINGIVAL AND/OR PERIODONTAL INFLAMMATION IN YOUNG ADULTS

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POTENTIAL ASSOCIATION BETWEEN PRE-DIABETIC CONDITIONS AND GINGIVAL AND/OR PERIODONTAL INFLAMMATION IN YOUNG ADULTS

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ABSTRACT

AIM:

To identify the potential association between pre-diabetic conditions and gingival and /or periodontal inflammation in young adults.

MATERIALS AND METHODS:

A total of 72 participants who were residents of Tamil nadu and free of diabetes were included in the study. An overnight fast of 8-14 hours blood glucose was collected. Gingival or periodontal inflammation was assessed by bleeding on probing, clinical attachment loss and calculus score. Physical parameters such as BMI and waist circumference were measured and the family history for diabetes was also recorded.

RESULTS:

When Fasting blood glucose level (FBG) was correlated against bleeding on probing and calculus score there exists a moderate correlation between FBG and bleeding on probing, and also a high correlation between FBG and calculus score.

CONCLUSION:

This study suggests associations between prediabetes and gingival and/or periodontal inflammation.

KEYWORDS:

Pre-diabetes, inflammation, calculus, gingiva, clinical attachment loss, fasting blood glucose

INTRODUCTION

Diabetes mellitus is a metabolic disorder defined by chronic hyperglycaemia with deranged fat, carbohydrate and protein metabolism that results from improper secretion or action of insulin.[1]. A study conducted in 2014 showed that about 8.5% of adults aged 18 years and older had diabetes worldwide. In 2016, diabetes was the direct cause of 1.6 million deaths[2].India is one of the 6 countries of the IDF SEA region and from the 425 million people who have diabetes in the world, 82 million people belong to the SEA Region and if this continues, by 2045 this will rise to 151 million. There were over 72,946,400 cases of diabetes reported in India in 2017.[3]

Recent studies have revealed that the occurrence of diabetes mellitus is increasing among children and adolescents in India.[4]

There are two main types of diabetes mellitus (DM): Type 1 DM results from the inability of the pancreas to produce enough insulin. Its cause is unknown. Type 2 DM occurs due to insulin resistance, in which the peripheral cells fail to respond to insulin properly. As the disease progresses, failure to produce insulin may also occur. The most common risk factor of type 2 DM is excessive body weight and sedentary lifestyle. Type 2 DM accounts for more than 90% of the diabetes cases worldwide. It is difficult to diagnose early, as it is mostly asymptomatic and usually presents with complications like nephropathy, cardiovascular disease, retinopathy, neuropathy, cerebrovascular disease and peripheral vascular disease.[5]

Recent studies have revealed that around half of the diabetics in the world are undiagnosed.[5] American Diabetic Association has introduced a new category of blood glucose levels, preceding the onset of diabetes, known as prediabetes. Individuals with prediabetes, have a higher risk of development of diabetes in the future.[6] American Diabetic Association has defined pre-diabetes as − Impaired Fasting Glucose, when fasting plasma glucose level ranges from 100 to 125 mg/dl and Impaired Glucose Tolerance, when plasma glucose level 2-h after an oral glucose tolerance test ranges from 140 to 199 mg/dl.[7 8] Screening for prediabetes can lead to early diagnosis and treatment and prevention of complications[7]

Bleeding on probing (BOP) is highly prevalent, and is a major component of routine periodontal examinations carried out in clinical settings and dental clinical research. However, its clinical relevance in the disease progression from chronic gingivitis to severe periodontal disease remains unclear. BOP is a classic sign of periodontal inflammation, and has been observed to be highly correlated to active periodontal disease. Thus, it could serve as an indicator of disease activity[9]Studies have suggested that diabetes is a systemic disease well documented as a risk factor for the development of periodontal disease[10]. As such, diabetes is an ideal model to study the natural history of this oral disease and its progression. Still, the mechanisms underlying the transition from chronic gingivitis to periodontal disease among people with diabetes are not known. It is not clear whether the transition rate is higher among those with type 2 diabetes or those presenting with prediabetic conditions compared with individuals in the general population showing no evidence of systemic disease. Therefore, comparing BOP, in addition to probing depth (PD) and clinical attachment loss (CAL), between individuals with or without prediabetic conditions is important. The findings of such a study could suggest means for prevention and control of both periodontal disease and diabetes among high- risk populations.[11]

Obesity has increased by 70% in adults aged 18–29 years, and type2 diabetes has increased in parallel by 70% in adults aged 30–39 years over the last decade, making young adults the fast growing adult group for both obesity and 5 type 2 diabetes[12]

The present study aimed to evaluate the potential association between prediabetes and the occurrence of gingival and/or periodontal inflammation among young adults [age group 19 to 23 years old] consisting of students from Indira educational institution.

MATERIALS AND METHODS

STUDY POPULATION

A cross-sectional study including 72 young adults within the age group of 18 to 23 years and residing in Tamil Nadu was carried out during the period of August and September 2018. Participants were excluded if they had diagnosis of diabetes (type 1 or 2), metastatic cancer, taking either insulin or other anti-diabetic drugs, having braces or orthodontic appliances that might make the periodontal examination difficult, being pregnant, hypoglycaemia, history of coronary heart disease, congenital heart murmur, heart valve disease, congenital heart disease, endocarditis, stroke, rheumatic fever, haemophilia or bleeding disorders, undergoing current dialysis treatment, undergoing current anticoagulant therapy, requiring antibiotic prophylaxis before a dental procedure.

Among the 72 participants who successfully completed all the study procedures 51participants who had elevated fasting blood glucose (FBG = 100-120mg/dl) were prediabetic, 34 participants had a positive family history for diabetes, 26 participants were obese (BMI>25), 10 males and 17 females had a greater waist circumference (males = > 34 inches; females = > 31 inches). Therefore, the final sample for statistical analysis included 72 participants. The pilot study was conducted for 25 eligible participants at Priyadarshini Dental College and Hospital and all participants provided signed informed consent before any study procedures.

MEASUREMENT OF FASTING BLOOD GLUCOSE

Participants were asked to fast for 8-14 hours before their appointments with no alcoholic consumption. Fasting blood glucose was measured using Glucometer (Accu chek instant active) after signing the informed consent.

PERIODONTAL EXAMINATION

Periodontitis was assessed by clinical measurements of probing pocket depth (PPD) and clinical attachment loss (CAL) at six sites (disto-buccal, mid-buccal, mesio-buccal, disto-lingual, mid-lingual, and mesio-lingual buccal) for all teeth excluding the third molars. All measurements were taken with a periodontal probe (William's periodontal probe) and rounded off upwards to the nearest millimetre. Periodontitis was defined according to the Centres for Disease Control and Prevention/American Academy of Periodontology (CDC/AAP)[13]. Severe periodontitis was defined as having at least two interproximal sites with CAL≥6 mm (not on the same tooth) and at least one interproximal site with PPD≥5 mm. Moderate periodontitis was defined as having at least two interproximal sites with CAL≥4 mm (not on the same tooth) or at least two interproximal sites with PPD≥5 mm (not on the same tooth). Mild periodontitis was defined as having at least two interproximal sites with CAL≥3 mm and at least two interproximal sites with PPD≥4 mm (not on the same tooth) or one

site with PPD≥5 mm. Full mouth clinical exams were conducted by two examiners.

During the measurement of PPD, a periodontal probe was inserted to the base of the sulcus or pocket with a maximum force of 20 g. BOP was present if the probed site bled about 20 seconds after probing the lingual and buccal surfaces of each tooth. BOP was classified as high if 30% or more teeth showed bleeding on probing, and as low otherwise[14].

The oral hygiene index simplified (1964) was done for 6 index teeth and calculus index scored were recorded. Scores were given based on the criteria as 0 for no calculus present, 1 for supragingival calculus covering not more than one-third of the exposed tooth surface, 2 for supragingival calculus covering more than one third but not more than two thirds of the exposed tooth surface or the presence of individual flecks of subgingival calculus around the cervical portion of the tooth or both and 3 for supragingival calculus covering more than two thirds of the exposed tooth surface or a continuous heavy band of subgingival calculus around the cervical portion of the tooth or both.

OTHER DATA COLLECTION

Participant's demographic data such as Name, Age, Sex, Address, and Occupation was gathered along with their medical history and family history. The BMI was calculated by measuring the height and weight of the participants. The waist circumference of the participants was measured using a measuring tape.

RESULTS

Of the 72 participants who completed the research procedures, 51 participants who had elevated fasting blood glucose (FBG = 100-120mg/dl) were prediabetic, 34 participants had a positive family history for diabetes, 26 participants were obese (BMI>25), 10 males and 17 females had a greater waist circumference (males = > 34 inches; females = > 31 inches).

Among 72 respondents, 31(43%) were males and 41 (57%) were females Figure 1 Distribution of Gender (n=72)

The Mean age of the sample is 22 years, minimum age is 19 years, and maximum age is 23 years.

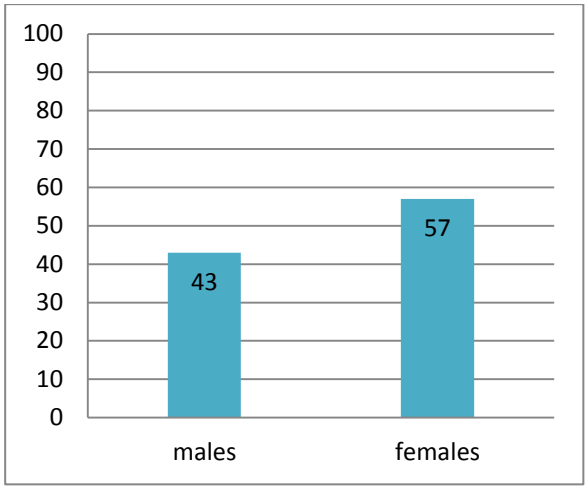

Figure 1 Distribution of study subjects based on gender (n=72)

Among 41 male study subjects around 3% were over 19 years of age (frequency-1), 13% were over 21 years of age (frequency-4), 61% were 22 years of age (frequecncy-19) and around 23% were 23 years (frequency-7)

S.no	Age(years)	Frequency (male)	Percentage (%)
1	19	1	3

2	21	4	13
3	22	19	61
4	23	7	23
5	Total	31	100

Table 1 Distribution of Male study subjects across age (in years)

Among 31 female study subjects around 2% were over 19 years of age (frequency-1), 10% were over 21 years of age (frequency-4), 68% were over 22 years of age (frequency-28) and 20% were 23 years of age (frequency-8)

S.no	Age in years	Frequency (female)	Percentage (%)
1	19	1	2
2	21	4	10
3	22	28	68
4	23	8	20
5	Total	41	100

No.	Age(years)	Male		Female		Total	
		frequency	%	frequency	%	frequency	%
1	19	1	3	1	2	2	3
2	21	4	13	4	10	8	11
3	22	19	61	28	68	47	65
4	23	7	23	8	20	15	21
	Total	31	100	41	100	72	100
	Respondent	Male		Female			
		31	43(%)	41	57(%)	72	100(%)

Table 2 Distribution of Female study subjects across Age (in years)

Table 3 Descriptive statistics (Age vs gender)

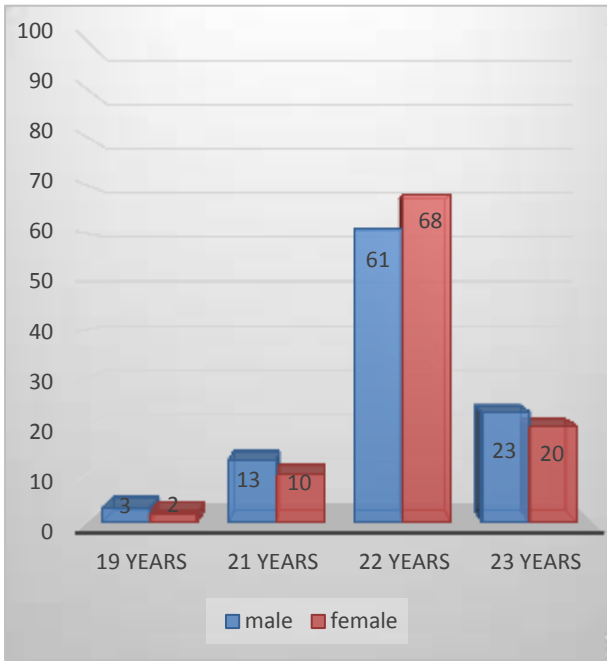

Figure 2 showing Age across Gender

Among the study subjects (n=72), 52.77% had no previous family history of diabetes, 29.16% had a positive family history of diabetes through their father and 18.05% had a positive family history of diabetes through their mother.

S.NO	FAMILY HISTORY OF DIABETES	FREQUENCY	PERCE
1	No previous family history	38	52.77
2	Through father	21	29.16
3	Through mother	13	18.05

Table 4 showing Family history across study subjects

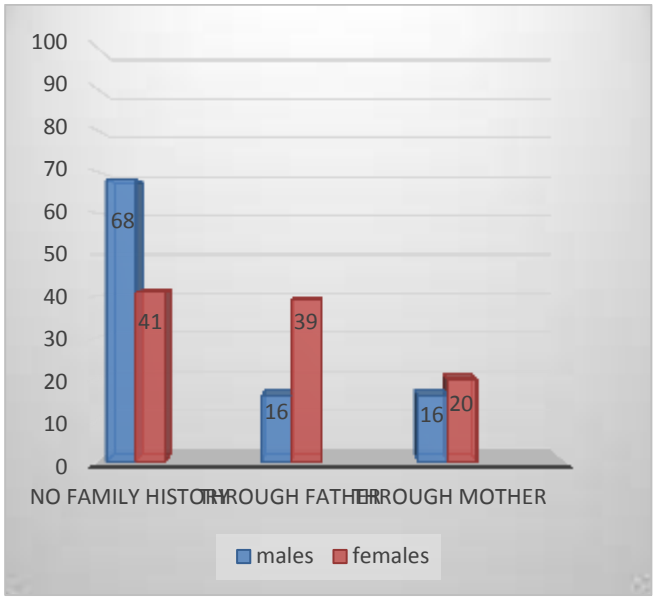

Figure 3 showing family history of diabetes across gender

Variables	N	Minimum	Maximum	Mean	Standard deviation
BMI	**72**	**17.30**	**37.30**	**24.26**	**4.4**
Waist circumference	**72**	**50.80**	**127**	**75.77**	**17.24**
Fast blood glucose level	**72**	**70**	**120**	**102.40**	**10.6**
Bleeding on probing	**72**	**0**	**1.00**	**0.5**	**0.24**
Calculus score	**72**	**0.3**	**3.00**	**1.4**	**0.7**

Table 5 Descriptive statistics

		BMI	Waist circumference	Fbg	bop	Calculus score
BMI	Pearson Correlation	1	.720**	.509**	.362**	.473**
	Sig. (2-tailed)		.000	.000	.002	.000
	N	72	72	72	72	72
Waist circumference	Pearson Correlation	.720**	1	.482**	.377**	.335**
	Sig. (2-tailed)	.000		.000	.001	.004
	N	72	72	72	72	72
F b g	Pearson Correlation	.509**	.482**	1	.563**	.722**
	Sig. (2-tailed)	.000	.000		.000	.000
	N	72	72	72	72	72
Bop	Pearson Correlation	.362**	.377**	.563**	1	.752**
	Sig. (2-tailed)	.002	.001	.000		.000
	N	72	72	72	72	72
Calculus score	Pearson Correlation	.473**	.335**	.722**	.752**	1
	Sig. (2-tailed)	.000	.004	.000	.000	
	N	72	72	72	72	72
Correlation is significant at the 0.01 level (sig 2-tailed)						

Table 6 Correlations

Therefore when BMI is correlated against bleeding on probing and calculus score, the r value is 0.362 and 0.473 respectively. Hence there exists a weak correlation between them.

When Waist circumference is correlated against bleeding on probing and calculus score, the r value is 0.377 and 0.335, so here also there is a weak correlation between them.

But when Fast blood glucose level (FBG) is correlated against bleeding on probing and calculus score, the r value is 0.563 and 0.722, so there exists a moderate correlation between FBG and bleeding on probing, and also a high correlation between FBG and calculus score. Therefore we can conclude that there exists correlation between pre diabetic and periodontal conditions.

DISCUSSION

This study assessed the cross-sectional associations between impaired fasting blood glucose with BOP and Periodontitis among diabetes free individuals of Tamil Nadu. Pre-diabetes was significantly associated with high BOP after extensive multivariable adjustment for confounders. Most of these associations remained significant or borderline significant when the analysis were restricted to obese individuals.

Findings from the present study suggested a potential association between impaired fasting plasma glucose level and prediabetes, and gingival and/or periodontal bleeding on gentle probing of the periodontal tissues. Multiple studies have postulated different mechanism pathways explaining the potential association between established diabetes and periodontal diseases[15]. Patients with diabetic mellitus have a higher risk for periodontitis development, probably because of vascular changes, neutrophil dysfunction, altered systemic inflammatory responses[16], altered collagen synthesis, microbiotic factors or genetic predisposition[17].

In contrast, the potential biological mechanisms explaining the association between moderate glycemic intolerance and periodontal status have been scarcely studied. It is important to assess early stages to better understand the natural history and interrelationships between the two diseases. Previous studies have assessed the potential role of reactive oxygen species in the association. Impaired glycemic status is associated with an increased production and accumulation of reactive oxygen species in the body tissues including the periodontium[18]

Although BOP measures are routinely carried out at dental clinical examination, BOP has not been given much attention. Gingival bleeding after stimulation of the gingival sulcus or pocket has been found to be associated with periodontal inflammation in clinical[19], histopathological[20]and bacteriological[17]aspects of the disease. Regarding the inherent ability of BOP to distinguish the disease condition, previous studies have reported a low sensitivity, but high specificity, of this measurement[21].All these findings could depend on the prevalence of the disease to be measured in the study population. BOP is frequently encountered in individuals at high risk of developing chronic systemic inflammatory diseases[22].As previously stated, the present findings suggested that BOP is more frequently found in participants with impaired fasting glucose or prediabetes among those with the presence of deep pocket depths (PD ≥5 mm) than without.

The associations of prediabetes, IFG, and IGT with severe periodontitis were consistent with few cross-sectional studies that have assessed the associations similar to the way they were modelled in this study. For example, Hong et al. (2016) found that individuals with IFG (111-125 mg/dL) had an increased odds of periodontitis (OR=1.33, 95% CI: 1.01-1.75) compared with subjects with normal fasting glucose (<90 mg/dL). Similarly, Saito et al. (2005) found that IGT was significantly associated with quintiles of mean PPD among Japanese

women. However, Kowall et al. (2015) found that prediabetes was neither associated with mean CAL and PPD in a large, population-based study. Other cross-sectional studies that have modeled the associations in the opposite direction have found positive findings. For example, Choi et al. (2011) reported that participants in the top quintile category of CAL and PPD had significantly higher odds of IFG (OR=1.55, 95% CI: 1.16-2.07; OR=1.39, 95% CI: 1.00-1.92; respectively). Arora et al. (2014)found that severe periodontal infection was significantly associated with IGT (OR=1.93; 95% CI: 1.18-3.17) but not with IFG. However, Demmer et al. (2015) found that higher tertiles of specific periodontal microbiota, but not moderate or severe periodontitis, were significantly associated with prediabetes.

Several biological mechanisms of the bidirectional connection between impaired glucose metabolism and periodontitis have been proposed. Periodontal pathogens and an ensuing inflammatory response lead to collagen destruction resulting in periodontitis, characterized by a deepening of the pockets around the teeth and loss of attachment and alveolar bone. Periodontal pathogens activate cytokines which are associated with increased levels of inflammatory markers and endothelial dysfunction, and altered lipid metabolism, which in turn could lead to increased glucose abnormalities, insulin resistance, and increased risk of diabetes[2324]. While increasing evidence supports systemic inflammation as one mechanistic link explaining the effects of periodontitis on diabetes, the Diabetes and Periodontal Therapy Trial showed that non-surgical periodontal treatment was not associated with six-month changes in serum biomarkers in patients with type 2 diabetes and chronic periodontitis [25] In contrast, a recent meta-analysis supports the hypothesis that periodontal therapy reduces systematic inflammation (hs-CRP and TNF-α) in people with type 2 diabetes[26].On the other hand, it is hypothesized that hyperglycaemia induces oxidative stress through increased intracellular formation of advanced glycation end products and increased proinflammatory cytokine production by monocytes, which can contribute to periodontal tissue destruction [27].

Thus, cross-sectional study findings can reflect either or both directions regardless of what is modelled as the outcome and exposure. Longitudinal studies are needed to better understand the bidirectional relationship between periodontitis and insulin resistance and glucose abnormalities and to assess potential mediators of these relationships.

In summary, this cross-sectional analysis indicates the potential role of prediabetes and insulin resistance in high BOP and severe periodontitis. Given the high prevalence of impaired glucose metabolism and periodontitis, the replication of these findings and assessment of the temporal sequence of these associations in longitudinal studies could have substantial implications in the prevention of these chronic conditions.

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