



A Study of Aetiopathology of Ulcers and Membranous Lesions of Oral Cavity and Oropharynx

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Abstract

Ulcers and membranous lesions of oral cavity and oropharynx is a common complaint encountered in E.N.T OPD. Proper knowledge of aetiopathology of these lesions is necessary to treat the underlying pathology.

Objective was to study etiology, incidence, duration, episodes, number, sex predilection and histopathological presentation of these lesions.

Method: The prospective study was carried out in 100 patients presented in department of ENT & Dermatology from February 2015 to August 2016 with complaints of ulcers/membranous lesions of oral cavity/oropharynx. After taking the detailed history of patients complete examination of ear, nose and throat was done. Investigations like biopsy and histopathological examination, and swab test for culture and sensitivity were also carried out for chronic lesions.

Result: out of 100 patients 80 patients had ulcers and 20 patients had membranous lesions. 56 patients had acute ulcers and 44 had chronic ulcers. Overall sex incidence ratio was 1:1. 52 cases had solitary lesions whereas 48 cases had multiple lesions. 65 cases out of 100 had first episode of lesions while 35 cases reported as recurrence. Out of 44 cases of chronic ulcers histopathological studies reported 13 cases were that of squamous cell carcinoma and 13 cases were of leukoplakia, 4 were lichen planus and candidiasis each and 3 were of pemphigus vulgaris.

Conclusion: ulcers and membranous lesions may be present due to various underlying pathologies. So proper diagnosis, through detailed history, clinical examination and investigations are warranted to find out cause and initiating treatment.

INTRODUCTION

An ulcer (Latin *ulcus*) is the breach of continuity of epithelium. Ulceration of oral mucosa is frequent occurrence producing The oral mucosa is fragile membrane and susceptible to erosions. The

word membrane is derived from the latin word "membrum" which is defined as a pliable sheet like structure acting as a boundary, lining, or partition in an organism. The membranous lesions of oral cavity and oropharynx are consequences of

infections (bacterial or fungal) or due to prolonged ill-effects of habit forming substances like tobacco, guthka etc. Present study is an algorithmic approach based on duration, recurrence, morphology, location and systemic symptoms of oral ulcers and membranous lesions which will be useful in evaluating etiology.

Material & Methods

The study was conducted from February 2015 to August 2016 on 100 patients diagnosed as cases of oral ulcers and membranous lesions of oral cavity and oropharynx.

Cases were selected from patients attending Ear Nose and Throat outpatient department and Dermatology out-patient department.

Informed consent was obtained from all individual participants included in the study. Patients of all age, sex, religion, and different socio-economic status with complaints of ulcers and membranous lesions in oral cavity and oropharynx were selected. Patients not willing for biopsy or swab test and patients with congenital lesions were excluded from the study. A detailed history and clinical examination was done in a systemic manner and noted on a specially designed proforma. Apart from detailed history and clinical examination investigations like biopsy and histopathological examination and swab test for culture and sensitivity were also carried out.

Results

In the present series, a clinical study was done on 100 cases of ulcers and membranous lesions of oral cavity and oropharynx. The salient features observed in the present series were as follows:-

80 cases were those of ulcers whereas 20 cases were those of membranous lesions. 56 cases were reported to be acute lesions while 44 cases were reported as chronic. (Table. 1) The peak age distribution was observed in the age group of 10-19 years that accounted 23% of patients, while minimum was in 0-9 age group. It accounted 5%. A secondary hike was seen in the age group of 50-59 due to chronic use of tobacco or smoking.

(Table. 2) Overall sex incidence ratio was 1:1. (Table. 3) Female preponderance (M:F::1:1.94) was noted in acute lesions whereas in chronic ulcers this Male:Female ratio was 2.67:1.

Out of the total 100 cases 52 cases had solitary lesions whereas 48 cases had multiple lesions. 65 cases had first episode of lesions while 35 case reported as recurrence of their ulcers/membranous lesions.

Major complaint of patients was ulceration (80%) followed by patches or membranes (20%) in mouth or throat. Associated complaints included burning sensation in mouth (45%), constipation (41%), trismus (32%), dyspepsia (29%), decreased appetite (27%), foul smell from mouth (26%), difficulty in swallowing (22%), bleeding from mouth (19%) and lesions at other parts of body (8%). (Figure. 1) The most common site of lesions was buccal mucosa (42%) followed by tongue (25%) whereas ulcers over anterior and posterior pillars (4%), retromolar trigone (4%) and gums (1%) were infrequent. (Table. 4)

The most common causes of oral and oropharyngeal lesions was tobacco /guthka chewing (35%) followed by psychological stress (29%) and bidi/cigarette smoking (28%). Other causes included anaemia (14%), trauma (6%) etc. (Table. 5)

60 cases were non smokers and 40 cases were having habit of smoking, tobacco/guthka chewing or both. (Table. 6)

Out of 44 cases of chronic ulcers histopathological studies reported 13 cases were that of squamous cell carcinoma and 13 cases were that of leukoplakia. 6 cases were reported as chronic non specific pathology. 4 cases were of lichen planus and candidiasis each and 3 cases were of pemphigous vulgaris. One case was reported as caseation necrosis with lymphocytic infiltrates suggestive of tubercular ulcer. (Figure. 2)

Table. 1: Acute Vs Chronic

S. NO.	Duration	Percentage
1.	ACUTE	56%
2.	CHRONIC	44%
3.	TOTAL	100%

Table 2: Age Distribution

AGE IN GROUP	NO. OF CASES	PERCENTAGE
0-9 years	5	5%
10-19years	23	23%
20-29years	18	18%
30-39years	16	16%
40-49years	14	14%
50-59years	16	16%
60-above	8	8%
TOTAL	100	100%

Table 3 : Sex Distribution

SEX	NO. OF CASES	PERCENTAGE
MALE	50	50%
FEMALE	50	50%
TOTAL	100	100

Table 4 : Site of Lesion

S.NO	SITE	NO. OF CASES	PERCENTAGE
1.	VESTIBULE(including lips)	17	17%
2.	GUMS	1	1%
3.	TONGUE	25	25%
4.	SOFT PALATE	7	7%
5.	BUCCAL MUCOSA	42	42%
6.	ANTERIOR /POSTERIOR PILLAR, TONSILLAR FOSSA	4	4%
7.	RETRO MOLAR TRIGONE	4	4%
	TOTAL	100	100%

Table 5 : Etiological Distribution

S.NO.	ETIOLOGY	NO. OF CASES	PERCENTAGE
1.	TRAUMA	6	6%
2.	ANAEMIA	14	14%
3.	ALLERGY	2	2%
4.	TOBACCO /GUTHKA CHEWING	35	35%
5.	SMOKING	28	28%
6.	PSYCHOLOGICAL STRESS	29	29%
7.	FAMILIAL ASSOCIATION	6	6%
8.	SYSTEMIC DISEASE	20	20%

Table 6 : Association of Smoking & Tobacco Chewing

S. NO.	SMOKING/TOBACCO CHEWING HABITS	NO. OF CASES	PERCENTAGE
1.	TOBACCO CHEWERS	13	13%
2.	SMOKERS	8	8%
3.	BOTH TOBACCO CHEWING AND SMOKING	19	19%
4.	NON SMOKERS/ NON TOBACCO CHEWERS	60	60%
	TOTAL	100	100%

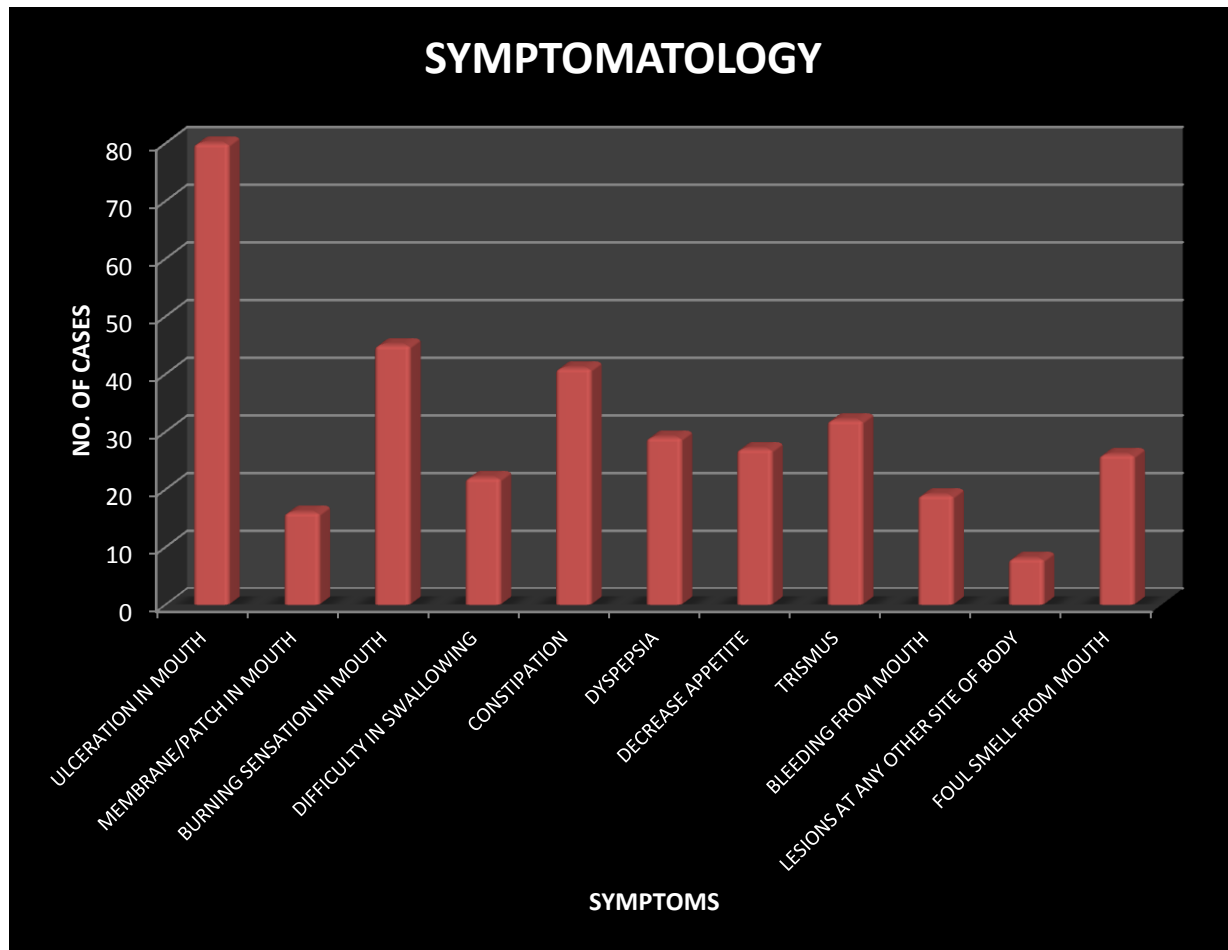


Figure 1. Showing symptoms in patients

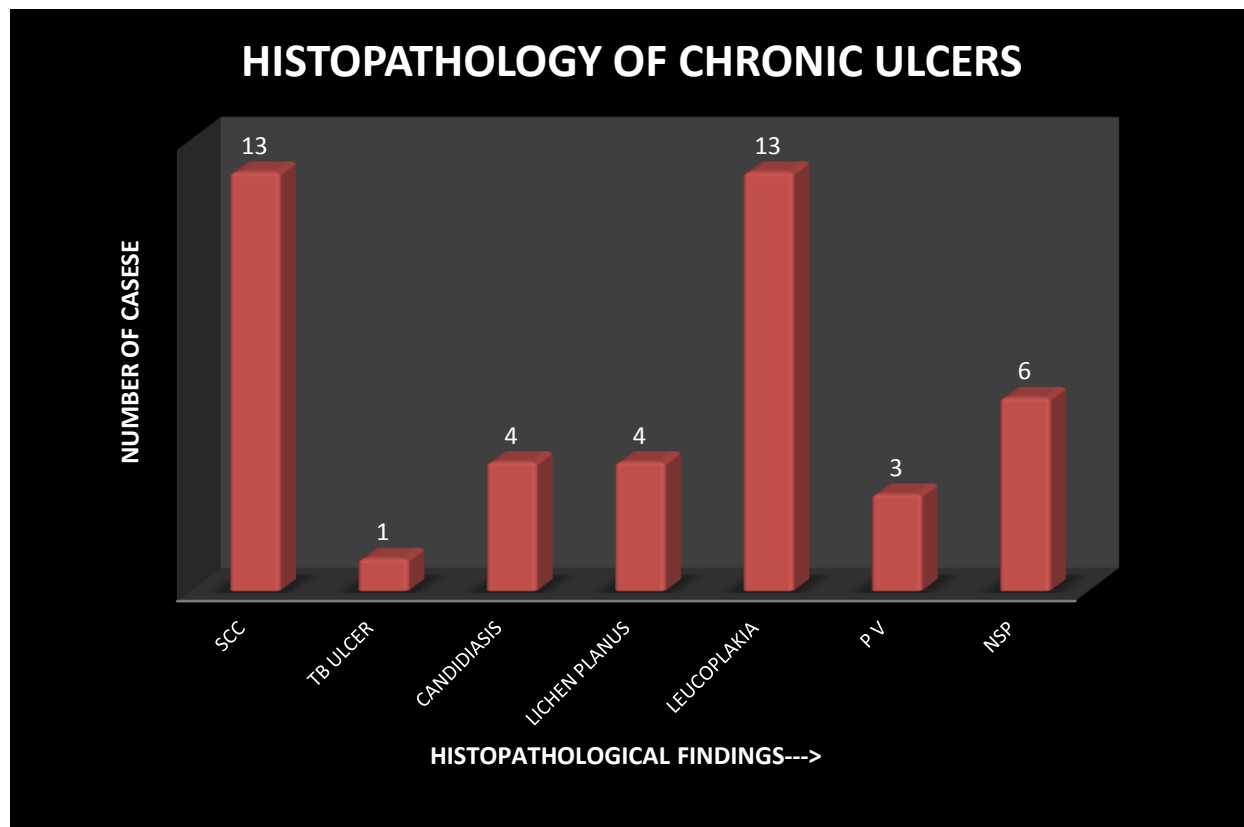


Figure 2. Showing histopathology of chronic ulcers

Discussion

As the data is collected for one and a half year duration (1.5years), thus for calculating incidence for one year data is divided by a factor of 1.5

Out of the total 49,954 new O.P.D cases seen during the period 14,686 cases were that of ulcers and membranous lesions of oral cavity and oropharynx i.e. incidence was found out to be 19.6 % person-years.

The incidence of lesions was highest in 10-19 years of age group and minimum in 0-9 years of age group. Distribution of these lesions was found equal in both genders.

The incidence of acute lesions was 10.9% and that of chronic lesions was 8.6%.The incidence of cases with single lesions was 12.7% and that of recurrent lesions was 6.8%.The incidence of cases with solitary lesions was 10.1% and that of multiple lesions was 9.4%.

Oral and oropharyngeal lesions are almost equally distributed among males and females. Tobacco chewing and smoking, nutrients deficiencies, viral and bacterial infections and traumatic irritation are frequent causes of ulcers and membranous lesions in oral cavity and oropharynx.

Relation of Lesions with Age

Out of the 100 cases of ulcers and membranous lesions selected for study, the maximum cases of mucosal lesions were reported in the age group of 10-19 years while the minimum cases were observed in 0-9 age group. The minimum age of the patient presenting with oral mucosal lesion was 1 year and maximum age was 70 years.

A rise in mucosal lesions in 20-29 years age group was seen due to development of habit of Guthka (Paan Masala), and tobacco chewing and smoking at early age.

Out of the 56 cases of acute oral ulcers & membranous lesions (<3 weeks duration) maximum cases were reported in the age group of 10-19 years. This age distribution coincides with the study done by Miller *et al.*^[1] (1980), Peretz (1994)^[2] Rennie *et al.*^[3] (1985).

The highest frequency of onset of Recurrent Oral Ulceration (ROU) is during the second decade of life and 67% to 85% of patients develop ROU in the first three decades. Church R. and Kelleher J. Sircus, W (1957)^[4], Lehner T.^[5] (1969); Aphthous ulcers usually appear during first and second decade of life and may continue throughout the entire life. Ship *et al.*^[6](1972).

Out of the 44 cases of chronic ulcers and membranous lesions most number of cases were reported in the age group of 50-59 years. These cases mainly were those of leukoplakia or carcinoma associated with prolonged history of tobacco chewing or smoking. Again, the minimum cases of chronic oral lesions were found to be in 0-9 years of age group.

Sex Distribution

Out of the 100 cases of ulcers and membranous lesions under study sex ratio was found to be as male: female:: 1:1.

Laronde (2008)^[7] and Naik Balachandra Ramachandra (2012)^[8] in their independent studies found out that the ratio of oral cancers in male and female was 1:1.

About 56 cases out of 100 were that of acute lesions (duration <3 weeks). Among these acute cases a slight female preponderance was seen i.e. a male:female ratio of 1:1.94.

This is in accordance with the study conducted by Saeedeh Eris *et al* (2007)^[9] among the students of Golestan Medical Science University in the North Of Iran where 60.5% patients were female i.e. a male:female ratio of 1.53:1.

Similar preponderance was noticed by Axell and Henricsson (1985)^[10], Field *et al* (1992)^[11] in case of oral ulcers.

ROU is more often found in females than males, but the ratio varies from 2:1 to 1.3:1. Church R. and Kelleher J. (1957)^[4], Lehner T. (1969)^[5].

Banoczy^[12] (1977) revealed the prevalence of leukoplakia in the age group of 51-60 years and sex distribution showed a male : female ratio of 3.2:1.

Number of Lesions (Solitary/Multiple)

In this study 52% of cases had solitary lesions in oral cavity and oropharynx whereas rest 48% cases had multiple lesions.

Cases having solitary lesions were mostly those of aphthous ulcers (16%), ulcers related to squamous cell carcinoma (13%), leukoplakia (13%), traumatic ulcers (6%) and lichen planus(4%).

Cases with multiple lesions in the mucosa of oral cavity and oropharynx were mostly those of ulcers with non-specific etiology (35%), candidiasis (4%), membranous tonsillitis (4%), pemphigus vulgaris (3%) and herpes zoster (2%).

Episodes

65 percent of cases under study had single episode of oral lesions. These mostly belong to ulcers with non specific etiology, traumatic ulcers, leukoplakic patches, membranous tonsillitis and malignant ulcers.

Symptomatology

Out of the 100 cases under study 80% cases presented with complaints of ulcers in mouth whereas 20% cases complained membranous lesions in mouth. Next frequent complaints were as described below:

Burning Sensation in Mouth

In our series about 45% of patients complained of burning sensation in mouth. Scully C, Campbell A (1982)^[13], also reported similar symptomatology in their study.

The prodromal stage of ulcerations is variable, but there is usually a sensation described as 'burning' or 'pricking' for a short period before the ulcers appear. Alison J, Bruce MD (2003)^[14].

Difficulty in Swallowing

In this study about 22% of cases complained of difficulty in swallowing. Mostly these cases had multiple ulcers in oral cavity or the ulcer was located over the soft palate, anterior or posterior pillars or there was membranous tonsillitis. Patients of pemphigus vulgaris having oral ulcers also complained of difficulty in swallowing.

In a study conducted by Rima Ahmad Safadi^[15] in Jordanian University claimed that ulcerations interfered with food eating and swallowing.

Constipation

In our series 41% of patients with ulcers or membranous lesions had a history of constipation. Patients who had leukoplakic patches had a common history of constipation and smoking or tobacco/guthka chewing.

Scully C, Porter S (1989)^[16] noted that change of gut flora and vitamin deficiency manifesting as constipation, gastrointestinal upset are one of the major predisposing cause of oral cavity ulcers.

Dyspepsia

Out of the 100 cases under study 29% of cases had associated symptoms of dyspepsia. Dyspepsia is often associated with gastro esophageal reflux and oral ulceration. Patients with oral ulcers and dyspepsia often have *H. pylori* infection.

In the Kangnam Hospital of Korea, Kim N *et al* ^[17] (2000) mentioned that in their study that *H. pylori* was detected in dental plaque and saliva from 7% and 14% respectively, of patients with *H. pylori*-positive gastric pathology, suggesting that the oral cavity may be an important reservoir of *H. pylori*.

In Venezuela, Berroteran *et al*^[18] (2002) investigated *H. pylori* infection in dental plaque from 32 dyspeptic patients, and its relationship with gastric pathology.

Decrease Appetite

Out of the 100 patients 27 % patients gave history of loss of appetite. These cases included patients with ulcers associated with constipation, burning sensation in mouth, dyspepsia and those chronic ulcers that were histologically diagnosed with malignancy.

Trismus

In this series 32% cases had complaint of restricted mouth opening. Most common reason of this was chronic tobacco chewing or smoking

leading to oral submucous fibrosis. Other causes included ulcer of buccal mucosa and retromolar trigone leading to painful mouth opening and trismus.

Oral submucous fibrosis is a commonly seen in people from the Indian subcontinent and in asian migrants in European. The exact aetiology is unknown but it is most commonly attributed to betel nut chewing. P.J. Dhanrajani et al (2002)^[19]

Bleeding From Mouth

19% of cases had associated complaints of bleeding from mouth. This chiefly included traumatic ulcers, ulcers those were histologically positive for cancer and herpes zoster.

Foul Smell From Mouth

26% of cases reported foul smell from mouth along with ulceration which signifies poor orodental hygiene resulting due to malignancy, tobacco addiction, smoking and dental caries.

Poor oral hygiene means accumulation of food particles and harmful agents for a longer period of time in oral cavity leading to exposure of oral mucosa to microorganisms.

Lesions at any other site of Body

8 cases out of 100 cases under study had lesions at other parts of the body. 3% cases were that of lichen planus having lesions at skin of limbs, 3% cases were that of pemphigus vulgaris having rashes over face and body and 1% was that of Behcet's disease having ulcers at genitals and ophthalmological symptoms.

Site of Lesions

The present study showed that the buccal mucosa is the most common site for oral mucosal lesions (42%) in which maximum number of cases were those of ulcers (aphthous ulcers, traumatic ulcers, and ulcers of non specific etiology) followed by leukoplakia. The next most common site of ulcers and membranous lesions in oral cavity was tongue (25%) and lesions found were leukoplakic plaques, malignant ulcers, and aphthous ulcers.

17% of ulcers were at vestibule and 7% were at soft palatal mucosa. These are common sites for aphthous ulcers and ulcers due to nutritional deficiencies (like vitamin B₁₂ deficiency). Lesions found over anterior and posterior pillar and tonsillar fossa were those of membranous tonsillitis (4%).

Etiology

Trauma: In this study 6% cases had trauma as the causative factor for oral ulcer. Various studies have shown that trauma is the common trigger for ulcers. Wray D, Ferguson M, Hutcheson W, Dagg J (1975)^[20].

In a trial conducted by Rees TD, Binnie WH (1996)^[21] involving 128 patients 16% claimed that a traumatic incident was associated with oral ulcers. This variation might be due to involvement of other type of oral lesions in this study, besides ulcers.

In our study it was observed that the trauma was because of cheek and tongue biting due sharp tooth, due to ill fitting dentures or due to acid ingestion.

In literature also similar cases have been observed. Salisbury III. PL, (1993)^[22] suggested that dentures can produce pressure ulcers which are typically small.

Herbert AA *et.al* 1997^[23], observed patients may also inadvertently produce traumatic ulcers through biting of oral mucosa either accidentally or through unconscious oral bites.

Anaemia

In the present study 14% cases anaemia (Hb <10%) was associated with oral ulcers. Both Iron deficiency anaemia, and pernicious anaemia may present with oral cavity ulcers. However, Olson *et.al.* (1982)^[24] found that vitamin B₁₂, folate and iron deficiencies were not significantly different between the patients with RAU and controls.

Other authors also suggested the role of anaemia as the etiological factor in oral ulcers. Wray *et.al.* (1975)^[20], Porter *et.al.* (1998)^[25]. Hematonic

deficiencies have been found in about 20% of patients with ROU. Brice SL *et.al* (2000)^[26].

Allergy

In the study population 2 cases reported allergy. One patient was on anti-depressant medication which resulted in drug allergy and oral ulcers. Other case was associated with drinking of alcohol already known allergic to him.

Abdollahi M, Radfar M,(2003)^[27] mentioned in their studies that the oral manifestations of drug reactions may be erythematous, vesicular, or ulcerative in nature. They may also mimic erosive lichen planus known as lichenoid drug reactions.

Many drugs acting locally or systemically can alter the ecosystem of the oral cavity or depress the immune system of the patient, increasing susceptibility to oral manifestations. Most of these infections are caused by overgrowth of organisms that are part of normal oral flora. Dr. Alan Tack & Roy S. RogersIII, (2002)^[28]

Tobacco/Guthka Chewing

35% cases in the study population had tobacco chewing addiction. These cases developed chronic ulcers or leukoplakic plaques. 13% of these chronic ulcers were histologically detected as squamous cell carcinoma.

Various studies show that the main risk factor for squamous cell carcinoma development worldwide is the habitual use of tobacco. Tobacco contains potent carcinogens, including nitrosoamines (nicotine), polycyclic aromatic hydrocarbons, nitrosodiethanolamine, nitrosoproline, and polonium.

Smoking: In this study out of total 56% cases with acute oral lesions 27% cases were smokers. Other study by P. Scheid, 2000^[29], has also shown that recurrent oral ulcers are less common among users of smokeless tobacco than among non users and among smokers than among non smokers.

Marija Bokor Bratic and Nada Vuckovic,^[30] 2002 mentioned that the higher percentage of smokers (94.3%) than non-smokers (5.7%) points to the accepted role of smoking tobacco use in the

development of oral leukoplakia. The results of this study also showed that longer the duration of smoking habits higher the prevalence of leukoplakia.

Chattopadhyay A, Chatterjee S. (2007)^[31], found in American adults that non smokers had a greater risk of RAU compared with those who smoked 10 cigarettes per day.

Stress: Out of the 100 cases, psychological stress factor was present in 29% of cases. This was mainly found in the young age groups of students and employed people. Many authors are today in the opinion that psychological stress may play a role in manifestation of recurrent aphthous stomatitis, it serves as a trigger or a modifying factor rather than being a cause of disease.

Earlier studies have documented an association between oral ulcers and a variety of psychological factors including anxiety, repressed hostility, as well as job related and other stressors. Ship *et.al* (1961)^[33], Miller *et.al.* (1977)^[34]

Familial Association

In the present study 6% patients reported that their family members (first degree relatives) have recurrent complaints of similar type of ulcers.

Ship (1965)^[34], Miller *et.al.* (1977),^[33] Miller *et.al.* (1980)^[35] suggested that patients with a positive family history of RAU (recurrent aphthous ulceration) develop ulcers at an earlier age.

The probability of a sibling developing RAU is influenced by the parents ROU status with increased risk in children of two affected parents (67-90%). Ship (1972)^[36]

Systemic Disease

Ulcers may be manifestations of disorders of the skin, connective tissue, blood, or gastrointestinal tract. The skin disorders most often associated with mouth ulcers are lichen planus, pemphigus, pemphigoid, erythema multiforme, epidermolysis bullosa, and angina bullosa hemorrhagica (blood-filled blisters that leave ulcerated areas after rupture).

Association of Smoking AND Tobacco Chewing

Tobacco in its many forms is a risk factor for oral cancer, oral mucosal lesions, periodontal disease, gingival recession, and coronal and root caries. Available evidence suggests that the risks of oral diseases increase with greater use of tobacco and that ceasing to use tobacco can result in decreased risks. The magnitude of the effect of tobacco on the occurrence of oral diseases is generally very high, with users having many times the risks of non-users. Tobacco use leads to additional consequences for persons with periodontal disease and oral cancer. Tobacco adversely affects healing after periodontal treatment, while among persons with oral cancer, continued use of tobacco increases the risk of a second primary cancers.

The risk for caries may be elevated in users as a consequence of the high amounts of sugar in chewing tobacco. There is an increasing recognition that genetic factors play a role in the development of tobacco-related oral diseases. Genetic factors affecting susceptibility to oral cancers include genotypes affecting metabolism of tobacco carcinogens and DNA repair. Specific genotypes for interleukin-1 are associated with adult periodontal disease.

Histopathological Studies

In the present study out of the 44 cases of chronic ulcers that were put under histopathological examination 13 cases were diagnosed with squamous cell carcinoma. Out of these 13 diagnosed cases 12 were male and 1 was female. Mean age of the cases was 48.92 years. The most common site was buccal mucosa (53.8%), followed by retromolar trigone (30%) lateral border of tongue (15%). Blot et. al. (1998)^[37], stated that tobacco smoking and alcohol drinking combine to account for approximately three-fourths of all oral and pharyngeal cancers in United States.

The study conducted by P Sharma et. al.^[38] (2010) for epidemiology of oral squamous cell carcinoma in west UP revealed a male:female ratio of 2.2:1,

with the largest number of Oral squamous cell carcinoma developing in the fourth and fifth decades of life

Squamous cell carcinoma is the most common type of oral malignancies. Age adjusted incidence rate in India is 44.8 years. About 40% of intra-oral squamous cell carcinomas begin on the floor of mouth or on the lateral and ventral surfaces of tongue.

Chronic Non-Specific Pathology

Out of the 44 cases whose oral lesions were biopsied 6 cases showed chronic non specific pathology on histopathological examination. The mucous membrane of these ulcers showed superficial tissue necrosis with a fibrinopurulent membrane covering the ulcerated area. The necrosis was covered by tissue debris and neutrophils. Epithelium was infiltrated by lymphocytes and few neutrophils. Intense inflammatory cell infiltration, predominantly neutrophils present immediately below the ulcer, mononuclear lymphocytes were seen in adjacent areas.

Caseation Necrosis with Lymphocytic Infiltrates

In one of the case of chronic ulcer, histopathological examination of biopsied ulcer revealed caseation necrosis with lymphocytic infiltrates which is specific finding of tuberculosis. Site of ulcer was tongue. The case was a known case of pulmonary tuberculosis.

Tubercular lesion of oral cavity are rare. Their incidence is 0.05-3.65% among patients with Tuberculosis.

Similar tuberculous ulcer case over tongue were reported by Prabhu SR, Daftary DK et al.(1978)^[39], A. Cakan et al (2001). According to them in secondary tuberculosis, lesions of the oral cavity may be seen simultaneously with lesions of the pharynx, lungs, lymph nodes or miliary tuberculosis.

Conclusion

It can be concluded that oral lesions have multifactorial etiology with dietary habits playing a major role. Acute ulcers were seen more often in non-smokers, while anaemia, allergy, cytotoxic drugs, trauma, psychological stress were other causes playing contributory role. The study faced certain limitations due to factors like unawareness and illiteracy of patients, lack of higher investigating facilities like serum immune markers and also the lack of medical insurance facilities in government institution which prevented the study to go another level.

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