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Oral Mucosa Alterations in Type 2 Diabetes Mellitus: Prevalence and Risk Factors - A Case Control Study in South Indian Population.

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ABSTRACT

To diagnose the oral mucosal changes associated with diabetes mellitus, investigate their prevalence and to identify possible risk factors associated with it. 500 known type-2 diabetic patients and 500 non-diabetic healthy controls were taken to answer a structured questionnaire designed to collect demographic data as well as history of diabetes. Clinical examination of the oral mucosa was carried out. A higher prevalence of oral mucosa changes was found in patients with diabetes than in patients without diabetes. Among the observed oral mucosal alterations in diabetic patients; gingivitis, coated tongue, fissured tongue ,leukoedema, fungal infections such as candidiasis as well as atrophy of tongue papilla/median rhomboid glossitis; and potentially malignant diseases, such as leukoplakia, lichen planus showed statistically significant value. In the multiple logistic regression age factor (>50) showed a significant increase on the risk and inadequate metabolic control as well as smoking habit elucidate a trend of increased risk of oral mucosal alterations in diabetes patients. The result shows the necessity of periodic oral health examination for early diagnosis and management of oral mucosa lesions in diabetics.

Keywords: Diabetes, Oral mucosal changes**,** potentially malignant diseases

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INTRODUCTION

According to World Health Organization diabetes mellitus is “a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentration of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves” [1].

The increased mortality and morbidity rate in diabetes mellitus is due to complications of this disease such as micro and macro vascular dysfunctions, impaired wound healing and higher susceptibility to infections.

Over past few decades the prevalence of diabetes mellitus has increased in such an alarming extent that the disease which was previously known as a mild disorder of elderly people now became a major cause of mortality and morbidity in our society. Considering the number of old as well as recently diagnosed cases, **India** can be called as **“Diabetic Capital of the World” [2]**.

The report published by the International Diabetes Federation (IDF) and the Madras Diabetes Research Foundation declared, India had 62.4 million people with type 2 diabetes in 2011 compared with 50.8 million the previous year. The IDF predicts, India will have 100 million people with diabetes by 2030 [3].

Several oral changes have been reported to be associated with diabetes mellitus. These complications include periodontal diseases, dental caries, burning mouth syndrome, impaired healing, various potentially malignant disorders, dysfunction of salivary flow and opportunistic fungal infections.

Among fungal infections, the majority of oral lesions are candida species related. They are median rhomboid glossitis, denture stomatitis, angular cheilitis as well as pseudomembranous candidiasis.

Few developmental conditions such as fissured tongue, benign migratory glossitis etc is also associated with diabetes.

On the other hand several studies have shown that among the potentially malignant disorders, leukoplakia, erythroplakia and lichen planus are more prevalent in diabetes mellitus, whereas other authors neither observed this association nor found an influence of diabetes on the duration, distribution or type of these lesions.

The purpose of this study is to diagnose the oral mucosal changes associated with diabetes mellitus, investigate their prevalence compared to non diabetic subjects, and to identify possible risk factors associated with it [4].

MATERIALS AND METHODS

The present study was approved by the Institutional ethical committee, Sree Balaji Dental College & Hospital, Chennai-600100; Ref no-SBDCECM104/13/13. All volunteers were informed about the aims and methods of study and they provided their written consent for participation.

The study group consisted of 500 known type-2 diabetic patients. Out of these 500 patients 153 were males and 347 were females. All these patients were between the ages of 25-90.

Both dentulous as well as edentulous known Type 2 Diabetes mellitus patients without other systemic disease with or without diabetic medication were included in this study.

Patients who presented with Type-1 Diabetes mellitus and Diabetes in pregnancy were excluded from the study. Physically and mentally challenged patients as well as patients, who were under Immunosuppressant and related drugs were also excluded from studies.

Both dentulous as well as edentulous 500 non-diabetic healthy subjects without any systemic disease were included in this study as control group. Out of these 500 healthy subjects 239 were males and 261 were females. All these healthy subjects were between the ages of 25-90.

The patients were selected from Sree Balaji Medical College & Hospital as well as Chennai and Ramakrishna Math Charitable Dispensary, Mylapore, Chennai. All patients were from different socioeconomic status and standards.

A structured questionnaire containing questions regarding demographic data, adverse habits and daily medication use was completed by subjects.

In relation to diabetes, history of diabetes in family, duration of diabetes metabolic control, use of medications (Oral drugs, insulin, or both) to control hyperglycemia and any diabetes associated complications according to the medical records of patients were noted.

An examination of the oral mucosa was done using artificial light, a mouth mirror mirror, gauze square etc. Diagnosis of different oral mucosal alterations was based on the clinical signs.

Appropriate treatment and follow up were established after diagnosis of oral mucosal disorder.

DATA EVALUATION AND RESULTS

The difference between the case and control groups for parametric data was analysed by a chi-square test (qualitative variables) and Student's t-test (quantitative variables). Nonparametric data were evaluated by the Mann–Whitney test. Multiple logistic regression was performed to evaluate the odds ratio of aspects which could represent a risk factor to oral mucosa changes.

In the present study 500 type-2 diabetes patients, out of which 153 (30.6%) were male and 347 (69.4%) were female and 500 healthy subjects out of which 239 (47.8%) were male and 261 (52.2%) were female were examined**.**

The mean age of the type-2 diabetes patients was 54.89 years (SD±10. 505) and healthy subjects was 43.98years (SD±13. 431)**.**

Diabetes data and data regarding adverse habits are shown in Table 1.

Table 1

	Present		Absent		Total
	N	%	N	%	N
Adequate Metabolic Control	236	47.2	264	52.8	500
Oral Medication	449	89.8	51	10.2	500
Insulin	6	1.2	494	98.8	500
Oral Medication And Insulin Both	25	5.0	475	95.0	500
Family History	165	33.0	335	67.0	500
Smoking Habit	26	5.2	474	94.8	500
Tobacco Chewing Habit	30	6.0	470	94.0	500
Alcohol Consumption Habit	19	3.8	481	96.2	500

Diabetes related data and data of adverse habit

To relate the number of complications associated with diabetes mellitus, it was found that 58% of diabetic patients were without any complications, 33.8% patients had only one complication, 7% patients had 2 complications and 1.2% patients had 3 complications.

The duration of diabetes was Up to 2 years for 37.0% patients, 2 – 4 years for 21.6 % patients, 4 – 8 years for 22.6% patients and above 8 years for 18.8% patients.

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Among the observed oral mucosal alterations in diabetic patients; gingivitis (65.8%), coated tongue (34.8%), fissured tongue(17.0%) ,leukoedema(3.2%), fungal infections such as candidiasis (1.4%) as well as atrophy of tongue papilla/median rhomboid glossitis (16.0%); and potentially malignant diseases, such as leukoplakia(2.8%), lichen planus(2.2%) showed statistically significant value. summarised in Table 2and Table 3.

Table 2

		Group				Total	
		Diabetes		Non Diabetes		N	%
		N	%	N	%		
Gingivitis	Present	329	65.8	272	54.4	601	60.1
	Absent	171	34.2	228	45.6	399	39.9
Coated Tongue	Present	174	34.8	59	11.8	233	23.3
	Absent	326	65.2	441	88.2	767	76.7
Fissured Tongue	Present	85	17.0	45	9.0	130	13.0
	Absent	415	83.0	455	91.0	870	87.0
Pigmentations	Present	44	8.8	30	6.0	74	7.4
	Absent	456	91.2	470	94.0	926	92.6
Leukoedema	Present	16	3.2	3	0.6	19	1.9
	Absent	484	96.8	497	99.4	981	98.1
Leukoplakia	Present	14	2.8	3	0.6	17	1.7
	Absent	486	97.2	497	99.4	983	98.3
Carcinoma	Present			2	0.4	2	0.2
	Absent	500	100.0	498	99.6	998	99.8
Lichen Planus	Present	11	2.2	2	0.4	13	1.3
	Absent	489	97.8	498	99.6	987	98.7
Nicotinic Stomatitis	Present	6	1.2	4	0.8	10	1.0
	Absent	494	98.8	496	99.2	990	99.0
Osmf	Present	5	1.0	5	1.0	10	1.0
	Absent	495	99.0	495	99.0	990	99.0
Candidosis	Present	7	1.4			7	0.7
	Absent	493	98.6	500	100.0	993	99.3
Angular Cheilitis	Present	11	2.2	5	1.0	16	1.6
	Absent	489	97.8	495	99.0	984	98.4
Denture Stomatitis	Present	4	0.8	1	0.2	5	0.5
	Absent	496	99.2	499	99.8	995	99.5
Atrophy Of Tongue Papillae	Present	80	16.0	37	7.4	117	11.7
	Absent	420	84.0	463	92.6	883	88.3
	Absent	491	98.2	495	99.0	986	98.6
Others	Present	27	5.4	37	7.4	64	6.4
	Absent	473	94.6	463	92.6	936	93.6
Total		500	100.0	500	100.0	1,000	100.0

Prevalence of oral mucosal alterations

Table3

	Chi square	p	Sig.
Gingivitis	13.55	< 0.001*	Highly Significant
Coated Tongue	74.00	< 0.001*	Highly Significant
Fissured Tongue	14.15	< 0.001*	Highly Significant
Pigmentations	2.86	0.091	Not Significant
Leukoedema	9.07	0.003*	Highly Significant
Leukoplakia	7.24	0.007*	Highly Significant
Carcinoma	2.00	0.157	Not Significant
Lichen Planus	6.31	0.012 †	Significant
Nicotinic Stomatitis	0.40	0.525	Not Significant
Osmf	0.00	1.000	Not Significant
Candidosis	7.05	0.008*	Highly Significant
Angular Cheilitis	2.29	0.130	Not Significant
Denture Stomatitis	1.81	0.179	Not Significant
Atrophy Of Tongue Papillae	17.90	< 0.001*	Highly Significant
Others	1.67	0.196	Not Significant

* Significant at 1 %; †Significant at 5 %

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Logistic regression

A logistic regression was performed to identify possible risk factors in type-2 diabetes mellitus group. (Shown in Table 4).

Table 4

	Risk Factors	B	p value	Odds Ratio	95.0% C.I.	
					Lower	Upper
Total sample	Age	0.058	< 0.001*	1.060	1.020	1.081
	Gender	0.167	0.313	1.182	0.483	1.814
Diabetic	Age	0.051	< 0.001*	1.052	1.022	1.083
	Gender	0.051	0.878	0.949	0.490	1.840
	Inadequate Metabolic Control	-0.052	0.259	3.298	0.414	26.244
	Oral Medication and Insulin Both	1.193	0.987	1.005	0.556	1.815
	Family History	0.005	0.330	2.922	0.337	25.304
	Smoking Habit	1.072	0.145	4.524	0.595	34.367
	Tobacco Chewing Habit	1.509	0.650	1.659	0.186	14.794
	Alcohol Consumption Habit	0.506	0.911	0.996	0.929	1.068
	Duration of Diabetes	-0.004	0.077	1.657	0.947	2.901

* Significant at 1 %

DISCUSSION

Though pathognomonic lesions associated with type-2 diabetes mellitus are not very common [4], yet in the present study we found some specific oral mucosal alterations are similar and frequently present in patients with type-2 diabetes mellitus irrespective of their age as compared to healthy subjects.

The oral mucosal alterations which showed statistically significant differences in our study were coated tongue, fissured tongue, gingivitis, potentially malignant disorders which included leukoplakia and lichen planus; as well as fungal infections such as candidosis and atrophy of tongue papilla/median rhomboid glossitis.

Although Farman et al [5] observed higher prevalence (28%) of fissuring of the dorsal surface of tongue in diabetes patients; Neville et al [6] suggested this alteration ranges only from 2%-5% of the overall population and described it as genetically determined. In this present study we found fissured tongue was more prevalent in type 2 diabetes group(17%) than the control group; which was accordance with the findings of Alliny de souza Bastos et al [4] who observed that, this alteration was present in 17.8% patients of type 2 diabetes mellitus compared to control.

Manfredi et al [7] documented conflicting results to correlate association between diabetes mellitus and geographical tongue. In our study we could not find any association between them. In contradiction to our study, Alliny de souza Bastos et al [4] reported significantly greater prevalence (5.4%) of benign migratory glossitis in type-2 diabetes patients.

Carlos et al [8] discussed that reduction in salivary flow and high salivary viscosity causes coating of tongue. This is due to reduction in action of salivary antimicrobial factors as well as cleaning capacity, which facilitates retention of debris, exfoliated mucous cells and proliferation of microorganisms on the tongue's surface.

In our study we found a significantly greater prevalence of coated tongue (34.8%) in type-2 diabetes patients compared to control which could be attributed to reduction of salivary flow and increased salivary viscosity in diabetes mellitus patients. Our finding is more prevalent than the observation of Alliny de souza Bastos et al [4] who found that coated tongue was only present in 28.7% of type-2 diabetes patients. Whereas Siddharth Gupta et al [9] recorded the coated tongue in 40% patients with uncontrolled diabetes mellitus; which was even more prevalent than our study.

Sadia Iqbal et al [10] showed that the gingivitis was statistically significantly higher among the type-1diabetes patients when compared with the control group. Rehana et al [11] recorded gingivitis as a very common oral manifestation (45%) of type-2 diabetes mellitus. Rohit Sharma et al

[12] in their study found that diabetic patients exhibited significantly higher level of gingivitis whereas there were no significant differences in gingival inflammation between uncontrolled diabetic and controlled diabetic patients. Giju George Baby et al [13] showed that there are changes in the gingival vascular membrane in diabetes mellitus patients.

In the present study we found a significantly greater prevalence of gingivitis (65.8%) in type-2 diabetes mellitus patients than in the control group. These changes could be due to gingival tissue response to local factors, microangiopathy as well as increased susceptibility and severity of infections in diabetes mellitus.

As per classification of oral Candidiasis [14] as proposed by Samaranayake (1991) and modified by Axell et al (1997), oral Candidiasis can be broadly classified as primary oral Candidiasis and secondary oral Candidiasis. Denture stomatitis, angular cheilitis and median rhomboid glossitis was classified under Candida associated lesions.

Maria Rozeli et al [15], Siddharth Gupta et al [13] and Lalit Shrimali et al [16] compared oral manifestations of controlled and uncontrolled type-2 diabetes mellitus patients and observed higher prevalence rate of oral Candidiasis and Candida associated lesions in uncontrolled type-2 diabetes mellitus patients.

Increased prevalence of acute and chronic Candidiasis as well as Candida associated lesions was probably due to xerostomia, immunological alterations, saliva composition, compromised local vascular circulation, reduced local resistance of the tissue as well as poor oral hygiene.

Alliny de souza Bastos et al [4] observed a significant prevalence of fungal infections (17.7%) in patients with type-2 diabetes mellitus without any significant difference between groups.

In our present study we recorded 16% prevalence of atrophy of tongue papilla, 1.4% prevalence of erythematous Candidiasis, 2.2% prevalence of angular cheilitis and 0.8% prevalence of denture stomatitis. Among these, there was a significant statistical difference in atrophy of tongue papilla (16%) and erythematous Candidiasis (1.4%) in type-2 diabetes mellitus patients in comparison to the control group.

This finding correlates with numerous studies [17-23] that demonstrated diabetes patients are more prone to oral Candidiasis and Candida associated lesions but was different from the findings reported by Maria Goretti de Menezes Sousa et al [24] who observed that healthy patients presented almost the same frequency of candidates as type-2 diabetes mellitus patients.

To correlate the hypothesis that progressive atrophy of oral mucosa due to xerostomia can increase its permeability to carcinogens, Albretcht M et al [26] recorded the prevalence of oral leukoplakia was higher among diabetic patients (6.2%) in comparison to control group (2.2%).

Alliny de souza Bastos et al [4] also found higher prevalence of potentially malignant disorders in type-2 diabetes mellitus patients as compared to control; however leukoplakia was observed only in 2.7% of patients with no significant difference from the control group.

Ajit Auluck (2007) [27] suggested that increased blood glucose levels cause excessive free radical formation as well as reduced activity of antioxidant scavengers and enzymes in diabetic patients, which invariably enhance oxidative damage to DNA to facilitate carcinogenesis.

In the present study leukoplakia was diagnosed in 2.8% of type-2 diabetes mellitus patients. It was significantly higher when compared to control group (0.6%).

In contradiction to the present study, Muralidhara Yadiyal et al [27] could not find any association between oral precancerous lesions and diabetes mellitus.

In 1963, Grinspan et al linked diabetes mellitus to oral lichen planus and systemic hypertension [7], but at present this association became controversial as the prevalence of lichen planus in diabetes may vary from 1.6% to 85%; even some studies could not verify this association.

In the present study, we observed significant prevalence of lichen planus/lichenoid reaction (2.2%) in type-2 diabetes mellitus patients compared to controls (0.4%). This increased rate of prevalence could be due to the use of oral hypoglycemic drugs.

This finding correlates with the study done by Albrecht et al [25] who recorded 1% occurrence of lichen planus in 1600 diabetes patients compared to control group (0.0%).

Alliny de souza Bastos et al [4] found a greater prevalence of lichen planus compared to our studies. According to their study 6.1% of the patients with type-2 diabetes had lichen planus which was significantly different from the control group (0.0%).

In contradiction to our study Siddharth et al [9] could not find any significant association of lichen planus in type-2 diabetes mellitus patients and mentioned that, lichen planus should not be considered as a factor to identify diabetes mellitus patients.

Various authors opinionated that impaired immunological response and microangiopathy [13] plays the key role in certain oral mucosal changes in diabetes mellitus patients, as these factors causes reduced blood supply and promote infections; whereas others believe that these changes are due to inadequate metabolic control [28].

In the present study a multiple logistic regression was performed to identify possible risk factors associated with oral mucosal changes among the diabetes mellitus patients. It was found that among the candidate factors included in the model only age factor (>50) showed a significant increase on the risk and inadequate metabolic control (odds ratio- 3.298 IC-0.414-26.244) as well as smoking habit (odds ratio- 4.524 IC-0.595-34.367) elucidate a trend of increased risk of oral mucosal alterations in diabetes patients.

In contradiction to our study Alliny de souza Bastos et al [4] could not find any candidate factor to increase the risk for oral alterations. But their study recorded that smoking, female patients and patients with at least one kind of diabetes related complications showed a trend of increased risk for oral mucosal alterations.

However, it was not possible to investigate the clear cut underlying mechanism; the present study showed a significant prevalence of oral mucosal alterations in type-2 diabetes mellitus patients compared to the control subjects.

CONCLUSION

The results of the study have shown a significant prevalence of oral mucosa alterations in the diabetic patients as compared to control subjects, which show the necessity of periodic oral health examination for early diagnosis and management of oral mucosa lesions in diabetics.

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