AN ANALYTICAL APPROACH TO EXPLORE CLINICO-BIOCHEMICAL RELATIONSHIP BETWEEN TYPE 2 DIABETES MELLITUS (T2DM) AND ORO-DENTAL DISEASES INCLUDING CHRONIC PERIODONTITIS

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ABSTRACT

CONTEXT
T2DM is associated with concomitant oral and dental manifestations that necessitate dental evaluation.

AIMS
The aim of this study was to analyse oro-dental conditions particularly chronic periodontitis and their correlation with glycaemic status and with other complications in patients with T2DM.

SETTINGS AND DESIGN
Comparative cross-sectional study.

MATERIALS AND METHODS
One hundred subjects with T2DM were studied for oral manifestations and underwent comprehensive periodontal examination.

RESULTS
Hyposalivation (58%) was the most common oral manifestation followed by periodontitis (50%), halitosis (45%), burning mouth sensation (25%), taste impairment (23%), stomatitis (18%), and oral candidiasis (8%) among 100 subjects with T2DM. T2DM patients with chronic periodontitis had significantly higher glycaemic indices including FPG, PPPG, HbA1C as compared to those without chronic periodontitis (p<0.05). T2DM patients with chronic periodontitis had more prevalent diabetes specific microvascular complications like neuropathy, diabetic kidney disease, retinopathy, as well as macrovascular disease as compared to those without chronic periodontitis. (p<0.05) There was statistically significant direct correlation between HbA1C and clinical attachment level and number of gingival sites with bleeding on probing. This association remained significant even after adjustment for serum creatinine, body mass index, plaque index, OHI-S. (r=0.29 p=0.048).

CONCLUSIONS
Our results suggest that glycaemic impairment is associated with increased severity of periodontitis. Also, periodontitis is associated with increased risk for diabetic complications. Further rigorous systematic studies with larger sample size are required to establish bidirectional relationship between chronic periodontitis and glycaemic status.

KEYWORDS
Type 2 Diabetes Mellitus, Oro-dental Diseases, Chronic Periodontitis, Diabetic Complications.

INTRODUCTION
Type 2 Diabetes Mellitus (T2DM) is a significant public health concern. International Diabetes Federation projects that 642 million individuals will have diabetes by the year 2040.[1] T2DM is associated with concomitant oral and dental manifestations. A two-way relationship between diabetes mellitus and chronic periodontitis has been proposed that not only patients with T2DM are more susceptible to chronic periodontitis, but the presence of chronic periodontitis also affects glycaemic control.[2] Interactions between these two diseases that have important clinical implications for dental professionals, physicians, and most importantly patients. There is scarcity of data on oral complications in patients with T2DM from India particularly the Eastern part till date. This study has been taken up to study various oro-dental conditions particularly chronic periodontitis and their correlation with glycaemic status and with other complications in patients with T2DM. The main objectives were to study oro-dental manifestations in patients with T2DM with particular emphasis on chronic periodontitis.

We also evaluated the association between chronic periodontitis and glycaemic status, microvascular, and macrovascular complications among individuals having T2DM with and without chronic periodontitis.

MATERIAL AND METHODS

This was a hospital-based cross-sectional study. The study was approved by the Institutional Ethical Committee and informed consent was obtained from study subjects.

INCLUSION AND EXCLUSION CRITERIA WERE GIVEN BELOW

Inclusion Criteria

T2DM patients with age between 18 years and 65 years.

Exclusion Criteria

1. Smokers and those consuming chewable tobacco.
2. Subjects with less than 20 teeth were excluded. This was to ensure that patients had sufficient teeth on which to assess periodontal health.
3. Systemic conditions affecting periodontal tissues other than T2DM like haemolytic anaemia, HIV infection, etc.
4. Medications with side effects shown to affect periodontal tissues like anticonvulsants (Phenytoin, phenobarbitone, valproate), calcium channel blockers (amlodipine, verapamil), and immunosuppressants (Cyclosporine).
5. Pregnant subjects.

All study subjects underwent meticulous clinical and laboratory evaluation as per standard practice of T2DM. HbA1c assay was done using Bio-Rad laboratory analyser by High Performance Liquid Chromatography method.

Hyposalivation was assessed by doing saliva collection. On day of saliva collection, patient was instructed to refrain from intake of any food or beverage (water exempted) one hour before the collection period. Saliva collection done by the patient was asked to void the mouth of saliva by swallowing. Patient was instructed to keep his/her mouth slightly open and to allow saliva to drain into Falcon 15 mL calibrated conical tube. Patient was classified as having hyposalivation if the saliva quantity was below 5 mL at end of 20-minute period.[3] Periodontal examination was done by a single examiner expert in periodontia to eliminate inter-examiner variability. Periodontal examination was conducted with all aseptic measures. Oral and dental examination was done according to WHO Oral Health Assessment Form.[4] Oral hygiene was assessed by OHI-S (Oral Hygiene Index-Simplified) were also assessed. Average individual debris and calculus scores were combined to obtain the OHI-S.[5,6] Measurements of probing pocket depth were performed at six sites per tooth: mesiobuccal, mid buccal, distobuccal, mesiolingual, mid lingual, and distolingual. Clinical Attachment Level (CAL) to the nearest millimeter was measured with calibrated University of North Carolina-15 probe (UNC-15) as the distance between the Cementoenamel Junction (CEJ) and the base of the pocket. Chronic periodontitis defined by presence of ≥2 Interproximal sites with CAL ≥4 mm or ≥2 interproximal sites with Probing Depth ≥5 mm developed by the Centres for Disease Control and Prevention (CDC) and the American Academy of Periodontology (AAP) Working Group. This was confirmed by radiological evidence of horizontal bone loss.[7]

STATISTICAL ANALYSIS

Data was collected and processed using SAS (Statistical Analysis System) version 9.1 for Windows, SAS Institute Inc. Cary, NC, USA. The results were presented as mean±SD for normally distributed data and median (min-max) for nonparametric data. Normality of data was determined using Anderson-Darling test, Shapiro-Wilk test, and QQ plot. For significant difference of continuous variables between two groups, p values were calculated using unpaired t-test with equality of variance tested using Levene's test and for nonparametric data. P-values were calculated using Wilcoxon Mann-Whitney test. To test significant difference of continuous variables between more than two groups, ANOVA with post hoc Bonferroni tests was used for normally distributed data and Kruskal-Wallis test with multiple comparisons Bonferroni method was used for non-normally distributed data. Correlation coefficient was determined using Pearson or Spearman partial correlation test depending on the distribution of data. $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 100 subjects with T2DM were studied for oro-dental manifestations. Hyposalivation was the most common oral symptom (58%) followed by halitosis (45%), burning mouth sensation (25%), stomatitis (18%), and taste impairment (23%) in subjects with T2DM. Periodontitis, tooth loss, dental caries were dental manifestations observed in 50%, 36%, and 24% respectively (Table 1).

Oro-Dental Manifestation	Percentage
Hyposalivation	58%
Halitosis	45%
Tooth loss	36%
Chronic periodontitis	50%
Burning mouth sensation	25%
Dental caries	24%
Taste impairment	23%
Stomatitis	18%
Oral candidiasis	8%
Table 1: Shows Distribution of Various Clinical Parameters of Oral Health in Subjects with T2DM (n=100)	

Prevalence of oro-dental complications was studied among subjects well-controlled glycaemic status (HbA1C<7%) and uncontrolled glycaemic status (HbA1C>7%). Oral manifestations were significantly higher among T2DM subjects with uncontrolled glycaemic status except stomatitis and burning mouth sensation (Figure 1).
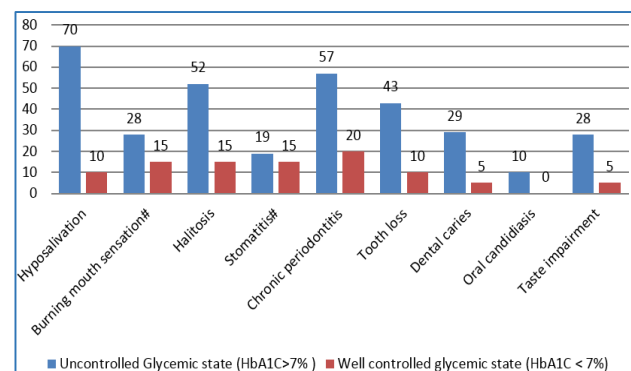
Fig. 1: Distribution of Various Clinical Parameters of Oral Health in Subjects with T2DM (percentage) in Uncontrolled and Well-Controlled Glycaemic Status

Patients with T2DM were analysed into two groups those with chronic periodontitis and those without chronic periodontitis. On comparison of glycaemic indices, it was observed that the FPG, PPG, HbA1c levels were higher in T2DM subjects with chronic periodontitis compared to those without a significant difference was observed between FPG, PPPG, and HbA1C values (p<0.05) among these groups. Duration of T2DM was more among T2DM with chronic periodontitis compared to those without (p<0.05). There was no significant difference between lipid parameters between two groups (Table 2).

| Parameter	T2DM with CP (n=50)	T2DM without CP (n=50)	P value
Age	47.27±9.19	47.22±7.44	0.89
Sex (Female)%	60	58	0.77
Toothbrush use (Once daily)	44	46	0.74
Duration of T2DM	5.53±2.93	4.36±2.58	0.03
BMI	25.92±2.97	25.58±3.04	0.57
FPG	133.39±26.46	119±22.55	0.004
PPPG	212.18±56.5	182.60±35.13	0.002
HbA1C	7.98±0.96	7.16±0.53	0.001
Total cholesterol	186.24±33.53	184.84±36.56	0.84
Triglycerides	159.27±60.09	151.46±62.85	0.52
HDL cholesterol	43.69±8.39	43.78±7.73	0.76
LDL cholesterol	108.31±27.87	109.12±31.1	0.89
eGFR	81.43±28.48	89.50±21.69	0.11
Neuropathy %	52	30	0.04
DKD %	36	16	0.03
Retinopathy %	38	20	0.04
CVD %	32	10	0.012
Number of teeth	29.48±2.88	31.56±1.16	0.004
Plaque Index	2.47±0.61	2.40±0.70	0.59
OHI-S	4.76±1.06	4.58±0.99	0.40
CAL	4.92±1.13	1.22±0.60	<0.001
PPD	4.20±1.55	0.32±0.47	<0.001
Sites with BOP	40.51±19.40	0	<0.001
Table 2: Showing Relationship Between Anthropometric Parameters, Metabolic Parameters, in Patients with T2DM with Chronic Periodontitis and Without Chronic Periodontitis			

FPG: fasting plasma glucose, PPPG: postprandial plasma glucose, HbA1C: haemoglobin A1C, GFR: estimated glomerular filtration rate, CVD: cardiovascular disease, DKD: diabetic kidney disease, OHI-S: oral hygiene index-simplified, CAL: clinical attachment loss, BOP: bleeding on probing, PPD: pocket probing depth.

Microvascular complications including diabetic kidney disease, retinopathy, neuropathy as well macrovascular complications were significantly higher among subjects with T2DM having chronic periodontitis as compared to those without (p<0.05) (Table 2). In the present study, most of the patients brushed only once a day in both groups. All of the

patients in both groups used toothbrush and toothpaste (Table 2). Plaque Index (PI) and OHI-S, which are the markers of oral hygiene suggested similar oral hygiene status in both the groups (Table 2). There was statistically significant direct correlation between HbA1c and clinical attachment level unadjusted as well after adjustment done for serum creatinine, body mass index, plaque index, and OHI-S. (r=0.29 p=0.048). (Figure 2).
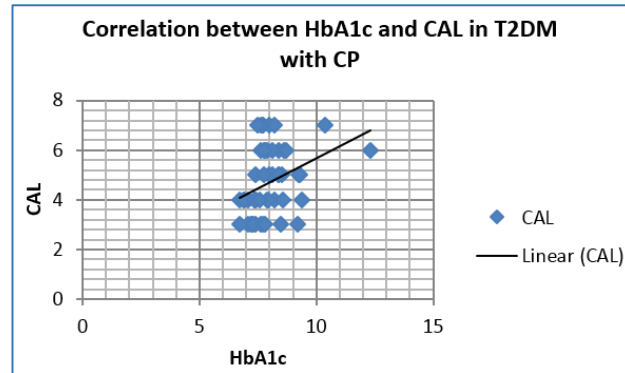
CAL- Clinical Attachment Level.

Fig. 2: Correlation between HbA1c and Clinical Attachment Level in Subjects with T2DM and Chronic Periodontitis

DISCUSSION
In the present study, hyposalivation (58%) was the most common oral manifestation. Hyposalivation being more common in present study was might be due to presence of neuropathy. Prevalence of hyposalivation varies among different studies. Similarly, Shrimali et al[8] reported significantly higher prevalence of hyposalivation among poorly-controlled patients with DM. Saliva possess lubricating and antimicrobial properties. Reduction in salivary quality and quantity results in increased susceptibility to dental caries, mucosal ulcers, and fungal infections.[9] In the present study, halitosis was observed among 45% subjects with T2DM. Halitosis is primarily caused by bacterial putrefaction and the generation of volatile sulfur compounds. Halitosis in individuals with DM is due to poor oral hygiene, periodontal disease.[10] Periodontitis, tooth loss, dental caries were observed in 50%, 36%, and 24% respectively (Table 2). Factors favouring an increased risk for dental caries among subjects with DM include increased glucose concentration in saliva and GCF, a reduced salivary flow rate.[11] The observations in present study were in accordance with studies conducted by Gibson.[12] and Sreebny.[13] Sreebny et al.[13] reported hyposalivation in 43% among 40 subjects with DM. Other oral complications included burning mouth sensation in 25%, stomatitis in 18%, taste impairment in 20%, and oral candidiasis in 8%. Oro-dental manifestations were significantly higher among T2DM subjects. Uncontrolled glycaemic status compared to well-controlled glycaemic status in the present study. Bajaj et al[14] reported periodontal disease in 34% followed by oral candidiasis in 24%, tooth loss in 24%, and dental caries in 24%, oral mucosal ulcers in 22%, taste impairment in 20%, halitosis in 16%, xerostomia and salivary gland hypofunction in 14%, and burning mouth sensation in 10% among 50 patients with DM.

In present study, glycaemic indices FPG, PPPG, HbA1c were higher in subjects with T2DM with chronic periodontitis than those without. In 4343 NHANES III (1988-1994) participants aged 45 years and older of whom 502 had diabetes, severe periodontitis was found in 14.3% of those with poorly-controlled diabetes (HbA1c >9%) and in 8.8% of those with "better" controlled (HbA1c ≤9%) diabetes compared to 4.1% among people without diabetes. After controlling for potential confounders, individuals with diabetes who had poor glycaemic control had 2.90 times and those with better control 1.56 times higher risk for periodontitis than individuals without diabetes.[15] In the present study, direct linear relationship between HbA1C and severity indicators of periodontitis, CAL, and number of sites with bleeding on probing was observed. Similarly, Anoop Kumar et al[16] observed positive correlation between worsening of glycaemic level and increase in severity of periodontitis. In this study, clinical attachment loss was found to be significantly associated with glycaemic control. Similarly, Collin et al[17] reported an association between advanced periodontal disease and impaired glycaemic control among 25 adults with DM. Apoorva et al[18] reported direct association between rising HbA1c levels and severity of periodontitis.

In the present study, microvascular complications as well as macrovascular complications were higher among the subjects with T2DM with chronic periodontitis compared to those without (Table 2). Diaz R et al[19] observed 41% prevalence of neuropathy among T2DM subjects with periodontitis. They observed significant association between severe periodontitis and edentulism with neuropathy among 436 patients with T2DM (Adjusted OR: 1.7; IC 95%: 1.1-2.6). In a longitudinal study of 529, Gila River Indian adults with type 2 diabetes, Shultis et al[20] observed that incidence of end-stage renal disease in individuals with moderate or severe periodontitis or in those who were edentulous were 2.3, 3.5, and 4.9 times as high respectively compared with those with none/mild periodontitis.

Thorstensson et al[21] more likely to have prevalent proteinuria and cardiovascular complications including stroke, transient ischaemic attacks, angina, myocardial infarction, and intermittent claudication compared to controls at followup. Noma H et al[22] from Japan observed that severity of periodontal disease was significantly correlated with the severity of diabetic retinopathy (p=0.0012). Moreover, the risk of proliferative diabetic retinopathy was significantly higher (2.8 times; p=0.036) in the presence of periodontal disease. Various mechanisms that explain the increased susceptibility to periodontitis in diabetes mellitus are increased MMP, adhesion molecules synthesis, impaired chemotaxis, prolonged inflammation, increased oxidative stress, increased GCF and salivary glucose levels, cytokine dysregulation, impaired bone formation and repair.[23]

To conclude, oro-dental manifestations are common in patients with T2DM, hyposalivation, periodontitis, halitosis, tooth loss, dental caries, burning mouth sensation, taste impairment are common oro-dental manifestations among patients with T2DM. Oro-dental manifestations are more common among T2DM patients with poor glycaemic status. Chronic periodontitis is associated with poor glycaemic control in patients with T2DM.

Chronic periodontitis is associated with diabetic microvascular and macrovascular complications. Further rigorous, systematic studies with larger sample size are required to establish relationship between chronic periodontitis and glycaemic status diabetic complications.

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