Frequency of Oral Lesions in Diabetic Patients on Oral Hypoglycemic Drugs and Insulin

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ABSTRACT
Background: Lichen planus is a pre-cancerous condition which is immune mediated. It is often linked with other autoimmune diseases such as Diabetes Mellitus. It is linked with both Type 1 and Type 2 DM.

Methods: A retrospective cross-sectional study that was conducted at Jinnah Sindh Medical University on data of patients coming to Oral Medicine OPD from January 2020- December 2022. Diabetic patient’s data was extracted, and secondary analysis was done on it to find out the frequency of the lesions in both types.

Results: Data of 211 patients were analyzed through SPSS ver. 20. Total of 30 patient with oral lesions presented with diabetes mellitus with 8 having hepatits c. Data was excluded of those with co-morbid. The predominant age group was 41-50 years, all males, presenting with type 2 DM. Gingivitis(N=10) was the commonest followed by Oral Lichen Planus(N=7), Periodontitis(N=3), and Infections(N=2).The lesions were predominant in patients on Glucophage and insulin.

Conclusion: Diabetes Mellitus predisposes patients to a variety of oral problems. Early diagnosis of these lesions and changes in medication as per requirement to treat these lesions may benefit the quality of life of these patients.

Keywords: Oral Lichen Planus, Diabetes Mellitus, Autoimmune disorder

INTRODUCTION
Lichen planus is a premalignant condition affecting skin and mucosa alike. It is an autoimmune disease having both papulonodular and mucocutaneous manifestations with prevalence of 1-2% in the general population1-4. Though it affects women more as compared to men with a ratio of 2:1, predominantly seen in the second and third decades of life. The disease is not associated with any racial ethnicity5.

Oral lichen planus occurs in the oral cavity bilaterally and symmetrically. Common sites are buccal mucosa (60%), tongue (65%), lips (20%), and only <10% cases are of floor of the mouth and palate.6 The oral lichen planus has six types: reticular, atrophic, papular, bullous, plaque, erosive and ulcerative.7 OLP has shown transformation rate of 5.3% to malignancy resulting in its classification as precancerous lesion in 1978 by World Health Organization. The highest rate of change is seen in erosive and atrophic types.8 It manifests in the oral cavity weeks before its appearance on the skin.1 It has variable etiologies like stress, systemic medication, chronic liver diseases and hepatitis C, genetics, tobacco smoking, dental material, and graft versus host response.9

The pathophysiology in oral cavity is unknown but there are several theories. One of the suggested mechanisms is an antigen specific activation of the cytotoxic T cells along with mast cell degranulation and matrix metalloprotein activation through non-specific process. Further, the increased production of cytokines increases the Langerhans cells resulting in OLP.1

It is linked with multiple autoimmune disorders including Diabetes Mellitus.10 The type 1 share common grounds with oral lichen planus. One of the postulates of this association is endocrine dysfunction is associated with an immunologic defect which aids in the development of Oral lichen Planus. Meta-analysis on the prevalence of OLP in DM concluded it affects diabetics in the range of 0.5 to 9.3% comparative to the control subjects (0-1.8%).10 Another study concluded that type 1 diabetes has a pervasiveness of about 5.76% while type 2 has 2.83%.11 The patients having both oral lichen planus and Diabetes Mellitus have a high level of salivary interferlein-8 in them supporting the hypothesis that they are related.12 The purpose of current study is to find the frequency of oral lichen planus along with the commonest type of lesion in patients diagnose with Diabetes Mellitus visiting tertiary care clinic.

MATERIALS AND METHODS
A retrospective cross-sectional study was conducted on the data record of patients who visited Sindh Institute of Oral Health Sciences from 2020 January to 2021 December who were diagnosed with oral lesions. Permission from Institutional review board of Jinnah Sindh Medical University was taken prior to data retrieval from records of the patients (IRB No: JSMU/IRB/2021/587). A performa was designed to collect the data specifically required for the study. Convenience sampling was done and data of patients who fulfill the criteria of having diabetes mellitus without any other comorbid was included. Co-morbid for exclusions were Patients with ulcerative colitis, alopecia areataes, vitiligo, myasthenia gravis, chronic active hepatitis, primary biliary cirhosis and thyroidoma. Incomplete record forms of patients were also excluded as part of protocol. The identity of the patients was kept confidential by replacing identifiable information with coding and only the principal researcher had access to the data file.

The objectives of this study were to determine the frequency of oral lesions in patients with type 1 and type 2 diabetes and to identify the most common lesion. Additionally, the study aimed to investigate whether the frequency of oral lesions varied depending on the mode of treatment. By examining these factors, the study sought to improve our understanding of the relationship between diabetes and oral health and to provide insights into potential strategies for managing oral lesions in diabetic patients.

RESULTS
A Total of 211 patients reported with oral lesions during the duration of January 2020 to December 2021 to OPD of Oral medicine in SIOHS, only 30 patients were diagnosed with Diabetes mellitus. Data analysis was done through SPSS ver. 20. We have excluded data of 8 patients reporting with Hepatitis C as part of the protocol. Among these large number of patients who presented with Diabetes mellitus and oral lesions were in age range of 41-50 years. Patients who presented with type 1 Diabetes mellitus were 0 while those with Type 2 were 22. The degradation of cases according to lesion is shown in figure 1.

Figure 1 shows the frequency of lesions, from highest to lowest frequency were Gingivitis(N=10), Oral Lichen Planus(N=7), Periodontitis(N=3) and Bacterial infections (N=2).Among the white lesions only Oral lichen planus was present while in infections category only bacterial infections were reported.
Table 1 shows cross tabulation of drugs prescribed to control diabetes mellitus in type 2 patients. We found out that most of the cases with Lichen Planus (N=7) and Gingivitis (N=8) were present in patients treated with Glucophage. While, in insulin dependent patients the highest cases reported were of Gingivitis (N=2) followed by Periodontitis (N=1). The only case reported in the sulfa group drugs were of Periodontitis.

Table 2 shows the results from paired t-test. A total of three pairings were made according to the objective of our study. Pair 1 was between Type of diabetes and Oral Lesion. It was significant at the level of 0.001. While the pair 2 was between medication and Oral lesion and it was non-significant. The 3rd group was between Oral lesions and co-morbid which was significant at the level of p=0.005. Co-morbid includes hypertension and arthritis.

Table 1: Cross Tabulation Of Medications For Diabetes Mellitus And Oral Lesion

<table>
<thead>
<tr>
<th>Medication</th>
<th>Oral Lesion</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ginivitis</td>
<td>Periodontitis</td>
</tr>
<tr>
<td>Injectable</td>
<td>Insulin</td>
<td>2</td>
</tr>
<tr>
<td>Oral Hypoglycemic</td>
<td>Glucophage</td>
<td>8</td>
</tr>
<tr>
<td>Sulfa drugs</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2: paired t-test between different variables to find out the significance with oral lesions.

<table>
<thead>
<tr>
<th>Variable</th>
<th>p-value</th>
<th>Confidence Interval (95%)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>0.001†</td>
<td>1.12</td>
<td>-</td>
</tr>
<tr>
<td>Medication</td>
<td>1.673</td>
<td>0.724</td>
<td>0.228</td>
</tr>
</tbody>
</table>

† p-value at the level of 0.001 significant
‡ p-value at the level of 0.05 significant

**DISCUSSION**

We analyzed the files of 211 patients, who attended the OPD of oral medicine in SIOHS, from January 2020 to December 2021 and found a total of 22 diagnosed cases of Diabetes Mellitus. The male: female ratio was 1.5:1. The patient ages most being in the range from 41 to 50 years. Diabetes Mellitus has been linked with several oral manifestations and lesion including Lichen Planus. In past 10 years several studies have been conducted to confirm this link. A study held in Brazil on 146 patients with type 2 diabetes mellitus reporting that nearly twice the number of diabetic patients (88%) had one or more oral lesions as compared to non-diabetic control subjects and the difference was statistically significant (P < 0.001) (13). In another study higher prevalence of oral mucosal disorders was found in patients with DM compared to non-DM patients. This prevalence ranged from 45–88% in Type 2 diabetes mellitus patients to 38-45% in non-DM groups and from 44.7% in Type 1 diabetes mellitus patients to 25% in the non-DM population. In our study, the prevalence of oral lesions is higher in Diabetic Mellitus patients as the 22 patients reported over the period of 2 years. 7 cases of lichen planus, 10 cases of gingivitis, 3 cases of periodontitis, and 2 cases of bacterial infection were reported. Studies conducted in Indiana, Brazil, Spain, and UAE all showed prevalence of oral lesions in Diabetic Mellitus patients. Three out of five correspond to prevalence and two to case-control studies. All studies showed that Type 2 Diabetes patient reported with oral lesions in which Oral lichen planus was reported in UAE, Brazil, and Spain in contrast, while gingivitis was highest in Indiana. In the present study, the association between Lichen Planus and DM was found. 7 cases of lichen planus were found in Glucophage medicated type 2 DM patients and none of found in sulfa drugs and insulin. Cases of lichen planus have been reported with drugs like Glucophage therapy.

Bastos et al. reported a significantly higher prevalence of lichen planus in DM type 2 patients (6.1%) than in control subjects. Similarly, Baykal et al., in a case-control study reported mean duration of LP to be significantly higher 54.29 months (SD 35.8) among diabetic patients compared to 23.17 months (SD 35.8) among non-diabetic group (P=0.034). Van Dis and Park observed lichen planus in 4% of patients with diabetes. Another study of Albrecht et al. examined 781 diabetic type 2 patients and reported a prevalence rate of oral lichen planus at 1%. Study of C Petrou Amerikanou et al have recorded 139 insulin-dependent diabetics and 353 patients with noninsulin-dependent diabetes mellitus. Our observation is in concordance with the study of C Petrou Amerikanou et al. In the present study, no lichen planus was recorded in type I but C Petrou Amerikanou et al has reported a prevalence of 5.76%. Yet, another study by Atefi et al. showed the treatment duration for LP to be significantly higher among the diabetic group (P=0.0024). Among the local studies held in Pakistan in 2012 in Karachi reported 63 patients reporting with Oral Lichen Planus during that year. Majority were males and presented between the age of 20-40 years. Out of these 4 were diagnosed cases of Diabetes Mellitus. Another study held in Lahore in 2014 on skin diseases in diabetic patients reported that 58% of the sample were female with 3.82% cases of Lichen planus, melasma and vitiligo. Skin infections(28.16%) were the second commonest cause of visit to the outpatient department with majority reporting with fungal infections(34%) followed by bacterial (27.3%).

Although it is said that there is no sexual predilection in LP, however in our study revealed that most of the patients with oral lichen planus in type 2 diabetic groups were male. In one study, 26(52%) of the cases were male and 24(48%) were female with a slight male preponderance with a male: female ratio of 1.08:1, similar to a study done by Mushtaq et al. In contrast, multiple studies support higher proportion of men than women among the population. In a recent study held at Sialkot, they found 18 patients out of 500 diagnosed cases of Diabetes Mellitus with Oral Lichen Planus reporting prevalence of 3.6% with male to female ratio of 1:1.9.

Among the patients presenting with Oral Lichen Planus the majority ranged in between the age 41-50 years. Similarly, Souza et al. have reported their association in the age range 40-50 years in a similar set of patients. Therefore, the finding in our study is comparable to the studies mentioned.

There were 8 people with Hepatitis C. Since multiple studies have noted a substantial association between Hepatitis C and Lichen planus. Hence, we have removed details of patients with hepatitis from data pool. In Jordan, it was discovered that individuals with oral and cutaneous LP had much more HCV antibodies than the control group did. The reported incidence of HCV infection in patients with LP does, however, vary widely by country, ranging from 0% in England to 63% in Japan.
Hence, our findings are in concurrence with earlier studies held on relationship between Diabetes Mellitus and OLP. Prevalence according to age group and gender are also like earlier findings. No previous data is present to compare the results of prevalence of OLP in diabetic patients using different hypoglycemics medications. Though the limited number of patients in this study due to the brief time slot, affects generalizability of the results but it opens a gap for future studies.

REFERENCES