

**“ORAL MUCOSAL LESIONS IN GERIATRIC POPULATION
A CLINICO-EPIDEMIOLOGICAL STUDY.”**

By:

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Under The Guidance Of

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ABSTRACT

BACKGROUND:

Oral health is important to individuals of all age groups. Oral mucosal lesions and its normal anatomical variations are very common in all age group. The oral mucosa performs essential protective functions that plays an important role in the general health status of an individual. Any decline in the protective functions of the oral mucosa could expose the aging individual to a variety of pathogens and chemicals. During aging, oral epithelium becomes thinner and collagen synthesis also decreases, which leads to decreased tissue regeneration and disease resistance. The oral mucosa becomes permeable to toxic substances and more vulnerable to external carcinogens.

OBJECTIVES:

1. To study the clinical pattern and the types of oral mucosal lesions in geriatric population.
2. To study the distribution and possible etiological factors of oral mucosal lesions in geriatric population.

MATERIAL AND METHODS:

The study was carried out from January 2016 to July 2017. All patients above 60 years of age, reporting to Dermatology OPD at R.L.Jalapa Hospital &

Research Centre, attached to Sri Devaraj Urs Medical College, Tamaka, Kolar were examined and evaluated for oral mucosal lesions. A detailed medical history including demographic data, chief complaints related to skin, presence of oral mucosal lesions, medical disorders, medications used, and habits (smoking, alcohol consumption, chewing of betel nut, other forms of tobacco use, prosthetic or other appliances use) taken and detailed general physical examination was made to see any associated lesions elsewhere in the body. The clinical diagnosis was established and classified. Correlation, if any, with etiological factor was assessed. In relevant cases, necessary investigations were done with a written consent from the patient, to establish the definitive diagnosis.

The final definitive diagnosis was based on histopathological examination given by pathologists and its clinical correlation. The data collected was documented in the prescribed proforma and further validated by the consultants.

RESULTS:

A total of 130 cases fulfilling above 60 years with oral mucosal lesions who presented to Dermatology OPD at R.L. Jalappa Hospital and Research centre, Tamaka, Kolar district, Karnataka during the period of from January 2016 - July 2017 were enrolled in this clinical study. In the present study, majority of

the patients, were in the age group of 60-69 years (71%), followed by the age group of 70-79 years (24%), least were the age group of 60-69 year (5%) and there was no cases above 90 years. Males (56.2%) were affected marginally more than females (43.8%). Buccal mucosa was the most frequently involved site in 58% of the study population. In the present study, common risk factors associated with oral mucosal lesions observed were smoking (40%), alcohol (17.7%), other forms of tobacco use (46.2%), betel nut chewing (52.3%), dentures (12.3%) and stress (13.8%). A total 130 conditions, classified into 8 various etiological categories. Malignancy (25.4%) was the most common etiology, followed by dermatological etiology (19.2%) and then premalignant and infective etiologies (16.9%). Other miscellaneous conditions (13.8%), inflammatory (4.6%), developmental (2.3%) and systemic etiologies (0.8%) were the uncommon observed etiologies. Amongst malignancy, squamous cell carcinoma was the common clinical type. The second most frequently observed condition was oral candidiasis (12.4%). Amongst dermatological conditions, most common was oral lichen planus 8%, followed by vitiligo 6%, pemphigus 3% and psoriasis (2%). The least conditions were Steven Johnson syndrome, systemic lupus erythematosus and discoid lupus erythematosus. Leukoplakia (8.5%) was the most common premalignant conditions, followed by oral submucous fibrosis(7.7%).

CONCLUSION:

The present study brings to light various oral mucosal lesions in geriatric population, which also highlights the importance of early diagnosis of oral precancerous lesions before it develops into malignancy.

LIST OF ABBREVIATIONS USED

WHO - World Health Organisation

OML - Oral Mucosal Lesion

OLP - Oral Lichen Planus

HPV - Human papilloma Virus

HIV - Human Immunodeficiency Virus

HSV - Herpes simplex virus

OSCC - Oral Squamous Cell Carcinoma

OSF - Oral Submucous Fibrosis

OHL - Oral Hairy Leukoplakia

CMC - Chronic mucocutaneous candidiasis

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INTRODUCTION



INTRODUCTION:

Oral health is important to all individuals as the oral mucosa performs essential protective functions that plays an important role in the general health status of an individual.¹ As per WHO definition, a population aging more than 60 years old should be considered to be an elderly population.²

In the aging individual, the systemic comorbidities and concurrent medications can cause decline in the protective function which could expose the oral mucosa to a variety of pathogens and chemicals. Aging can cause atrophic changes like thinning of oral epithelium and reduction in collagen synthesis which leads to impaired tissue regeneration and disease resistance.²

Various oral carcinogens including smoking, alcohol, other forms of tobacco and habits of chewing betel quid or areca nut have been found as etiological factors for oral precancerous and cancerous lesions.^{2,3} Cancers are the increasing cause of mortality in patients with oral mucosal lesions. It can be seen on the lip, buccal mucosa, floor of the mouth, palate as well as on the tongue. Oral cancer is one among the top three types of cancers in India.³

Reduced salivary gland function in aging, can predispose to infections of oral mucosa, commonly oral candidiasis.^{2,3} Dermatologic diseases have got special attention in oral medicine as oral mucosal lesion (OML) can be the

primary clinical feature or sometimes the only sign for various mucocutaneous diseases.⁴

Since there is a paucity of literature in various studies about oral mucosal lesions in the Indian geriatric population, the present study aimed to document the clinical types of oral mucosal lesions in geriatric population and also to study their distribution with possible etiological factors which will be valuable in planning future oral health studies.

AIMS & OBJECTIVES



AIMS AND OBJECTIVES

1. To study the clinical pattern and the types of oral mucosal lesions in geriatric population.
2. To study the distribution and possible etiological factors of oral mucosal lesions in geriatric population.

REVIEW OF LITERATURE

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REVIEW OF LITERATURE

An Indian study on prevalence and distribution of oral mucosal lesions (OMLs) in a geriatric population conducted in 5100 patients with age ranging from 60 – 98years. There were 3100 males and 2000 females, with an average age of 69 + or – 6.3years. 64 % of the patients presented with one or more oral lesions, associated to tobacco, betel nut consumption and lesion secondary to trauma and prosthesis. Males were affected more than females and this difference was clinically not significant. The most common observations were smoker's palate (43%), denture stomatitis (34%), oral sub mucous fibrosis (30%), frictional keratosis, leukoplakia (22%) and pyogenic granuloma (22%). Hard palate was the most commonly affected site (23%). Leukoplakia was the most common pre-malignant lesion in the study and squamous cell carcinoma were diagnosed as the most common malignant condition which was confirmed by microscopic analysis. They came to a conclusion as increased number of aged individuals with oral mucosal lesions implies an important demographic change all over the globe.¹

A study on oral mucosal lesion in elderly dental patients in Sana'a, Yemen was conducted with an objective to obtain baseline data on the prevalence and to investigate differences in the presentation of these findings in relation to age, gender, education level and the wearing of dentures. The overall prevalence of OMLs was 77.1% with a significant difference between men

and women. The prevalence of OMLs indicated a significant decrease with advancing age. The most frequently observed lesions were fissured tongue (34.2%), benign tumours (17.1%), hairy tongue (16.5%) and qat induced white lesions (12.6%). The presence of one or more lesions mostly significantly associated with low education levels. Certain OMLs showed a significant association with smoking and qat chewing.²

According to the study done in Chennai on prevalence of oral cancers in India most oral cancers affected the people from the lower socio-economic status of society and people in rural area due to a higher exposure to risk factors such as the use of tobacco, alcohol, betel nut chewing and human papilloma virus (HPV).³ In India, 90-95% of oral cancers are squamous cell carcinoma. Early detection has better curing rates, so preventive measures can reduce the incidence and mortality of oral cancer with better survival. Because of the high population in India, cancer control activities should be prioritized to make maximum use from the limited resources. People less than 40 years who are habitual cigarette smokers, alcohol consumers, and betel quid chewers must undergo oral mucosa screening regularly so that oral cancer can be identified as early as possible.³

A cross sectional Study in Sudan studied 315 patients with OML in skin disease attending a dermatological clinic. This study showed a significant male preponderance (males 54.6% versus females 45.6%, $p < 0.05$) .Tongue

lesions were the most frequently diagnosed followed by white lesions (19.1%) red and blue lesions (11%) and vesiculobullous diseases (6%). Presence of OML in skin diseased patients was most frequent in older age groups (62.4% older versus 52.7% younger), 63.2% males versus 52.6% females and among current users smokeless tobacco (77% current use versus 54.8% no use) . They came to a conclusion that OML were diagnosed in skin diseased patients and varied systemically with age, gender, systemic conditions and use of tobacco.⁴

ANATOMY OF ORAL MUCOSA^{5,6}

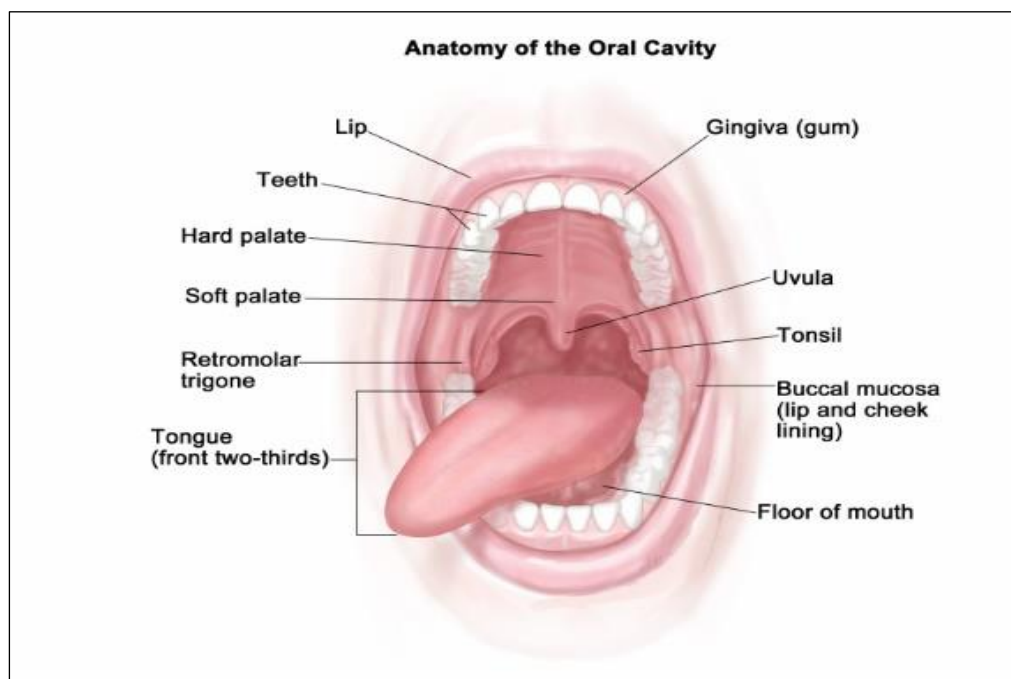


Fig 1: Anatomy of oral cavity.

Oral mucosa is a moist lining of the oral cavity. It consists of:

1. A covering epithelium

2. An underlying connective tissue – the lamina propria.

Oral mucosa is composed of:

- a. Epithelial tissue which is a stratified squamous epithelium.
- b. The underlying loose connective tissue component is called lamina propria. Epithelium is separated from the lamina propria by a basal lamina-basement membrane complex.
- c. Sub mucosa.

The epithelial tissues of gingiva and hard palate are keratinized, although in many individuals the gingival epithelium is para keratinized. The cheek, faucial and the sub lingual tissues are non- keratinized.

Lamina propria is composed of cells, fibres and amorphous ground substance. It also contains blood vessels and nerves.

Sub mucosa lies beneath the lamina propria and consists of connective tissue of varying thickness, minor salivary glands, blood vessels, nerves and adipose tissue. Lymphoid nodules are found at the base of tongue.

Types of oral mucosa

3 types according to functionally:^{5,6}

- a. Masticatory Mucosa: 25% of total mucosa. Gingiva (free, attached and interdental) and hard palate. Primary mucosa to be in contact with food during mastication. Masticatory mucosa is usually keratinized.
- b. Lining Mucosa: 60% of total mucosa. Covers the floor of mouth, ventral tongue, alveolar mucosa, cheeks, lips and soft palate. Does not function in mastication hence minimal attrition. Non-keratinized; soft and pliable.
- c. Specialized Mucosa: 15% of total mucosa. Covers dorsal tongue and composed of cornified epithelial papillae.

Functions of the Oral Mucosa⁷

- a. Protection: Barrier for mechanical trauma and microbiological insults
- b. Sensation: Temperature (heat and cold), touch, pain, taste buds, thirst; reflexes such as swallowing, etching, gagging and salivating
- c. Secretion and Excretion: Salivary secretion
- d. Mastication

Classification of the oral mucosal lesions

- 1. Developmental or Congenital
 - a. Fordyce spot
 - b. Melanoplakia
 - c. Intraoral nevi

2. Inflammatory/ reactive
 - a. Nicotinic stomatitis
 - b. Frictional, chemical, and thermal keratosis
 - c. Cheilitis
3. Infective
 - a. Candidiasis
 - b. Oral hairy leukoplakia
 - c. Herpes simplex Infection
 - d. Warts
4. Oral manifestation of Systemic disorders
 - a. Jaundice
 - b. Haematological disorders
5. Oral manifestation of Dermatological disorders
 - a. Psoriasis
 - b. Lichen planus
 - c. Pemphigoid
 - d. Pemphigus
 - e. Vitiligo
 - f. Systemic lupus erythematosus
 - g. Discoid lupus erythematosus
 - h. Steven Johnson syndrome
 - i. Toxic epidermal necrolysis

6. Premalignant
 - a. Oral submucosal fibrosis
 - b. Florid oral papillomatosis
 - c. Leukoplakia
 - d. Erythroplakia
7. Malignant
 - a. Squamous cell carcinoma.
 - b. Malignant melanoma
 - c. Kaposi's sarcoma
8. Miscellaneous
 - a. Recurrent aphthous stomatitis
 - b. Drug induced mucositis
 - c. Tongue lesions

DEVELOPMENTAL OR NORMAL ANATOMICAL VARIATION

1. **FORDYCE SPOT** (Fordyce granules)

Introduction

Fordyce spots are ectopic sebaceous glands, containing neutral lipids similar to those seen in skin sebaceous glands, lacking an association with hair follicle. Although uncommon, these may also be found in the

esophagus, gastrointestinal junction, uterine cervix, sole of the foot, thymus or tongue.⁸

Etiopathogenesis

Even though the sebaceous glands are present since birth, this condition is not common before puberty. The incidence continues to increase with age and the prevalence in adults is 70% to 80%, with a slight male predominance.⁹

The pathophysiology of Fordyce's spots is unknown. It can be due to ectopic disposition of sebaceous glands during embryonic development, which is considered as a variation of normal anatomy.⁸

Clinical Features

Fordyce spots appear as asymptomatic, multiple 0.1 to 1-mm yellow to yellow-white papules often occurring bilaterally, and they may occasionally form plaques. It is seen most commonly on the lips adjacent to the vermilion border, buccal mucosa, particularly inside the commissures, and sometimes in the retromolar regions.⁹

Treatment

No treatment is indicated, other than reassurance. The spots may become less prominent with oral isotretinoin, but on stoppage of treatment recurrence are also reported. Other therapies found effective on trial studies are bi-chloro acetic acid (BCA), CO2 laser and 5-aminolaevulinic acid-photodynamic therapies.¹⁰

2. MELANOPLAKIA

It is a physiologic pigmentation of oral mucosa, characterized by multifocal or diffuse melanin pigmentation with variable prevalence in different ethnic groups. The pigmentation depends on amount of melanin in the normal oral mucosa which varies in intensity and distribution with racial differences varying for the greatest.¹¹

Clinical features

Clinically presents as a diffuse or multifocal melanin pigmentation which is symmetric, persistent and does not alter the normal architecture of the tissues affected. Intraorally the most commonly affected site is gingiva but, can also occur on buccal mucosa, alveolar mucosa, tongue and to a lesser extent in soft palates. The pigmentation of gingiva produces black discoloration of gingival which is commonly known as Black Gum.¹²

Histology

Histopathologic evaluation shows increased melanin pigmentation with normal number of melanocytes. The melanin pigment is found in surrounding basal keratinocytes and subjacent macrophages.¹¹

Clinical differential diagnosis are Smoker's melanosis, Addison's disease, melanoma.^{11,12}

INFLAMMATORY / REACTIVE

1. SMOKER'S MELANOSIS¹³

Clinically, it is seen as white palatal proliferation with central red areas representing inflamed or obstructed minor salivary gland ducts.

Histology

Histopathologic evaluation shows hyperkeratinized epithelium and marked squamous metaplasia with deep rete ridge penetration in to the connective tissue lamina propria with diffuse inflammation that frequently surrounds small ducts with associated minor salivary glands.¹⁴

2. FRICTIONAL, CHEMICAL, AND THERMAL KERATOSES

Keratoses are characterized by whitish plaques develop as a result of an identifiable source which usually resolve once the causative factor is eliminated. Commonly observed causative factors are friction, chemicals and heat.¹⁵

Frictional keratosis is commonly seen in young adults. The sources of friction resulting in hyperkeratosis may be an ill-fitting denture, malocclusion, para-functional habits, or poor brushing techniques.¹⁵

Chemicals causing burning of the mucosa and resultant hyperkeratosis include aspirin, sodium hypochlorite, hydrogen peroxide, formocresol, paraformaldehyde, cavity varnish, or mouthwashes, to name a few.¹⁶

Thermal keratosis due to thermal burns in the oral cavity caused by excessively hot foods or heat generated from smoking. Lesions are commonly seen on the tongue and palate.¹⁶

In tobacco-related form of keratosis (Nicotine stomatitis) both chemical and thermal factors play a part.

Clinical features

Frictional keratosis is typically characterized by a poorly demarcated rough area, which can be peeled off occasionally, leaving focal areas of pink mucosa. Lips, lateral surface of tongue, and buccal mucosa are commonly affected sites. Persistent masticatory trauma often results in thick white corrugated lesions on the retromolar pad areas.¹⁵

Chemical keratosis is characterized by variably symptomatic white, irregularly shaped plaques typically located on the mucobuccal fold or the gingival mucosa.¹⁶

Thermal keratosis is characterized by a white lesion with focal areas of ulceration associated with mild to moderate pain.¹⁶

Differential diagnosis

Thermal and chemically induced lesions are almost always painful. The keratotic plaque has to be differentiated from white lesions of Morsicatio buccarum. In Morsicatio buccarum, lesions are asymptomatic with bacterial colonization of the plaque.^{15,16}

The white lesions of leukoedema do not rub off and disappearance of the opalescence on stretching of the oral mucosa is diagnostic. It should also be differentiated from leukoplakia, candidiasis, white sponge nevus, oral hairy leukoplakia, and squamous cell carcinoma.^{16,17}

Treatment

Removal of the causative factor leads to resolution of the lesions. No active intervention is needed as these lesions do not show any malignant potential.¹⁷

3. CHEILITIS

Inflammation of the lips are called cheilitis. It can affect the perioral skin, vermillion border and the labial mucosa. Usually presents as dryness, fissuring oozing and crusting. Sometimes can occur secondary to seborrheic dermatitis, atopic dermatitis, psoriasis, post-retinoid therapy and chronic exposure to sunlight. Dyes in lipstick and mouthwashes with allergic or irritating substances may be causative factors. Cheilitis can also occur in Plummer Vinson syndrome and in Human Immunodeficiency virus infection.¹⁸

Allergic contact cheilitis: Over 90% of patients are women and vermillion border is more likely to be affected. It can result from the use of topical medications, mouth washes, antichap agents and other dental

preparations. Cosmetics like lipsticks, sunscreen containing lip-balms, nail polish, fragrances are also observed to cause allergic cheilitis. Treatment includes discontinuation of offending agents and topical medications like topical calcineurin inhibitors, or corticosteroid preparations.¹⁹

Actinic cheilitis: Actinic cheilitis results from chronic exposure of the lips to sunlight. Usually lower lip is the one affected, becomes dry, fissured and atrophic. A high proportion of patients can develop squamous cell carcinoma, when not diagnosed and treated in early stages. Any suspicious lesion, biopsy should be done to rule out malignancy. Avoiding sun exposure and using sunscreen containing lip balms can minimize further damage. Topical 5-fluorouracil, imiquimod are effective. Cryosurgical treatment are effective for localized lesions.^{18,20}

Glandular Cheilitis: It is characterized by swelling and eversion of the lower lip, with numerous pin head sized orifices from which mucus exudes freely to form a gluey film that may cause the lips to stick together during the night. On palpation the enlarged mucus glands feel like pebbles beneath the surface. The lower lip is the site of predilection, with a male preponderance. Cheilitis glandularis has been reported to eventuate in OSCC, but can be by chronic sun exposure. Topical immunomodulators and cryosurgical therapies are effective. Surgical debulking is necessary in most cases. Intralesional triamcinolone may be

beneficial in some. Combination of minocycline and tacrolimus ointment are also tried effective.^{18,21}

Granulomatous (Meischer's) Cheilitis: Characterized by progressive and chronic enlargement of the lips- usually the upper, without ulceration or scaling leading to permanent macrocheilia. It may be part of a triad of recurrent lip edema, facial paralysis and scrotal tongue - Melkersson Rosenthal syndrome. Clinically, episodic nontender swelling of one or both lips and occasionally, other parts of the face, hyperplastic gums, regional lymphadenopathy. Histology reveals a perivascular and interstitial infiltrate of lymphocytes, plasma cells, histiocytes, focal noncaseating epithelioid granulomas, multinucleated cells of the Langerhans type. The main differential diagnosis is *Morbus Morbihan* – a persistent erythema and edema of the mid third and upper aspect of the face. Treatment is surgical reduction cheiloplasty combined with intralesional steroid.^{18,22}

Plasma Cell Cheilitis (Plasma Cell Orificial Mucositis): A rare inflammatory disorder of the lip characterized. By circumscribed, flat to slightly raised, eroded area of the lip. The cause of plasma-cell cheilitis is unknown. Histologically by a band-like infiltrate of plasma cells in the upper dermis. It is considered an oral counterpart of Zoon's balanitis. The treatment is often disappointing. Topical and intralesional corticosteroids are suggested to be the best forms of therapy.²³

INFECTIVE

1. ORAL CANDIDIASIS

Candidiasis is a common opportunistic infection of the oral cavity, oropharynx and corners of the mouth.²⁴

Etiology

Candida albicans represents the most common candidial species, whereas *C. tropicalis*, *C. krusei* and *C. glabrata* are uncommon. Commensal existence of oral *Candida* species varies from 20% to 50% in a healthy dentulous population. *Candida* carriage rate has been shown to also increase with age, smoking, cancer radiation therapy, diabetes, and HIV infection.²⁵

Pathogen

Most instances of oral candidiasis are caused by *Candida albicans*, despite the fact that an extensive number of other yeast species possibly discovered intraorally. These incorporate *C. tropicalis*, *C. krusei*, *C. parapsilosis*, and *C. guilliermondii*. In oral candidiasis, *C. albicans* by and large records for around half of cases.²⁵

The etiology of oral candidiasis isn't a solitary element rather, a mix of hazard factors like glycaemic control, sex, age, smoking and wearing of dentures.²⁶

Host

Local factors: Denture wearing, steroid inhaler utilize, decreased salivary stream (xerostomia), high sugar slim down.

Systemic factors: Extremes of age, endocrine issue (e.g. diabetes), malignancies (e.g. leukemia), receipt of expansive range anti-microbials, that modify the typical microflora.²⁶

Other factors are smoking, Cushing's syndrome, immunosuppressive conditions such as HIV infection and nutritional deficiencies.²⁷

In HIV patients, oral candidiasis is the most common opportunistic infection occurring in as many as 90% of patients at some point during the course of infection. It is a marker for increased rate of progression to HIV infection.^{27,28}

Though the reported prevalence of oral candidiasis in patients receiving systemic steroids is 30-35%, the relationship between candidal carriage or infection and systemic steroid therapy is not yet clear.

Some soreness in the denture-bearing area is said to affect nearly one-quarter of all denture wearers and most, but not all cases appear to be caused by candidiasis. Elimination of *Candida* alone does not usually result in complete recovery, and it is likely that other factors such as chronic mechanical irritation and bacterial colonization also have a role in the pathogenesis.²⁸

Clinical features

Oral candidiasis may have various clinical presentations as discussed bellows:²⁹

1. Pseudomembranous candidiasis (oral thrush)

Acute Pseudomembranous candidiasis is characterized by sharply defined superficial curd like white patches covered by a pseudomembrane which, on scraping leaves an erythematous base.²⁹ These white patches occur on the surface of the labial and buccal mucosa, hard and soft palate, periodontal tissues, and oropharynx. In immunocompromised patients, the tongue may be affected as well. Diagnosis is usually clinical and can be confirmed microbiologically either by staining a smear from the affected area or by culturing a swab from an oral rinse.³⁰

Chronic pseudomembranous candidiasis is seen in immunocompromised patients.

2. Atrophic candidiasis

Acute atrophic candidiasis (acute erythematous oral candidiasis; antibiotic sore tongue) is characterized by marked soreness and focal or diffuse areas of denuded atrophic erythematous mucosa, particularly on the dorsum of the tongue. It is especially associated with antibiotic therapy. Also develop in HIV-positive subjects and patients taking inhaled steroids.

Chronic atrophic candidiasis (chronic erythematous candidiasis; denture sore mouth; denture stomatitis) presents as a variable bright-red or dusky area of erythema with a pebbly or velvet surface confined to the upper denture-bearing area, the palate and gums. Often associated with an angular cheilitis.²⁸⁻³¹

3. Angular cheilitis

This can occur secondary to both fungal and bacterial infection. The clinical presentation consists of soreness along with erythema and fissuring at the commissures, most often bilateral.³¹⁻³⁴

4. Chronic hyperplastic candidiasis

Also known as chronic hypertrophic candidiasis or chronic leukoplakia, presents as very persistent, firm, non-scrapable irregular white plaques in the mouth commonly on the buccal mucosa or tongue. Sometimes surrounded by a margin of erythema. Usually asymptomatic or with mild soreness noticed. It is commonly seen in above 30 year aged males and associated with smoking. Must be differentiated from leukoplakia.³⁵

5. Median rhomboid glossitis

Appears as an asymptomatic diamond or oval shaped erythematous depapillated area in the midline of the dorsum of the tongue, just anterior to sulcus terminalis. The surface is smooth or lobulated. Usually asymptomatic, but sometimes burning sensation can occur. However involvement of palates can be indicative of immunosuppression.³⁵

6. Chronic multifocal candidiasis

It is defined as the presentation of candidiasis in more than one location, such as concurrent dental stomatitis and angular cheilitis. Additional clinical criteria for this condition include the presence of lesions for more than 4 weeks, the absence of any predisposing medical conditions, and the exclusion of patients who are on immunosuppressive drugs.³⁶

Chronic mucocutaneous candidiasis (CMC) is a rare inherited form, and can present during early childhood. It presents as persistent *Candida* infection of the mouth, the skin and the nails, refractory to conventional topical therapy. Oral lesions are superficial and diffuse.³⁵ Lip involvement in the form of petechiae is common. Underlying immune defects, including thymoma, should be excluded. It can also form a part of the autoimmune polyendocrinopathy candida ectodermal dystrophy syndrome (APECED).³⁶ Oral lesions start as pseudomembranous candidiasis, and then proceeds to become chronic hyperplastic candidiasis.

Diagnosis

The diagnosis of this condition is by positive direct microscopy. On 10% potassium hydroxide mount, pseudohyphae or budding cells consistent with the *Candida* morphology can be demonstrated. A cytologic smear or biopsy stained with periodic acid–Schiff is also useful. This method stains the abundant carbohydrates in the fungal cell walls and the fungi

appear in bright magenta color.¹⁴ The most frequently used primary isolation medium for *Candida* is Sabouraud's dextrose agar (SDA).³⁸

Treatment

The main stay of treatment is identification and treatment of underlying predisposing factors; frequent toilet in the seriously ill, and denture hygiene in other patients. Depending on its virulence, location and type of candidiasis there will carry on one treatment or another.³⁹

First has been supported the use of conservative measures before starting drug treatment, promoting good oral hygiene along with removing the dentures at night, thereby it will benefit the removal of the biofilm layer generated in the prosthetic surface.²⁸

Regarding the pharmacological treatment of candidiasis can be distinguished between two procedures.

Topical antifungal therapy alone is sufficient to treat in majority of cases.^{32,39}

Regular amphotericin lozenges, nystatin or amphotericin tablets or oral nystatin suspension are effective in non-immunocompromised patients. In acute cases, 10-14 days of treatment is adequate.³³ Angular stomatitis usually responds to treatment of the primary oral condition, although a topical antifungal applied to the area may speed recovery.^{34,36}

Systemic treatment is indicated in unresponsive and chronic cases, like those with hyperplastic candidiasis, with HIV infection or chronic

mucocutaneous candidiasis. With antiretroviral therapy (ART) the therapeutic outcome improves significantly in HIV infection patients. For systemic treatment, commonly used are triazoles, fluconazole and itraconazole. The usual daily doses are itraconazole 100–200 mg and fluconazole 100–400 mg.^{32,33,40}

In immunosuppressed patients, risk of recurrence is high. Because of the risk of resistance developing with continuous therapy, intermittent therapy should be given. Treatment is usually continued until there is symptomatic recovery.³⁹

In patients with chronic oral candidiasis, a biopsy may be justified to exclude leukoplakia.³⁵

2. HERPES SIMPLEX INFECTION

Herpes simplex virus (HSV) infections are among the infections most frequently encountered by humans. Two types of HSV infections have been identified HSV-1, which usually causes orolabial disease, and HSV-2, which is more frequently associated with genital and newborn infections. Usually, HSV causes mild and self-limited disease of the mouth and lips or at genital sites.⁴¹

Primary Herpes Simplex Infection

It is caused by HSV-1 but might be seen with HSV-2. Also known as gingivostomatitis, inflammation of oral mucosa and gingiva.⁴¹ It affects 60% to 90% of the population. It develops commonly in young

population and less commonly in adults, without primary immunity. Usually spreads through direct contact with an individual with active primary or recurrent disease.

Clinical features

The primary herpetic gingivostomatitis develops following a direct contact with infected person, in an incubation period of 3-7 days. Prodromal symptoms like local burning sensation followed by erythema are usually missed by patient. Within 2 days a sudden onset of grouped vesicular eruption which are readily rupture, forming painful coalescing ulcers with a yellowish membrane. In the initial phase both keratinized and non-keratinized regions are affected, involving the palate, gingiva, tongue, lip, and perioral area. One third of these patients are associated with recurrences.⁴²

Recurrent Herpes Simplex Infection

Recurrent infections, typically give rise to vesiculo-ulcerative lesions at mucocutaneous junctions particularly the lips (herpes labialis). Recurrent HSV-1 infection within the mouth is uncommon in otherwise healthy patients. Although in immunocompromised patients, recurrent infection can be more extensive and/or aggressive. The diagnosis of common herpetic infection can usually be based upon the clinical history and presenting features. Confirmatory laboratory diagnosis is, however, required when patients are, or may be, immunocompromised.^{42,43}

Diagnosis

Usually diagnosis is made by classical clinical presentation. In case of recurrent oral vesiculo-ulcerative lesions, can confirm the diagnosis by Tzanck smear (cytology). A smear preparation is obtained by unroofing a fresh intact vesicle, scraping the base and smearing the collected vesicular fluid. Smear is stained with Giemsa stain and microscopic examination reveals infected keratinocytes enlarged by ballooning degeneration with multilobulated viral inclusions.⁴⁴

Treatment

The management is generally symptomatic and supportive. Sponging, high fluid intake and antivirals therapy with acyclovir 400mg 3 times for 7-10 days in the early stage of the infection are mainstay of treatment.^{41,44} Recurrent herpes labialis and recurrent intraoral HSV infections can be effectively treated with systemic Acyclovir 400 mg 3 times for 5 days or systemic valacyclovir 500-1000mg twice a day for 3 to 5 days (longer in the immunocompromised).^{43,44}

3. WARTS

Common (verruca vulgaris) and venereal warts (condyloma acuminatum) are caused by human papilloma virus (HPV).

Epidemiology and aetiopathogenesis

Warts are infrequent in oral cavity but are commonly seen in HIV individuals. Oral verruca vulgaris are more frequent in children than in adults. The lesions develop in oral cavity following auto- inoculation from hands and fingers. Condyloma acuminatum is the most common sexually transmitted disease and arises in the oral mucosa because of autoinoculation or more commonly by orogenital sexual transmission. It is common in HIV infected patients, with a striking increase seen on starting highly active antiretroviral therapy.⁴⁵

Clinical features

Verruca vulgaris appear as solitary or multiple, asymptomatic, exophytic growths with roughened or verrucous surface identical to cutaneous warts. Lesions are either pedunculated or sessile and range in color from pink to white. Individual lesions usually achieve an average size of about 0.5 to 1 cm. The lesions develop in sites of inoculation, mainly the labial mucosa, tongue, and gingiva.

Condyloma acuminate lesions are frequently present on the labial mucosa, followed by lingual frenum, soft palate, and gingiva. They present as asymptomatic, pink, sessile, less frequently pedunculated, exophytic cauliflowerlike growths. They are multiple rather than single. They are usually larger than verruca vulgaris, ranging from 1 to 3 cm.⁴⁵

Histopathology

Warts are characterized by a proliferation of hyperkeratotic stratified squamous epithelium arranged into finger-like projections with connective tissue cores. The converging or “cupping” arrangement of the peripheral rete ridges and a prominent granular cell layer with coarse, clumped keratohyaline granules is characteristic. Numerous koilocytes with pyknotic nuclei and perinuclear vacuoles are present.

Diagnosis

The diagnosis of wart is confirmed by histopathology of the suspected lesion. Electron microscopy, immunoperoxidase staining, or in situ hybridization can detect HPV viral particles in the biopsy samples.

Treatment

Lesions can be removed by surgical excision, cryosurgery, electrosurgery, and laser therapy. Imiquimod and 20% podophyllin solution in tincture of benzoin have been used with some success.⁴⁵

4. ORAL HAIRY LEUKOPLAKIA

Oral hairy leukoplakia (OHL) was first observed in 1981 and presents as a common, benign, asymptomatic, corrugated or “hairy” white patch of the lateral borders of the tongue. Epstein Barr Virus has been implicated as causative factor. Seen in patients with human immunodeficiency virus infection and other immunocompromised states like renal transplant

individuals, hematological malignancies. Rarely in normal healthy population.⁴⁶ Oral hairy leukoplakia was observed in nearly 50% of asymptomatic HIV infected individuals and prevalence is higher in those with less CD4 count (less than $0.3 \times 10^9/L$). Thus, it is considered as a cutaneous marker of HIV infection and its severity.⁴⁷

The pathogenesis of oral hairy leukoplakia is complex and includes an interplay of persistent Epstein–Barr virus replication and virulence, systemic immunosuppression and suppression of the local host immunity.⁴⁷

Histopathology

Histopathologic evaluation shows hyperkeratosis and acanthosis of epidermis. Presence of koilocytes with the margination of the nuclear chromatin (nuclear beading) is a characteristic feature.⁴⁸

Treatment

It does not require specific treatment and frequently resolves under HAART, if associated with HIV infection. Use of antivirals like acyclovir, zidovudine showed resolution, but the lesions reappear once the medication is stopped.⁴⁹

ORAL MANIFESTATIONS OF DERMATOLOGICAL DISORDER

1. MUCOSAL VITILIGO

Introduction

Vitiligo is an acquired mucocutaneous pigmentary disorder with progressive loss of melanocytes. Oral mucosal vitiligo can occur as a part of generalized vitiligo or as an isolated condition.⁵⁰

Epidemiology

The exact incidence of vitiligo of oral mucosa is not known. Various studies in different populations report an incidence between 10-70%. Oral mucosal vitiligo can occur at any age and affects both sexes equally.⁵¹

Clinical features

Oral mucosal vitiligo classically presents with uniformly white macules or patches. Commonly, vitiligo affects the vermilion zone and spares the wet labial mucosa. Other uncommon presentations are sparing of vermilion and band-like involvement of the labial mucosa and involvement of only the most lateral part of the lips.⁵²

Histopathology

Histopathologic evaluation helps to confirm the diagnosis of vitiligo. Lesions typically appear unremarkable with only scant inflammatory cell infiltrate and few or no melanocytes.⁵¹

Diagnosis

Diagnosis of oral mucosal vitiligo is made clinically. Diascopy and Wood's lamp examination are helpful in detecting clinically subtle macules of vitiligo.⁵³

Differential diagnosis

Differential diagnosis for oral vitiligo includes lichen sclerosus, chemical leukoderma and oral submucous fibrosis. Although both vitiligo and chemical leukoderma are acquired conditions but later is mostly associated with repeated exposure to certain chemical mostly containing phenolic group. To differentiate lichen sclerosus from vitiligo microscopic examinations is required. Lichen sclerosus is characterized by reduced thickness of epithelium along with hydropic degeneration of basal cells also active melanocytes can be identified in it.⁵²

Treatment:

Depigmentation of the lips and labial mucosa is cosmetically embarrassing and socially stigmatizing in pigmented individuals. Mucosal vitiligo is more resistant to medical therapies.

In early vitiligo, topical tacrolimus and pimecrolimus are effective. The success rate of various surgical procedures for lip vitiligo varies widely.⁵³

The cosmetic outcome with individual procedures also varies significantly. Micropigmentation (tattooing) gives immediate results and excellent colour matching has been reported in various studies, especially

in dark individuals. Punch grafting has been found to be effective, but it is associated with cobble stoning. Similarly, thin split thickness grafts may be associated with thickened edges and milia formation.

Recently, autologous melanocytes transfer via epidermal graft has been found to be an effective and safe therapeutic option for stable vitiligo of the lips.^{51,54}

2. ORAL LICHEN PLANUS

Introduction:

The word, lichen planus (LP) is derived from the Greek word “leichen” meaning tree moss and the Latin word “planus” meaning flat. The true cause of lichen planus remains obscure. Treatment is generally geared to alleviating symptoms. Oral lesions are chronic, rarely remissive, and are frequently the source of morbidity.⁵⁵

Epidemiology and aetiology:

Lichen Planus has a varied prevalence based on different geographic regions, but it generally affects approximately 1% to 2% of the world’s population.² Oral lichen planus constitutes 9% of all oral white lesions.³ In India, the prevalence of oral lichen planus ranges between 0.5% and 3% of all white lesions affecting oral cavity. Genital LP is associated with approximately 20% of OLP, whereas cutaneous LP is associated with approximately 15% of oral lichen planus.

However, some studies suggest that the association between cutaneous LP and oral lichen planus is closer to 70% to 77%.⁵⁵

Women are affected more commonly than men.⁵⁸ Typically OLP affects individuals in the age group of 30-60 years. It is rare in children, but a higher prevalence of OLP is reported in Indian population, suggesting differences in the genetic and/or environmental factors.⁵⁶

Although OLP patients do not seem to have an increased risk of diabetes and hypertension, an association between OLP, diabetes mellitus, and hypertension has been described, the triad being termed the Grinspan syndrome.⁵⁹

Etiopathogenesis

The exact aetiology of OLP is unknown. Oral lichen planus is classified as an immunologically mediated mucocutaneous disorder, mediated by T cell lymphocytic reaction to antigenic components within the epidermal layer or by exogenous antigens that trigger an immune response.⁶⁰

Genetics, familial clustering, and human leukocyte antigen association, although initially implicated to play a role in the pathogenesis of OLP, are no longer considered critical factors. Polymorphisms and genetic variations in the expression of cytokines have been linked with the risk of developing lesions of OLP and govern whether lesions are limited to the oral cavity (INF- γ), or skin (TNF- α).⁶¹

Various viruses like varicella zoster virus, Epstein-Barr virus, cytomegalovirus, human herpes virus, human papilloma virus, and hepatitis C virus (HCV) have been implicated in development of OLP, but only the role of HCV has been extensively studied. The definite pathogenic role of HCV in the development of OLP is still not clear.⁶⁰ It is believed that the immune reaction mediated by HCV replication may cause damage to the basal layer cells and result in OLP lesions. Some studies suggest that the HCV exerts an indirect effect, possibly mediated by the modulation of cytokines and lymphokines in the pathogenesis of oral erosive LP.⁶²

Even though the association of dental amalgam with increased risk of OLP is reported, the exact mechanism is not clear; allergic and/or irritant reaction to mercury in amalgam is postulated.⁶³

Stress, anxiety and depression are known to significantly influence the development of OLP.⁶⁴

The triggering factors and pathogenic mechanism of OLP are still not conclusively identified. Most data suggest that OLP is a CD8⁺ T cell-mediated autoimmune disease. However, there seems to be no definite role of B cells, plasma cells, immunoglobulins, or complements in the mediation of LP.⁶⁰ These CD8⁺ T cells are believed to induce keratinocyte apoptosis and cause epithelial basal cell layer damage via several possible suggested mechanisms: (1) secretion of tumor necrosis factor- α (TNF- α), which binds the TNF- α receptor 1 on the keratinocyte surface; (2) the binding of CD95

(Fas) on the keratinocyte surface with CD95L, which is expressed on the T cell surface; and (3) entry and assimilation of granzyme B secreted by T cells into the keratinocytes by perforin-induced membrane pores.⁶⁵

A variety of factors are believed to trigger the cytotoxicity of CD8+ T cells.

One is the expression of major histocompatibility complex class (MHC) II presented by the langerhans cells and keratinocytes, which secrete interleukin-12 (IL-12) thus activating the CD4+ T cells. This activation of CD4+ T cells and subsequent expression of interleukin-2 (IL-2) and interferon- γ (INF- γ), in association with the MHC class I, which are associated with basal keratinocytes, promotes cytotoxic CD8+ T cell induction of keratinocytes apoptosis.⁶⁰ The immunologic abnormality leads to a delay in the growth of mucosal epithelium that is responsible for hyperkeratosis.⁶⁶

Another nonspecific mechanism in the development of OLP is believed to be the degranulation of mastocytes and activation of matrix metalloproteinases, which degrades components of the extracellular matrix and basal membrane and also participates in the migration of lymphocytes through the epithelium. OLP lesions have more than 60% of degranulated mastocytes in comparison with normal mucosa.⁵⁵

Clinical features:

The oral mucosa may be involved alone or in association with lesions on skin or other mucosa, and oral lesions may precede, accompany or follow lesions elsewhere.⁶⁷

The clinical presentation oral lichen planus is nearly always in a bilateral, symmetric pattern. Lesions are often asymptomatic but may cause soreness. The buccal mucosa, tongue, and gingiva are the most common affected sites, whereas palatal lesions are uncommon.⁶⁸

Clinically, 6 subtypes of OLP are seen individually or in combination: papular, reticular, plaquelike, atrophic, erosive, and bullous.⁶⁹ The more common of these are the reticular, erosive, and plaquelike subtypes.⁶⁸

Reticular subtype: This is the most common form of lichen planus. Characteristically, it presents as a network of small, raised, whitish-gray, lacy lesions known as Wickham striae, which may be surrounded by a discrete erythematous border. The buccal mucosa is the site most commonly involved. They may also be seen on the lateral border of tongue and less often on the gingiva and the lips.

Papular subtype: This form presents as small white pinpoint papules about 0.5 mm in size. It is rarely seen and being small possibly overlooked during routine oral examination.

Plaque subtype: This lesion resembles oral leukoplakia and occurs as homogenous white patches. The plaque like form may range from a slightly

elevated and smooth to an irregular form and may be multifocal. The primary sites are the dorsum of the tongue and the buccal mucosa.

Atrophic subtype: The atrophic type is diffuse, red area with white striae at the margins that radiate peripherally. The gingiva is often involved and the condition is commonly referred to as 'chronic desquamative gingivitis'. This condition can cause burning sensation particularly when in contact with certain foods.

Bullous subtype: Appears as small bullae or vesicles that tend to rupture easily leaving behind an ulcerated painful surface. The bullae or vesicles range from a few millimeters to several centimeters in diameter. The bullous form is commonly seen on the buccal mucosa, particularly in the postero-inferior areas adjacent to the second or third molar teeth. The next most common site is the lateral margin of the tongue.

Erosive subtype: This is the second most common type. The erosions are often large, slightly depressed or raised with a yellow slough, and have an irregular outline. The surrounding mucosa is often erythematous and glazed in appearance. The periphery of the lesion is usually surrounded by reticular or finely radiating keratotic striae. Erosive LP frequently affects the dorsum and lateral borders of the tongue or the buccal mucosae on both sides.⁶⁸

Histopathology:

Definite diagnostic histologic findings include liquefactive degeneration of the basal cells, colloid bodies (Civatte, hyaline, cytoid), homogeneous

infiltrate of lymphocytes in a dense, bandlike pattern along the epithelium-connective tissue interface in the superficial dermis, cytologically normal maturation of the epithelium, sawtooth rete ridges, and hyperkeratosis (orthokeratosis or parakeratosis). In addition, the surface epithelium may show signs of ulceration, typically seen in erosive LP.⁵⁷

Several histologic criteria that are considered as exclusionary in diagnosing OLP include the absence of basal cell liquefaction degeneration, polyclonal inflammatory infiltrate, abnormal cytology suggestive of dysplasia, abnormal keratinization, flat rete ridges, and absence of colloid bodies.⁷⁰

Diagnosis:

Table 1: Modified WHO diagnostic criteria of OLP and oral lichenoid lesions
Clinical criteria:
• Presence of bilateral, more or less symmetric lesions • Presence of a lacelike network of slightly raised gray-white lines (reticular pattern) • Erosive, atrophic, bullous, and plaque-type lesions are only accepted as a subtype in the presence of reticular lesions elsewhere in the oral mucosa
Histopathologic criteria:
• Presence of a well-defined, band like zone of cellular infiltration that is confined to the superficial part of the connective tissue, consisting mainly of lymphocytes ○ Signs of liquefaction degeneration in the basal cell layer ○ Absence of epithelial dysplasia

- When the histopathologic features are less obvious, the term “histopathologically compatible with” should be used.
- Final diagnosis of OLP or oral lichenoid lesions: To achieve a final diagnosis, clinical as well as histopathologic criteria should be included.

Biopsy with immunofluorescence is often indicated to exclude keratosis, lichen sclerosus, lupus erythematosus, malignancy and other disorders. Direct immunofluorescence studies of OLP have shown a linear pattern and intense positive fluorescence with antifibrogen outlining the basement membrane zone and cytooid like bodies with positive Ig M labeling.^{55,71}

Treatment:

OLP does not have a cure, largely because the cause remains unknown. Thus treatment is only supportive and palliative.

The primary goal of OLP management is to alleviate symptoms and to prevent and screen for malignant transformation.⁶⁹ Asymptomatic reticular lesions may require simple observation without any medical intervention.

Multiple treatment modalities available for the treatment of OLP are corticosteroids, topical and systemic retinoids, calcineurin inhibitors (cyclosporine, tacrolimus, pimecrolimus), azathioprine, phototherapy, griseofulvin, hydroxyquinone, dapsone, mycophenolate, thalidomide, low-molecular-weight heparin and CO2 laser.⁶⁰

The treatment modality for OLP depends on factors such as severity of symptoms, location and extent of the lesions in the oral cavity and the patient's overall health, precipitating psychological factors, possible drug interactions, and compliance of the patient.⁷²

The most widely used treatment for OLP is topical steroids, which is often required for a prolonged period because of multiple symptomatic episodes. Among topical steroids, clobetasol propionate has been reported to have good efficacy; alternatively, triamcinolone and fluocinonide acetonide, are also effective.⁵⁷ It is critical to have contact between the mucosal surface and the steroid drug for a few minutes, and therefore formulations such as an oral rinse or adhesive paste are often recommended.⁶⁹ Depending on the extent of oral involvement and access to OLP lesions, elixirs containing triamcinolone, dexamethasone, or clobetasol, or topical steroids in adhesive bases are used. Gingival lesions respond better to topical corticosteroids delivered in occlusive customised vinyl carriers as this method of drug delivery increases contact time of the topical agent to the gingiva. The patient should be advised to refrain from eating or drinking for 1 hour after use of any formulation of topical steroids.⁵⁷

The use of intralesional steroids has been reported, but their efficacy is not well documented.⁶⁹

Systemic steroids are used only for short-term alleviation of acute or refractory flares of OLP, or for widespread LP when other mucosal sites are

also affected.⁵⁷ Depending on the severity of the lesion and the patient's weight and response to treatment, short courses of high-dose corticosteroids, such as prednisone 0.5 to 1.0 mg/kg/d are used. Prednisone 40 to 80 mg daily is usually effective in bringing about a response, and once a therapeutic response is achieved the steroid should be gradually tapered by reducing the dosage to 5 to 10 mg/d.⁵⁵

Tacrolimus 0.1% ointment has been reported to show efficacy in the treatment of OLP in cases refractory to topical steroids.⁶⁹ Although Tacrolimus has proved to have potentially better clinical outcomes, it can cause local irritation, transient taste alterations, possible lesional flare-up after drug withdrawal, and mucosal pigmentation.

Pimecrolimus 1% cream has also been found to be effective in the management of OLP.⁷³

Topical retinoids for treatment of OLP have shown less effectiveness than 0.1% Fluocinolone acetonide in orabase. Unclear results have been reported with systemic use.⁷⁴

Extracorporeal photochemotherapy has been tried for treatment of severe refractory erosive OLP.

Surgical removal of OLP, especially isolated plaques or nonhealing erosions, has been performed but limited data exist to advocate this procedure.⁵⁷

Cryosurgery and laser surgery have been used to treat OLP, but more studies are needed to prove their efficacy.

Patient education and measures for reducing provoking factors such as mechanical trauma (sharp tooth, ill-fitting prosthesis, amalgam dental fillings), chemical irritation (acidic, spicy food or beverages), and good oral hygiene to reduce bacterial plaque can help in alleviating symptoms of OLP. Tobacco and alcohol use should also be discouraged.^{55,57}

3. PEMPHIGUS

Introduction

Pemphigus is a group of potentially life-threatening autoimmune diseases characterized by cutaneous and/or mucosal blistering. Pemphigus can be classified into six types: pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosus, pemphigus foliaceus, paraneoplastic pemphigus, and IgA pemphigus. Pemphigus vulgaris, which has multiple clinical variants, is an autoimmune blistering disorder of skin and mucous membranes, usually affecting the elderly, with a strong immunogenetic link and showing oral lesions as an initial manifestation in 50% of cases.⁷⁵ the peak incidence of pemphigus vulgaris occurs between the fourth and sixth decades of life with a male-to-female ratio of 1:2. Clinically, the oral lesions are characterized by blisters that rapidly rupture, resulting in painful erosions. While any area in the oral cavity can be involved, the soft palate, buccal mucosa, and lips are predominantly affected.⁷⁶

Etiopathogenesis

The etiology of pemphigus vulgaris is still unknown although the disease has raised much concern. The pemphigus-group diseases are characterized by the production of autoantibodies against intercellular substances and, therefore, classified as autoimmune diseases. The presence of a viral infection may also be involved in autoantibody production. In some cases, it may have a strong genetic basis as it has been reported more frequently in certain racial groups, for example, the ashkenazi jews and those of mediterranean descent.⁷⁷ Strong associations with certain hla class ii alleles have been demonstrated in pemphigus vulgaris. Other initiating factors reported include certain foods (garlic), infections, neoplasms, and drugs. The drugs commonly implicated are those in the thiol group, in particular captopril, penicillamine and others such as rifampicin.⁷⁸

In pemphigus vulgaris, autoantibodies are produced against desmosomes (adhesion proteins), specially desmoglein 3 (dsg 3). Another important component of desmosomes is termed desmoglein 1 (dsg 1). The latter is the target of the autoantibody formation in pemphigus foliaceus that affects the cutaneous site only. Dsg 3 is predominantly expressed in oral epithelium while both dsg 1 and dsg 3 are expressed in the skin (although dsg 1 is expressed more intensely in the superficial layer while dsg 3 is found more abundantly in basal and suprabasal layers). Dsg 1 and dsg 3 are components of desmosomal cadherin responsible for holding the cells of the epithelium

together. The loss of the adhesive function among the spinous cells due to anti-dsg 3 antibodies results in bullae formation immediately in the suprabasal region in pemphigus vulgaris.

Clinical features

The primary lesion is thin-walled flaccid to tense bulla with clear fluid on a normal or erythematous skin, which easily rupture to form moist erosions with less tendency to heal. Lesions heal slowly but without scarring. On the oral mucosa, primary bullous lesions are short lived and rupture easily to form erosions/ ulcerations. Majority of cases present clinically with painful erosions or ulcerations. The principal dermal and mucosal changes involve the loss of coherence among layers of keratinocytes. This can be demonstrated by nikolsky sign, where on lateral pressure on clinically normal appearing skin cause separation of epidermis from underlying dermis.⁷⁹

Diagnosis

Histological evaluation shows acantholysis, the loss of coherence of epidermal cells and their subsequent detachment, is the main histological finding. Light microscopy shows that this process starts by the development of oedema among keratinocytes situated above the stratum basale. In the next stage, a suprabasal crevice develops that widens to give rise to a bulla. In cellular material scraped from the base and sides of a bulla, typical acantholytic cells can be found by cytological examination (tzanck test).⁷⁷

Immunofluorescence methods are used to detect igg antibodies in the intercellular space of the epidermis or epithelium and circulating antibodies in serum. The igg antibodies targeting dsg-3 are deposited at the periphery of the epithelial cells, resembling a fishnet pattern in dif. The autoantibodies that are directed against dsg-1 and dsg-3 can be detected by using an indirect immunofluorescence assay in the circulating blood serum.⁷⁹

Differential diagnosis

Other etiologies for vesiculobullous oral lesions should be ruled out like mucous membrane pemphigoid, , dermatitis herpetiformis, bullous fixed drug eruption, erythema multiforme.⁷⁸

Treatment

The aim of treatment is to induce disease remission which should be followed by a maintenance treatment using the minimum drug doses required for the disease control. The mainstay of treatment is systemic immunosuppression with corticosteroids and non-steroidal agents. Mild localized oral lesions can be treated with topical corticosteroid rinses or creams (clobetasole proprionate).^{78,80} For resistant local lesion intra lesional triamcinolone may be used. Cyclophosphamide in combination with high dose with dexamethasone is also used as pulse therapy. By weekly rituximab infusions also shown to be successful.

The prognosis of pemphigus vulgaris remains guarded on the basis of the managing strategies to suppress the disease and the risk of systemic infection as well as treatment related adverse effects.⁸⁰

4. PEMPHIGOID

Mucous membrane pemphigoid (MMP) is considered an autoimmune blistering disease that predominantly affects mucous membranes. It is also cicatricial pemphigoid usually characterized by subepithelial bullae formation. Sites of mucosa involvement include ocular, nasopharyngeal , oral , laryngeal , nasal and oesopharyngeal areas.⁸¹

This disease is predominant in females, and it usually occurs in individuals with older age, between 60 and 80 years old.⁸²

Etiology

The main etiology is the formation of IgG and /or IgA auto antibodies directed against the basement membrane zone components. The major sequelae includes scarring and lose of function, except for some cases where exclusive oral mucosal involvement can be present Pathogenic factors include antibodies to bullous pemphigoid antigen 2 , both $\alpha 6\beta 4$ integrin subunits , and bullous pemphigoid hemidesmosomal antigen 180(BP 180) , laminin 311, laminin 332 (formerly laminin 5, epiligrin) and type VII collagen.⁸¹

Clinical features

In MMP oral mucosa is the most commonly involved site followed by ocular, nasal, nasal pharyngeal mucosa. Ocular and nasal mucosa shows erythematous skin with vesiculobulbous lesions. Primary lesion is tense bulla with pseudo membrane covering underlying ulcer. In oral mucosa most common sites are keratinized tissues of the palate and gingiva. Less commonly, the buccal mucosa will be involved.⁸³ Intra oral lesions not always shows scarring whereas scarring is the frequent ocular complication including symblepharon, ankyloblepharon, corneal opacification and entropion.⁸⁴ Scarring can also occur within the larynx and oesophagus.

Diagnosis

Histopathology of the lesion shows a sharply defined sub epithelial cleft in the absence of significant inflammation is always characteristic of mucous membrane pemphigoid. Direct immunofluorescence testing of perilesional mucosa will show linear immune deposits at the epithelial basement membrane zone composed of anyone or a combination of IgG, IgA and C3 in a homogenous pattern.⁸¹ This pattern of fluorescence can rule out vesiculoerosive diseases such as lichen planus, pemphigus vulgaris, erythema multiforme and drug induced lesions.

Treatment

Treatment must be depending upon the specific site of involvement as well as the severity of involvement. In the stage of rapidly progressive disease,

systemic immunosuppression in the form of prednisolone, cyclophosphamide, azathioprine and mycophenolate should be considered as mono therapy or combination therapy. When only the oral mucosa is involved topical corticosteroids could be the initial agents used. Severe or unresponsive oral lesions may require oral prednisolone with or without steroid sparing agents such as mycophenolate. Use of rituximab also shown effective.^{82,84}

5. PSORIASIS

Psoriasis is a chronic, remitting and relapsing inflammatory skin disorder with a strong genetic predisposition. Psoriasis affects 1–3% of the world's population in their early lives representing a disabling condition with significant social and economic impact. Oral involvement by psoriasis is uncommon.⁸⁵

Clinical features

The first oral manifestation of psoriasis was documented by Oppenheim and Thimm in 1903. The first case had a scrotal tongue. The second case had an extensive involvement of the buccal mucosa from commissure of the lip anteriorly to the anterior faucial pillar posteriorly by a coarse, interlacing network of grayish-white striae interspersed with unaffected mucous membrane; histologically, however, neither of the two cases presented typical features of psoriasis.⁸⁶

A higher prevalence of geographic tongue and fissured tongue in psoriatic patients compared to the general population has also been reported in many studies.^{86,87} Geographic tongue or Benign migratory glossitis is a common inflammatory condition of unknown etiology affecting the dorsum and lateral borders of the tongue. It develops from localized desquamation of filiform papillae resulting in asymptomatic multifocal erythematous patches surrounded by white, raised serpentine borders which expand centrifugally. Few patients complain of burning, particularly upon exposure to spicy foods. Benign migratory glossitis and wandering rash of the tongue are the synonyms for this condition.⁸⁸ The association between geographic tongue and psoriasis has been described in various studies, based on observation of its fundamental lesions, microscopic similarity between the two conditions and the presence of a common genetic marker, human leukocyte antigen (HLA) HLA-C*06.⁸⁶

Fissured tongue or scrotal tongue is characterized by an anteroposteriorly oriented fissure with branching fissures and is believed to be an inherited trait. It occurs in 2-5% of the general population and the incidence increases with age.

Ulmansky et al. postulated that benign migratory glossitis represents a transient and fissured tongue a delayed, more stable expression of oral psoriasis. Fissured tongue and benign migratory glossitis may also represent

non pathognomonic oral changes which are more likely to develop in the context of cutaneous psoriasis.⁸⁶

Differential diagnosis

Differential diagnosis of oral psoriasis includes lichen planus, candidiasis, leukoplakia, vesiculobullous conditions, idiopathic gingivostomatitis, Reiter's syndrome, and squamous cell carcinoma.⁸⁷

Treatment

Management is not well described, most of these lesions are asymptomatic. Multiple treatment strategies, be they topical or systemic, have been applied to these patients for symptom relief but not for cure.⁸⁸

6. SYSTEMIC LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus is a multi-organ system autoimmune disease with clinical and serological heterogeneity.⁸⁹

Clinical features

Clinical manifestations that can differentiate SLE patients from healthy people such as skin lesions, arthritis, renal disorder, neurologic disorder, hematologic changes and others are included in ACR criteria. The formulation of initial criteria for SLE was first proposed by the American College of Rheumatology and appeared in 1971. In 2012, the Systemic Lupus Collaborating Clinics proposed the SLICC criteria for SLE in view of new knowledge of autoantibodies and the importance of low complement.⁹⁰

Table 2: ACR Criteria for SLE
Clinical: malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis (pleura, pericardium or peritoneum), renal disorder, neurologic disorder(seizure, psychosis).
Laboratory abnormalities: Blood abnormalities: hemolytic anemia, leukopenia, thrombocytopenia Immunological: ANA, anti- DNA, anti-Sm.
<i>The diagnosis of SLE requires the presence of four or more of 11 criteria</i>

Table 3: *SLICC classification criteria for SLE⁹¹	
Clinical criteria:	Immunological criteria
Acute cutaneous lupus Chronic cutaneous lupus Oral or nasal ulcers Nonscarring alopecia Serositis Renal Neurologic Hemolytic anemia Leukopenia Thrombocytopenia	ANA Anti-DNA Anti-Sm Antiphospholipid antibody Low complement (C3,C4,CH50) Direct Coomb's test
<i>>4 criteria (atleast 1 clinical and 1 laboratory criteria) OR biopsy- proven lupus nephritis with positive ANA or Anti-DNA</i>	
*SLICC: Systemic lupus International Collaborating Clinics	

Laboratory diagnosis: ^{91,92}

- Screening tests
 - Erythrocyte sedimentation rate

- Complete blood counts
- Creatinine
- Urinary status and sediments
- Antinuclear antibodies (ANA)
 - If screening tests positive, immunological tests
- ANA profile (anti-Sm, -Ro, -La, -U1RNP)
- Complement (C3,C4,CH50)
- Antiphospholipid antibody
 - Organ specific tests, if required

Treatment:

In every patient with SLE treatment with antimalarials is recommended unless there are contraindications. Hydroxychloroquine and chloroquine are licensed for the treatment of SLE. Apart from their good efficacy against arthritis and LE-specific skin lesions, antimalarials maintain SLE in remission, are associated with fewer disease flares, and reduce damage in the course of the disease.⁹²

Glucocorticoids are the topical treatment of choice for skin lesions in SLE.⁹³

An alternative is the off-label use of topical calcineurin inhibitors. These agents can be applied as long-term treatment without the above-mentioned risks associated with the extended use of glucocorticoids.

In patients without organ-threatening manifestations (e.g., LE-specific skin lesions, arthritis, pleurisy), long-term treatment with antimalarials should be

sufficient. Due to the delayed onset of action of antimalarials, most patients temporarily need additional, short-term effective medication, usually non-steroidal anti-inflammatory drugs or glucocorticoids.

Almost as important as immunosuppression is the co- medication, which is determined by the comorbidities (infections, arteriosclerosis, hypertension, dyslipidemia, diabetes, osteoporosis, avascular necrosis, and malignancies, among others) and the damage that has already occurred.^{92,93}

7. DISCOID LUPUS ERYTHEMATOSUS

Chronic cutaneous lupus erythematosus (CCLE), also known as discoid lupus erythematosus, is an inflammatory disease of the skin predominantly among females in fourth decades. Most often involves sun exposed areas like face and scalp.

Clinical features

Cutaneous lesions characterized by coin shaped (i.e., discoid) red-violaceous plaques covered by a prominent, adherent scale that extends into the orifices of dilated hair follicles. The lesions typically expand with erythema and hyperpigmentation at the periphery leaving hallmark atrophic central scarring, telangiectasia, and hypopigmentation.⁹⁴ Whereas oral lesions appear as circumscribed, little elevated white papules or plaques with surrounding telangiectatic halo. Incidence of oral lesions of DLE is about 20 to 50%. They are not always associated with skin lesions.

Diagnosis

Histopathological examination is mandatory before the final diagnosis, to rule out other differential diagnosis.

Differential diagnosis

Oral lesions are similar to those of erosive form of lichen planus. Discoid lesions most often seen on the buccal mucosa, the gingiva, labial mucosa and vermillion border. Clinically, difficult to differentiate from oral leukoplakia or from the lesions seen in oral lichen planus.

Treatment

Oral lesions may be the first clinical manifestation of DLE, so proper diagnosis is required for early detection and to establish better treatment planning, this promotes resolution of established lesions and prevents scarring of skin lesions and also, reduces discomfort of the patients. The labial lesion near vermillion border are prone for malignant transformation. These patients should avoid excessive sun exposure, can apply ultraviolet barrier cream to the lips.⁹⁴

8. STEVEN JOHNSON SYNDROME & TOXIC EPIDERMAL NECROLYSIS

Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN).⁹⁵

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are

acute life threatening muco cutaneous reactions, predominantly drug induced.⁹⁶

Clinical features

TEN and SJS are characterized by more or less extensive painful erythematous and erosive lesions of the skin, conjunctiva and mucous membranes resulting from massive apoptosis of epithelial cells, and are considered to be two ends of a spectrum of severe epidermolytic adverse cutaneous drug reactions, differing only by their extent of skin detachment.⁹⁷

Drugs are identified as the main cause of SJS/TEN in most cases, but *Mycoplasma pneumoniae* and Herpes simplex virus infections are also documented in etiology. In few etiology remains unknown. Drugs including allopurinol, antibiotics, anticonvulsants and NSAIDs of the oxicam type are the main cause of SJS/TEN in most cases.⁹⁸

The two pathomechanism explained are genetic susceptibility and cell mediated cytotoxic reaction against keratinocytes leading to apoptosis. The pathogenesis of SJS/TEN is not fully understood but is believed to be immune-mediated, as re-challenging an individual with the same drug can result in rapid recurrence of SJS/TEN.⁹⁸

Diagnosis

The histopathology of SJS/TEN lesions show that keratinocyte apoptosis followed by necrosis is the pathogenic basis of the widespread epidermal

detachment observed in SJS/TEN. In order to rule out autoimmune blistering diseases, direct immune fluorescence staining should be additionally performed and no immunoglobulin and/or complement deposition in the epidermis and/or the epidermal-dermal zone should be detected.^{96,97}

Differential diagnosis

Differential diagnosis includes linear IgA dermatosis and paraneoplastic pemphigus, pemphigus vulgaris and bullous pemphigoid, acute generalized exanthematous pustulosis (AGEP), disseminated fixed bullous drug eruption and staphylococcal scalded skin syndrome (SSSS).⁹⁷

Treatment

Due to the high risk of mortality, management of patients with SJS/TEN requires rapid diagnosis, evaluation of the prognosis using SCORTEN, identification and interruption of the culprit drug, specialized supportive care ideally in an intensive care unit, and consideration of immunomodulating agents such as high-dose intravenous immunoglobulin therapy. SJS and TEN are severe and life-threatening.^{96,98,99}

ORAL MANIFESTATIONS OF SYSTEMIC DISORDER

1. JAUNDICE

Jaundice is a metabolic condition characterized by yellowish discoloration of skin, oral mucous membrane and the sclera. The discolouration may be due to an increase in the concentration of bilirubin and deposition of bile pigment

in the tissues. Serum concentration of bilirubin exceeding 2-3mg /dl causes discoloration.

Discolouration of oral mucosa is most apparent at the junction of hard and soft palates. This is due to the fat in this area that accentuate the yellow colour. Depending on the underlying pathology, jaundice exhibits various clinical symptoms such as pruritus, pain and enlarged liver. The faeces will be very light in colour if there is any biliary obstruction and urine will be darker.

2. ORAL MANIFESTATIONS OF HEMATOLOGICAL DISORDER¹⁰⁰

Hematological conditions can present with various manifestations in the oral cavity. Sometimes these manifestations may be the first clinical presentations, hence recognizing them can help for early diagnosis and treatment of underlying hematological condition.

Table 4: Oral manifestations of hematological disorders

Hematological disorder	Oral mucosal manifestations
Iron deficiency anemia	Mucosal pallor, angular cheilitis, glossitis and risk of candidiasis
Vitamin B12 deficiency	Angular cheilitis, mucositis, stomatitis, soreness of mouth, gingival bleeding, ulcerative gingivitis, aphthous ulcer, glossitis (beefy tongue).

Folic acid deficiency	Angular cheilitis, mucositis, stomatitis, glossitis and risk of candidiasis
Aplastic anemia	Petechiae, oral hemorrhagic bullae, risk of oral candidiasis, gingival hyperplasia and bleeding
ITP	Angina bullosa hemorrhagica ¹⁰¹ (sudden onset of blood blisters on oral mucosa), oral hematoma, palatal purpura, echymotic lesions on palate and tongue.
Acquired hemostasis (liver disease, uremia)	Angina bullosa hemorrhagica, oral hematoma, petechiae, echymotic lesions.

PREMALIGNANT AND MALIGNANT DISORDERS

1. ORAL LEUKOPLAKIA

The term leukoplakia was first used in 1877 by Schwimmer to denote any white lesion of the oral cavity.¹⁰² In 1978, WHO defined leukoplakia as "a keratotic white patch or plaque that cannot be scraped off and cannot be characterized clinically or pathologically as any other disease". Therefore, a process of exclusion establishes the diagnosis of the disease.¹⁰³

It is agreed that leukoplakia represents the most common premalignant oral mucosal lesion; however most cases are benign and remain so over time. The concept of malignant transformation is essentially related to the development

of cancer; preinvasive or otherwise, that is further characterized by variable degrees of epithelial dysplasia.¹⁰³

Epidemiology

Leukoplakia is most commonly seen in elderly age group with male preponderance. It is uncommon in men under 30 years of age; prevalence rises to nearly 30% in men over 80 years of age and rates are significantly higher where the use of betel (areca nut extract) and tobacco is common.¹⁰³

Etiology

Although the exact cause of oral leukoplakia is unknown, several associations with habits and behaviours are reported. Many physical agents have been implicated, including tobacco, alcohol, chronic friction, electro-galvanic reaction between unlike restorative metals, and ultraviolet radiation. Most strong association is with use of tobacco in its various forms, including smoked tobacco and other smokeless tobacco. In India, the use of areca (betel) nut preparations with or without tobacco forms an additional risk for this condition in patients.¹⁰³

Clinical features

Clinically, leukoplakia can be subdivided into 2 types.

1. **Homogeneous type:** Clinically characterized as a white, thick and opaque patch with generally smooth surface. Surface textural alterations can vary from a fine granularity to a slightly papillary outline. Common in the buccal (cheek) mucosa and usually of low premalignant potential.

2. ***Non-homogeneous type:*** Consist of white patches or nodules (“erythroleukoplakia”) in a red, often eroded, area of mucosa. They have a high risk of malignant transformation.¹⁰²

In addition leukoplakia can appear ulcerative, erosive, speckled, nodular, or verrucous to the naked eye.

Proliferative verrucous leukoplakia: a subtype of verrucous leukoplakia.

Its exact etiology is unknown, association with presence of human papilloma virus has been suggested but, not yet confirmed. It is characterized as irregular white patches or plaques that progress slowly across the oral mucosa membranes with nearly a 100% risk of malignant transformation and a high risk of recurrence after removal.¹⁰³

Leukoplakias are known to occur at almost all places in oral cavity. However, they are most frequent in buccal mucosa and mandibular mucosa. Two-third of the oral leukoplakias occurs at the vermillion, buccal mucosa and gingival surface. High-risk sites for malignant transformation include the soft palate, ventrolateral tongue and floor of the mouth.¹⁰²

Histopathology:

To fulfill a diagnosis of leukoplakia, no other definable lesion should be observed microscopically. Benign lesions display hyperkeratosis with or without acanthosis. A variable number of chronic inflammatory cells is seen in the underlying connective tissue. Epithelial dysplasia is commonly found in nonhomogeneous lesions.¹⁰⁴

Diagnosis:

There are no signs or symptoms that reliably predict whether a leukoplakia will undergo malignant change, and thus histology must be used to detect dysplasia.¹⁰⁵

Brush biopsy was designed for those clinical lesions which initially based on clinical features did not require a biopsy. This is a noninvasive technique which collects the basal layer cells using a brush. It can be used for mass screening campaigns. It eliminates the need for surgical procedure in doubtful lesions.¹⁰³

An early biopsy would provide much desired insight into the clinical severity of these lesions, whereas a delay in the biopsy would also mean overlooking a frank malignant lesion or a severe dysplastic lesion.¹⁰⁵

Scalpel or punch biopsy is generally mandatory for those leukoplakias that exhibit the following characteristics:

- Found in patients with previous or concurrent head and neck cancer
- are non-homogeneous, i.e. have red areas and/or are verrucous and/or are indurated
- in a high-risk site such as floor of mouth or tongue
- focal with symptoms
- without obvious etiological factors.¹⁰⁴

Differential diagnosis:

Lichen planus, cheek biting, frictional keratosis, tobacco-induced keratosis, nicotinic stomatitis, leukoedema, white sponge nevus, candidiasis, and lupus.¹⁰²

Prognosis and malignant transformation:

The prognosis of leukoplakia varies. There is clear evidence of the malignant potential of some oral leukoplakias. Overall, around 2–5% of leukoplakias become malignant in 10 years and 5–20% of leukoplakias are dysplastic. Of leukoplakias with dysplasia, 10–35% proceed to carcinoma.^{102,104}

Malignant transformation of leukoplakias depends on multiple factors:

- Female gender (more in females)
- Long duration of leukoplakia
- Leukoplakia in nonsmokers (idiopathic leukoplakia)
- Location on the tongue and/or floor of the mouth • Size > 200 mm²
- Nonhomogeneous type
- Presence of *Candida albicans*
- Presence of epithelial dysplasia.

Over the recent past, much effort has gone into identifying tissue markers of malignant potential,^{106,107} in particular the genetic changes that underlie oral carcinoma, resulting in the identification of biomarkers such as DNA

ploidy, p53, and chromosome 3 and 9 changes that might predict neoplastic change in potentially malignant lesions.^{108,109}

Treatment:

Leukoplakias have a relatively low risk of malignant transformation. Hence, the recommended treatment should produce the fewest adverse effects.

Initial treatment involves the elimination of all possible known risk factors, following which the patient should be re-examined 3 months later. If the lesion regresses, no further treatment is indicated. Persistent lesions warrant a biopsy.^{108,109}

“Benign” biopsy diagnosis may over time undergo dysplastic changes; therefore regular follow-up of these lesions is of utmost importance.

Surgery (scalpel or laser excision) is an obvious option for the management of leukoplakias with a high predisposition to malignant transformation.

Other treatment modalities include cryosurgery, retinoids, b-carotene, bleomycin, calcipotriol, photodynamic therapy, and vitamin A.

No definite measures have been devised for the prevention of development of leukoplakia or oral carcinoma. Avoidance of smoking and alcohol, and consumption of fresh fruits and vegetables may have a protective effect. Oral cancer screening programmes can help in early diagnosis of these lesions, and improve the prognosis and treatment success.^{109,110}

2. ORAL SUBMUCOUS FIBROSIS

Oral submucosal fibrosis (OSMF) is an irreversible, chronic disease of unknown etiology. It is characterized by fibroelastic changes and inflammation in the mucosa. It can affect oral, oropharyngeal, and at times esophageal mucosa.

Eventhough exact etiology unclear, strong correlation of OSMF with consumption of spicy food, areca nuts as well as vitamin B deficiency and protein malnutrition is reported.¹¹¹

A genetic predisposition involving human lymphocytic antigen (HLA) A10, DR3, DR7, and probably B7 has been found.

Clinical features:

Common symptoms are burning sensation on eating spicy foods and non-specific stomatitis. Later on examination asymptomatic symmetrical fibrosis of the cheeks, lips or palate, which are seen as bands running through the mucosa. More advanced lesions demonstrate palpable fibrous bands causing significant restriction in opening of mouth, speech, swallowing, and decrease in salivary flow.^{111,112}

Oral submucous fibrosis may predispose to the development of oral carcinoma, which occurs in 2–10% of patients over a period of 10 years.

Histopathology

Histology shows presence of chronic inflammatory cells, with several eosinophils in the lamina propria. Epithelial atrophy, hyalinized collagen, and loss of vascularity is seen in established cases. Fibrosis of minor salivary glands is also evident.

Biopsy is mandatory to confirm the diagnosis and to rule out differential diagnosis such as amyloidosis, scleroderma, oral lichen planus and ongoing malignant changes.¹¹²

Treatment:

Management is difficult and treatment focuses on improving mouth movement and relieving symptoms. In the early stages, sub-mucosal injections of corticosteroids and collagenases, as well as exercises are effective. Severe fibrosis needs surgical intervention. Pentoxifylline and lycopene also shown some effect. Close follow-up is required because of the high potential of malignant transformation.¹¹²

3. ERYTHROPLAKIA

It is defined as “a fiery red patch that cannot be characterized clinically or pathologically as any other definable disease”. Erythroplakia commonly seen in middle aged and elderly population. It is considered as the oral mucosal lesion with greatest potential for malignant transformation in the oral cavity.

Erythroplakia is much less common than leukoplakia. The aetiology is unknown, but tobacco and alcohol are probably predisposing factors.¹¹³

Clinical features

The clinical appearance of erythroplakia can be as a flat or depressed erythematous lesion with a smooth or granular surface. Sometimes a more common entity is erythroleukoplakia where a mixture of red and white lesions appear.¹¹³ The generally solitary presentation is helpful in differentiating clinically from erythematous lichen planus and erythematous candidiasis, since the latter conditions often manifest in multiple sites, usually bilateral, more or less symmetrical in distribution.¹¹⁴

Diagnosis

The gold standard for diagnosis of dysplasia is histopathological examination. But scalpel biopsy is an invasive procedure, with the disadvantage of tumor seeding. It is usually done when the lesion displays either symptoms or clinical features of malignancy, while many innocuous appearing early stage oral cancers are merely observed clinically and left undiagnosed. Thus various adjunctive and non-invasive tools have been developed both at the clinical as well as molecular level to assess the oral lesions of uncertain biologic significance. One such technique is vital staining, including toluidine blue. Vital staining is the process of dyeing

living cells or tissues. The staining reveals the otherwise un-apparent cytological details.^{115,116}

Toluidine blue is a basic metachromatic dye that stains the acidic cellular components. Since cancer cells contain quantitatively more DNA and RNA than normal epithelial cells, toluidine blue has greater affinity for these cells. Additionally, malignant epithelium contains wider intracellular canals, which facilitate the greater penetration of the dye. Thus toluidine blue is able to delineate areas of malignancy. It is a simple, fast, and inexpensive technique.¹¹⁷

Histopathological analysis reveals moderate to severe dysplasia and often even ongoing malignant transformation as carcinoma in situ or invasive carcinoma.¹¹⁵

Treatment

In view of the high malignant potential of these lesions, the recommended treatment is surgical excision, including laser. Data on laser excision, however, is only limited. Even after surgical excision, the recurrence and development of malignancy at the same site is very high. Reliable data, however, on this aspect is also insufficient. Even then, long term follow-up is warranted after surgical removal.¹¹⁸

4. ORAL CARCINOMA

Introduction

More than 90% of malignant neoplasms in the mouth are squamous cell carcinomas. Oral cavity squamous cell carcinoma (OCSCC) accounts for 2% to 3% of all malignancies.¹¹⁹

Epidemiology

There is marked inter-country and intra-country ethnic differences in incidence and mortality from OSCC. In many countries there is evidence for an increase in oral squamous cell carcinoma (OSCC) over recent years, especially in young persons. In most regions of the world, about 40% of head and neck cancers are known to be squamous cell carcinomas developing in the oral cavity. Similarly, in Asia, 80% of head and neck cancers are usually found in the oral cavity and oropharynx.¹¹⁹

Oral squamous cell carcinoma mainly afflicts patients older than 40 years of age, whereas the tumour remains very uncommon among young adults.

A plethora of lifestyle and environmental factors has been identified as the risk factor for oral cancers. However Tobacco and alcohol are the two most important known risk factors for the development of OSCC. Cofactors include dietary factors, immunodeficiency and micro-organisms like candida and HPV 16/18.

Premalignant conditions that can progress to OSCC include:¹²⁰

- Erythroplakia

- Leukoplakia
- Lichen planus- including lichenoid dysplasia
- HPV infection
- Discoid lupus erythematosus
- Submucous fibrosis
- Atypia in immunocompromised patients
- Dyskeratosis congenita
- Fanconi anaemia
- Paterson–Kelly syndrome (sideropenic dysphagia, Plummer–Vinson syndrome).

Clinical features:

OSCC may present as the following.

- A red lesion (erythroplasia)
- A granular ulcer with fissuring or raised exophytic margins
- A white or mixed white and red lesion
- A lump sometimes with abnormal supplying blood vessels
- An indurated lump/ulcer, i.e. a firm infiltration beneath the mucosa
- A non-healing extraction socket
- A lesion fixed to deeper tissues or to overlying skin or mucosa
- Cervical lymph node enlargement, especially if there is hardness in a lymph node or fixation.

Nearly 30% of all squamous cell carcinomas affect the lip; some 25% affect

the tongue, the most common intraoral site.¹ Most intraoral cancers involve the posterolateral border of the tongue and/or the floor of the mouth (the 'graveyard' area). In betel chewing, the buccal mucosa is a common site for carcinoma.

Histopathology

Findings range from well-differentiated (low grade) lesions, in which the tumors resemble normal epithelium, to poorly differentiated or anaplastic (high-grade) lesions, where the tumor cells lose their resemblance to the epithelial tissues.

Tumor consists of irregular masses of epidermal cells that proliferate downward into the dermis. The invading tumor masses are composed in varying proportions of normal squamous cells and of atypical (anaplastic) squamous cells. The number of atypical squamous cells is higher in the more poorly differentiated tumors.

Atypicality of squamous cells expresses itself in such changes as great variation in the size and shape of the cells, hyperplasia and hyperchromasia of the nuclei, absence of intercellular bridges, keratinization of individual cells, and the presence of atypical mitotic figures. Keratinization often takes place in the form of horn pearls, which are very characteristic structures composed of concentric layers of squamous cells showing gradually increasing keratinization toward the center. The center shows usually incomplete and only rarely complete keratinization.

Diagnosis

Early diagnosis is important since it improves prognosis and minimizes the extent of interventions.¹²¹ There should be a high index of suspicion, especially of a solitary lesion present for over 3 weeks: biopsy is invariably indicated. Scalpel biopsy is required and toluidine blue staining may help highlight the most appropriate area for biopsy.

The whole oral mucosa should be examined. Frank tumours should be inspected and palpated to determine extent of spread; for tumours in the posterior tongue, examination under general anaesthesia may facilitate this. OSCC should be staged according to the TNM classification of the International Union against Cancer.

Treatment

The prognosis of OSCC is around 30% survival at 5 years. The treatment of oral cancer involves one or a combination of radiotherapy, surgery and, very occasionally, chemotherapy. Serious consideration must be given to the complications of the various modalities and the quality of life achieved.^{122,123,124}

OTHER MISCELLANEOUS ORAL MUCOSAL LESIONS

1. DRUG INDUCED MUCOSITIS

Adverse drug events in the oral cavity are common and will likely increase as newer therapeutic agents are approved. Oral mucosal reactions to drugs have a variety of clinical presentations such as xerostomia, lichenoid reactions, oral ulcers, fixed drug eruptions, erythema multiforme pigmentations, pigmentation, infection, angioedema, and malignancy.¹²⁵

Table 5 : Common oral drug reaction and causative drugs

Xerostomia	Antidepressants, antihistamines, beta blockers, diuretics, ACE inhibitors, opioids, decongestants, antimigraine drugs, systemic retinoids, proton pump inhibitors. ^{125,126}
Lichenoid drug eruption	NSAIDs, oral antihypertensive agents (diuretics, ACE inhibitors, Beta blockers, calcium channel blockers), sulfonylurea antidiabetics (glipizide), antifungals (ketoconazole), anticonvulsants (carbamazepine), lithium, allopurinol, gold, penicillamines. ^{126,127}
Oral ulcers	NSAIDs, beta blockers and potassium channel blockers. chemotherapy agents like 5-fluorouracil, cisplatin, methotrexate, and hydroxyurea. ¹²⁵
Fixed drug eruptions	Griseofulvin, ciprofloxacin, norfloxacin, tinidazole,

	tetracycline. ^{128,129}
Erythema multiforme	Anticonvulsants like carbamazepine, barbiturates, phenytoin, NSAIDs, penicillins, azithromycin, tetracyclines, fluconazole, lamotrigine, antiretroviral drugs. ^{125,129}
Pigmentations	Tetracyclines, minocyclines, antimalarial drugs (e.g., hydroxychloroquine, mepacrine, and quinacine), and phenazine dyes (e.g., clofazimine). ¹²⁵
Infections	long-term immunosuppressive therapy, methotrexate, abatacept, and alefacept, infliximab and adalimumab. ¹²⁵
Angioedema	Ibuprofen, metronidazole, ciprofloxacin, amoxicillin, cefadroxil. ¹²⁵
Malignancy	Chemotherapy and immunomodulating agents have been shown to increase the risk of lymphoproliferative disorders and neoplasms. ¹²⁵

2. RECURRENT APHTHOUS STOMATITIS

It represents the most common non traumatic oral ulceration. In general population its incidence is 20% - 40%. It chiefly affects the oral and oropharyngeal mucosa, rarely the genital mucosa. It is a diagnosis of exclusion, and other causes of ulcerative stomatitis should be explored before a diagnosis of RAS is made.¹³⁰

Etiology

The specific etiopathogenesis is not well known but, wide range of associations or conditions exists as given in table below.¹³¹

Table 6: TRIGGER FACTORS: APHTHOUS STOMATITIS
Psychological stress
Traumatic/ Iatrogenic traumas(Sharp tooth, ill fitted dentures, prosthetics)
Associated systemic diseases and syndromes:
Crohns disease/ ulcerative colitis
Behcet disease
Malabsorption/ gluten sensitive enteropathy
Human immunodeficiency virus
Hematinic and other deficiency states
Sweet syndrome (acute febrile neutrophilic dermatosis)
PFAPA syndrome (perodic fever, aphthous ulcers, pharyngitis, and adenitis)

Drug induced aphthae are seen with nonsteroidal anti-inflammatory drugs, beta blockers and potassium channel blockers. Drug induced aphthae will resolve with the withdrawal of offending drug.¹³⁰

Clinical features

The based on the clinical presentations and severity of RAS, ulcer size being the major differentiating feature, the stomatitis is represented by one of three subtypes- minor, major and herpetiform types.¹³¹

- **Minor RAS (Miculiz's aphthae):** It is the most common variant, almost 80% of RAS. Ulcers vary from 8 to 10 mm in size. Commonly seen in the nonkeratinized mucosa such as labial mucosa, buccal mucosa, and floor of the mouth. Self-limiting and heal within 10–14 days without scarring.
- **Major RAS (Sutton's disease):** Affects about 10–15% of patients. Ulcers size exceed 1 cm. Seen on the lips, soft palate, and fauces. Less commonly involve masticatory mucosa like dorsum of tongue or gingiva. The ulcers persist for up to 6 weeks and heal with scarring.
- **Herpetiform ulceration** is characterized by recurrent crops of multiple (may be up to 100 in number) pinpoint size ulcers which later may coalesce to form large irregular ulcers. These ulcers last for about 10–14 days. To differentiate from herpetic ulcers, these are not preceded by vesicles and do not contain viral infected cells. More common in women.

Differential Diagnosis:

The differential diagnosis for recurrent aphthous ulcerations is extensive and ranges from idiopathic benign causes to even inflammatory bowel diseases. A thorough history and review of systems can assist the clinician in determining whether it is related to a systemic inflammatory process or truly idiopathic. The common differential diagnosis are described in the table below.

Table No. 7 : Differential diagnosis of acute and chronic oral ulcers¹³¹
Recurrent aphthous stomatitis (idiopathic)
Drug induced: fixed drug eruption, linear Ig A dermatoses, drug induced pemphigus, drug induced pemphigoid, Steven Johnson syndrome, toxic epidermal necrolysis
Autoimmune diseases: Crohns, Behcet disease, Lichen Planus, systemic lupus erythematosus, Wegener's granulomatosis
Trauma induced
Hematological: anemia, neutropenia, hyper-eosinophilic syndromes
Fever syndromes: PFAPA, Sweet syndrome, Familial Mediterranean fever
Vesiculobullous disorders: Pemphigus vulgaris, linear IgA, erythema multiforme
Nutritional deficiency: Iron/ folate/ zinc, B6, B12
Infections: Tuberculosis, syphilis, herpes simplex, EBV, HIV.

Treatment

Mild and infrequent episodes of minor aphthous ulcers generally require little more than symptomatic management and chlorhexidine rinses. The

general mainstay of treatment is with topical steroids in combination with topical analgesic agents or other topical anti-inflammatory drugs. Short term systemic corticosteroids are effective in case of severe, recurrent outbreaks. Other systemic medications found effective for RAS are clofazimine, dapsone, colchicine, pentoxifylline, thalidomide, zinc 50mg/day.^{131, 132}

TONGUE LESIONS

GEOGRAPHIC TONGUE

Geographic tongue is also known as benign migratory glossitis, erythema migrans, lingual geographica or glossitis areata exfoliative. Few studies pointed towards an association with diabetes, psoriasis, seborrheic dermatitis, HIV and atopy, but not found to be pathognomonic. The term "annulus migrans" is used when geographic lesions occur in association with psoriasis or Reiter's syndrome. Clinically, dorsum of tongue develops areas of papillary atrophy that appear smooth with sharply demarcated raised serpiginous border, making tongue resemble a map.

The condition is benign and localized requiring no treatment other than reassurance. Antihistamine mouth rinses can reduce tongue sensitivity.¹³³

FISSURED TONGUE

Also known as scrotal tongue, is seen associated with Down's syndrome, acromegaly, psoriasis, Cowden syndrome and Sjogren syndrome. It is seen in Melkersson-Rosenthal syndrome characterized by a triad of severe fissuring,

relapsing orofacial edema and facial nerve palsy. These typically occur with aging and require no treatment.^{133,134}

ATROPHIC GLOSSITIS

It is also known as bald tongue because of the smooth, glossy appearance with a red or pink background, as a result of atrophy of filiform and fungiform papillae. It is a manifestation of underlying nutritional deficiencies of iron, folic acid, vitamin B12 and niacin. Other etiologies like systemic infection like syphilis, localized infection like candida, amyloidosis, celiac disease, malnutrition should be ruled out. Resolution of lesion may occur with treatment of underlying pathology.¹³⁵

MEDIAN RHOMBOID GLOSSITIS

Typically a red, depapillated, rhomboid area in the midline of the dorsum of the tongue, just anterior to sulcus terminalis. It is more commonly seen in association with candidial infection, and responds to antifungals. Men are affected three times more often than females. Other predisposing conditions are smoking, HIV infection, diabetes. Presence of palatal inflammation may be indicative of immunosuppression.^{133,136}

MATERIAL & METHODS

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MATERIAL AND METHOD

The study was carried out from January 2016 to July 2017. All patients above 60 years of age, coming to Dermatology OPD at R.L.Jallapa Hospital & Research Centre, attached to Sri Devaraj Urs Medical College, Tamaka, Kolar were examined and evaluated for oral mucosal lesions.

A detailed medical history of all such patients collected including demographic data, chief complaints related to skin, presence of oral mucosal lesions, medical disorders, medications used, and habits (smoking, alcohol consumption, chewing of betel nut, other forms of tobacco use, prosthetic or other appliances use).

During the clinical examination the following elements were analyzed: morphology of the lesion, anatomical location and extension. Clinical evaluation included anatomical location, morphology and extension of the lesion. To assess changes in texture and its extension, digital palpation done. A detailed physical examination was made to see any associated lesions elsewhere in the body.

The clinical diagnosis was established and classified. Correlation, if any, with etiological factor was assessed. In relevant cases, necessary investigations like gram stain, KOH mount, Wood's lamp examination,

biopsy and histopathological examination were done to establish the definitive diagnosis.

The biopsy was taken under local anesthesia on an out-patient basis by researcher after patient's consent. For the cases with autoimmune diseases two biopsy samples were taken, one sample for routine histological examination and the other for immunofluorescent technique. The final definitive diagnosis was based on histopathological examination given by pathologists and its clinical correlation.

The data collected was documented in the prescribed proforma and further validated by the consultants.

Criteria for selection:

a. Inclusion criteria:

- All patients above 60 years having oral mucosal lesions.
- Irrespective of treatment taken

b. Exclusion criteria:

- Patients with medical emergencies like toxic epidermal necrolysis, burns, corrosive lesions and trismus grade 3.

The collected data were analyzed by the SPSS 22 version software. Chi-square test was used as test of significance for qualitative data.

RESULTS

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OBSERVATIONS AND RESULTS

A total of 130 cases fulfilling inclusion criteria attending to dermatology OPD at R.L. Jalappa Hospital and Research centre, Tamaka, Kolar district, Karnataka during the period of from January 2016 - July 2017 were enrolled in this clinical study.

PREVALENCE OF ORAL MUCOSAL LESIONS

In our study after screening 5257 patients above 60years, 130 patients with oral mucosal lesions were enrolled for the study, showing a prevalence of 2.47%.

AGE DISTRIBUTION

Majority of the patients, 93 (71%) were in the age group of 60-69 years, followed by 31 (24%) cases in the age group of 70-79 years, 6 (5%) cases in the age group of 80 years and above and there was no cases above 90 years.

Table 8: Age distribution of the study population.

AGE DISTRIBUTION		
	Number	Percentage
60 to 69 years	92	70.8%
70 to 79 years	32	24.6%
80 years and above	6	4.6%

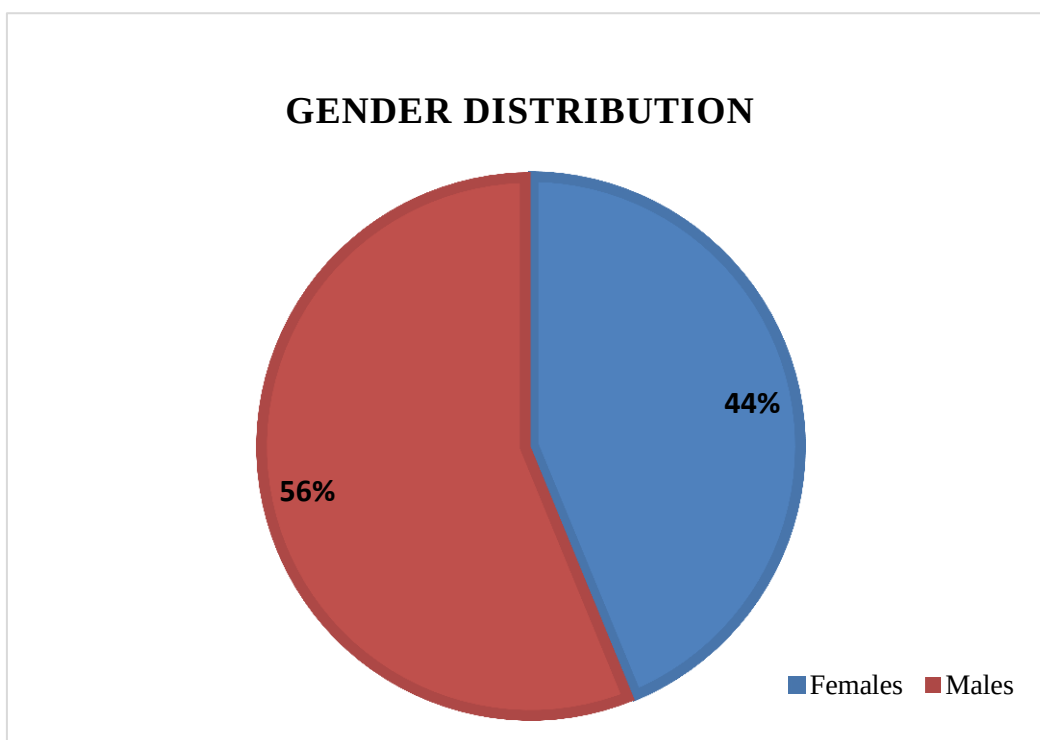
GENDER DISTRIBUTION

In the study 43.8% were females and 56.2% were males.

Table 9: Gender wise distribution of the study population

GENDER DISTRIBUTION		
	Number	Percentage
Male	73	56%
Female	57	44%
Total	130	100

Graph 1: Pie diagram showing gender wise distribution



ASSOCIATION OF AGE AND GENDER DISTRIBUTION

In the study both the gender, majority of subjects were in the age group 60-69 years, with 73.7% of females and 68.5% of males. There was no significant association between age and gender distribution.

Table 10: Association of age and gender distribution of the study population.

AGE	GENDER			
	Male		Female	
	Number	Percentage	Number	Percentage
60 - 69 years	50	68.5%	42	73.7%
70 - 79 years	19	26.0%	13	22.8%
80 years and above	4	5.5%	2	3.5%

p value = 0.769

SITE OF INVOLVEMENT

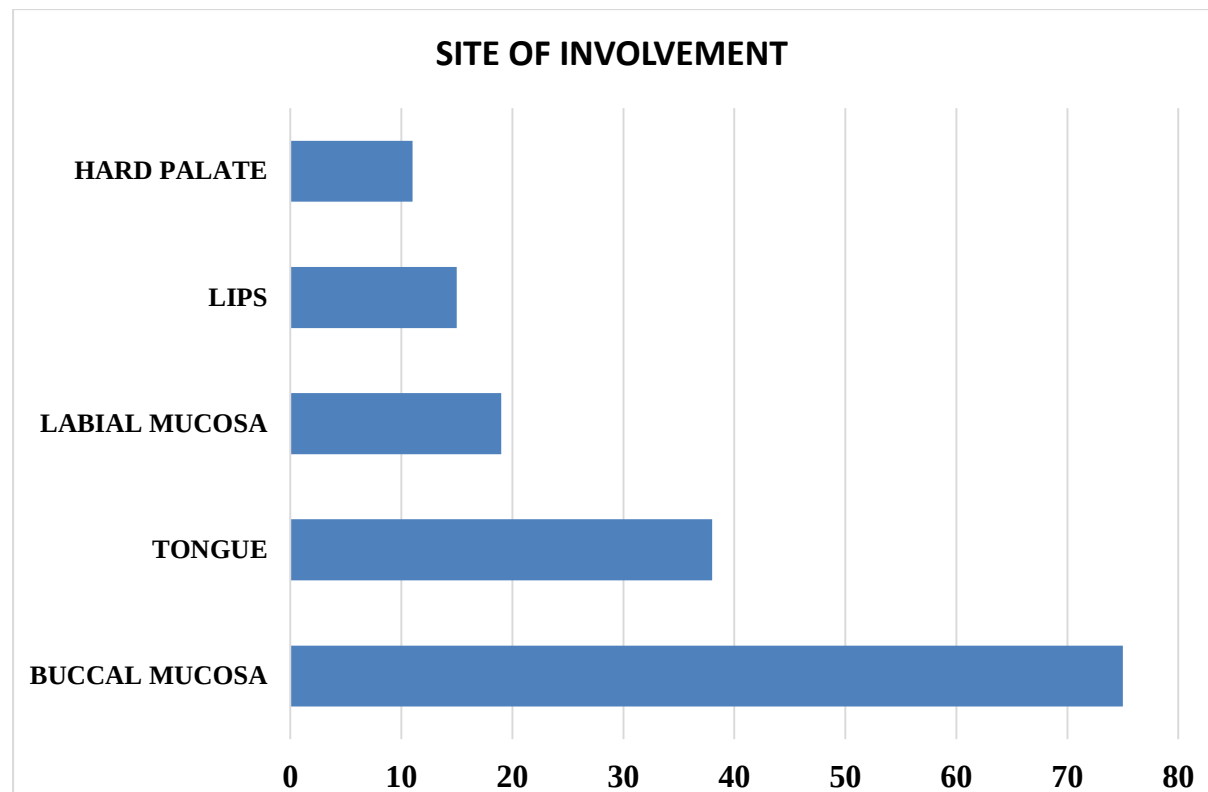
In the present study, the commonest site affected was the buccal mucosa in 75 cases (58%), next being involved in patients were tongue in 38 cases(29%), labial mucosa in 19(15%), lips in 15(12%) and hard palate in 11(8%).

Table 11: Distribution of oral mucosal lesions.

Site* of involvement	Number	Percentage
Buccal mucosa	75	58%
Tongue	38	29%
Labial mucosa	19	15%
Lips	15	12%
Hard palate	11	8%

*more than one site may be involved.

Graph 2: Site of involvement



RISK FACTORS

In the study 52.3% were chewing betel nut, 46.2% were consuming Tobacco, 40% were smokers, 17.7% were alcoholics, 12.3% had ill fitting dentures and 13.8% had stress. Most of the patients had more than one risk factors for the development of oral mucosal lesions. When the common risk factor in males was smoking, use of other forms of tobacco and betel nut chewing, females were addicted to betel and areca nut chewing followed by other forms of tobacco usage and stress.

Table 12: Risk factors associated with oral mucosal lesions.

		Number	Percentage
Betel quid	No	62	47.7%
	Yes	68	52.3%
Tobacco	No	70	53.8%
	Yes	60	46.2%
Smoking	No	78	60.0%
	Yes	52	40.0%
Alcohol	No	107	82.3%
	Yes	23	17.7%
Stress	No	112	86.2%
	Yes	18	13.8%
Dentures	No	114	87.7%
	Yes	16	12.3%

Graph 3: Bar diagram showing risk factors in the study population

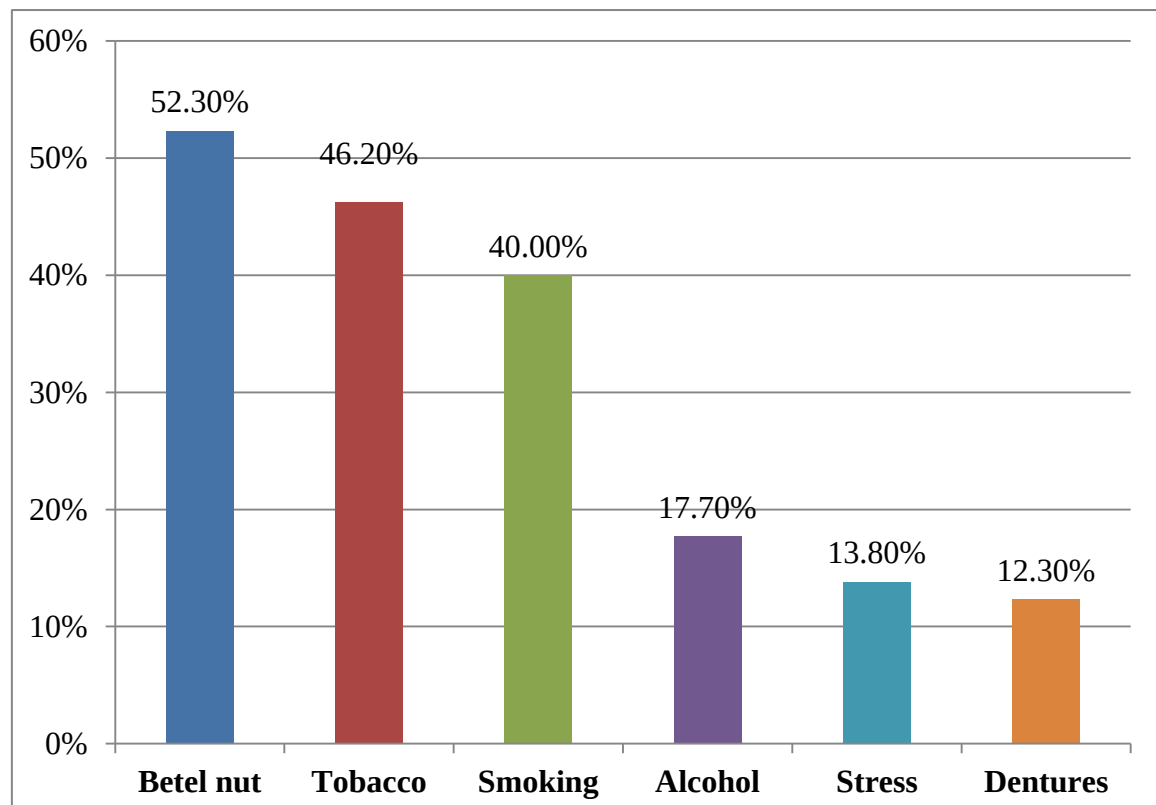
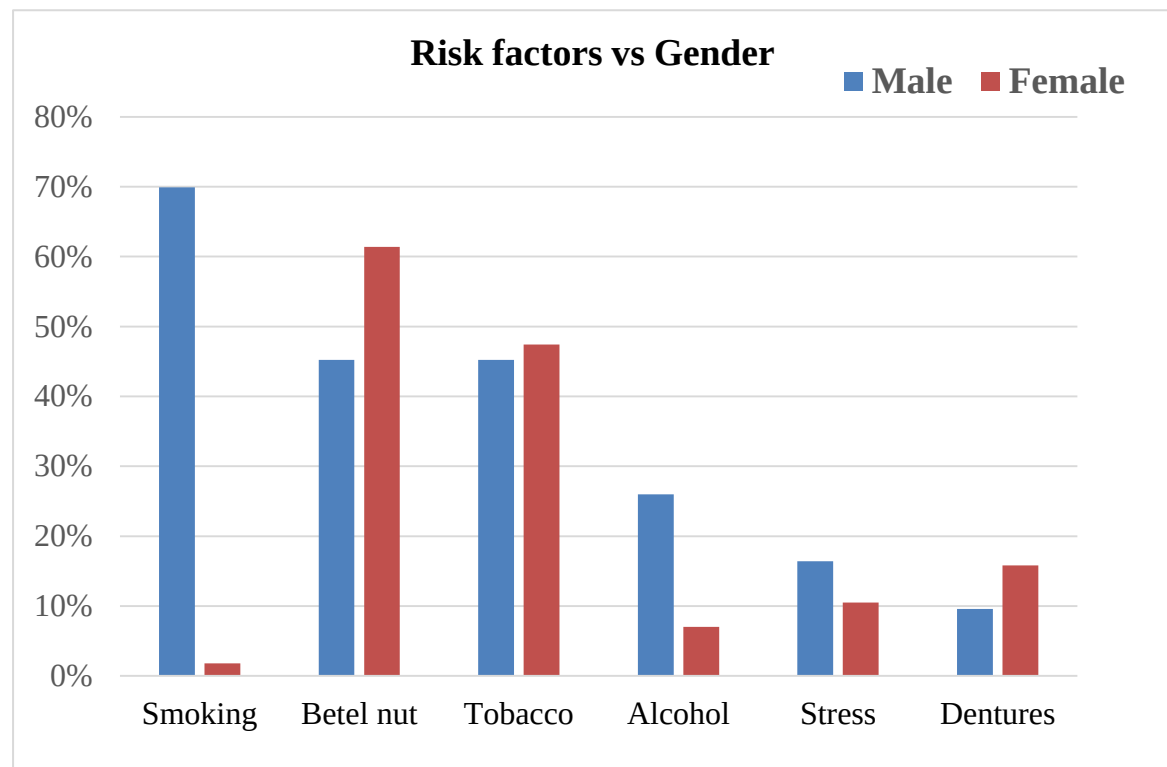


Table 13: Gender wise distribution of risk factors in the study population

Risk factors	Gender				P value
	Male		Female		
	Number	Percentage	Number	Percentage	
Smoking	51	69.9%	1	1.8%	<0.001*
Alcohol	19	26.0%	4	7.0%	0.005*
Tobacco	33	45.2%	27	47.4%	0.806
Betel quid	33	45.2%	35	61.4%	0.067
Dentures	7	9.6%	9	15.8%	0.286
Stress	12	16.4%	6	10.5%	0.333

Graph 4: Gender wise distribution of risk factors in the study population



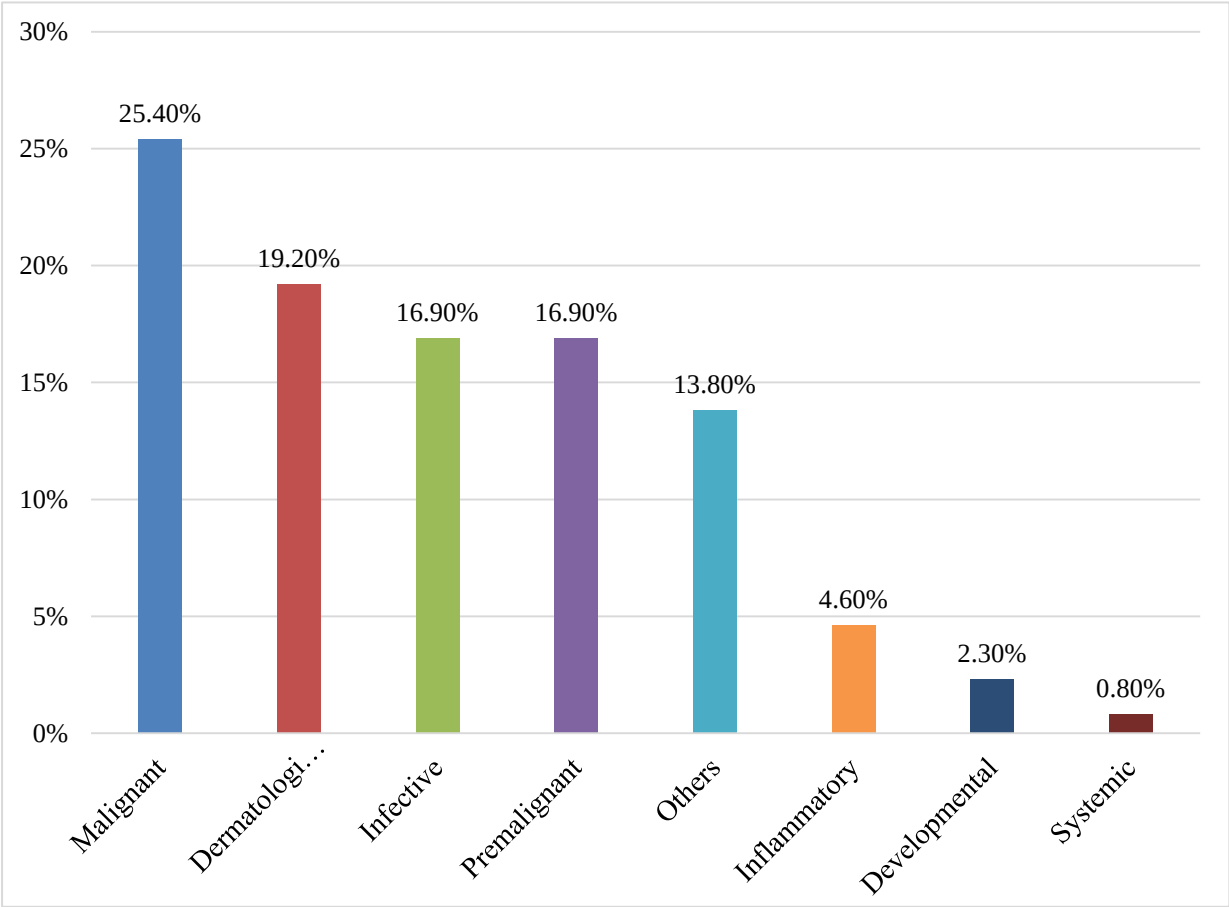
ETIOLOGICAL CLASSIFICATION

Most frequently observed etiology for oral mucosal lesions in the present study population were malignancy with 33 cases (25.4%) followed by dermatological with 25 cases (19.2%), premalignant and infectious etiology observed in 22 cases (16.9%). Least observed were other miscellaneous (13.8%), inflammatory (4.6%), developmental (2.3%) and systemic (0.8%).

Table 14: Etiological classification of oral mucosal lesions in the study

ETIOLOGICAL CLASSIFICATION		
Etiologies	Number	Percentage
Malignant	33	25.4%
Dermatological	25	19.2%
Infective	22	16.9%
Premalignant	22	16.9%
Others	18	13.8%
Inflammatory	6	4.6%
Developmental	3	2.3%
Systemic	1	0.8%

Graph 5: Etiological classification of oral mucosal lesions in the subjects



CLINICAL TYPES OF ORAL MUCOSAL LESIONS

Each etiological conditions were subdivided as following clinical types and their subtypes based on clinical and histopathological evaluation.

Table 15: Clinical types of oral mucosal lesions in the study population.

Clinical types	Number	Percentage
Oral Carcinoma 33(25.4%)		
Squamous cell carcinoma	32	97%
Adenoid cystic carcinoma	1	3%
Oral Candidiasis 16 (12.4%)		
Hypertrophic type	12	75%
Atrophic type	4	25%
Leukoplakia 11 (8.5%)		
Homogenous	8	73%
Speckled	3	27%
Oral Lichen Planus 10 (7.7%)		
Reticular type	7	70%
Atrophic type	2	20%
Actinic type	1	10%
Vitiligo 8 (6.2%)		
Vitiligo vulgaris	2	25%
Mucosal vitiligo	6	75%
Aphthous Ulcer 8 (6.2%)		
Minor aphthous ulcer	6	75%
Major aphthous ulcer	2	25%
Herpes Simplex 7 (5.4%)		
Herpes labialis	7	100%

Pemphigus 4 (3.1%)		
Pemphigus vulgaris	3	75%
Pemphigus foliaceus	1	25%
Cheilitis 2 (1.5%)		
Granulomatous cheilitis	1	50%
Actinic cheilitis	1	50%
Others		
Oral Submucous Fibrosis	10	7.7%
Drug Induced Mucositis	6	4.6%
Smoker's Melanosis	4	3.1%
Fissured Tongue	3	2.3%
Fordyce Spot	2	1.5%
Geographic Tongue	2	1.5%
Angina bullosa haemorrhagica	1	0.8%
Melanoplakia	1	0.8%
Discoid Lupus Erythematosus	1	0.8%
Steven Johnson Syndrome	1	0.8%
Systemic Lupus Erythematosus	1	0.8%
Erythroplakia	1	0.8%

AGE WISE DISTRIBUTION OF ETIOLOGIES

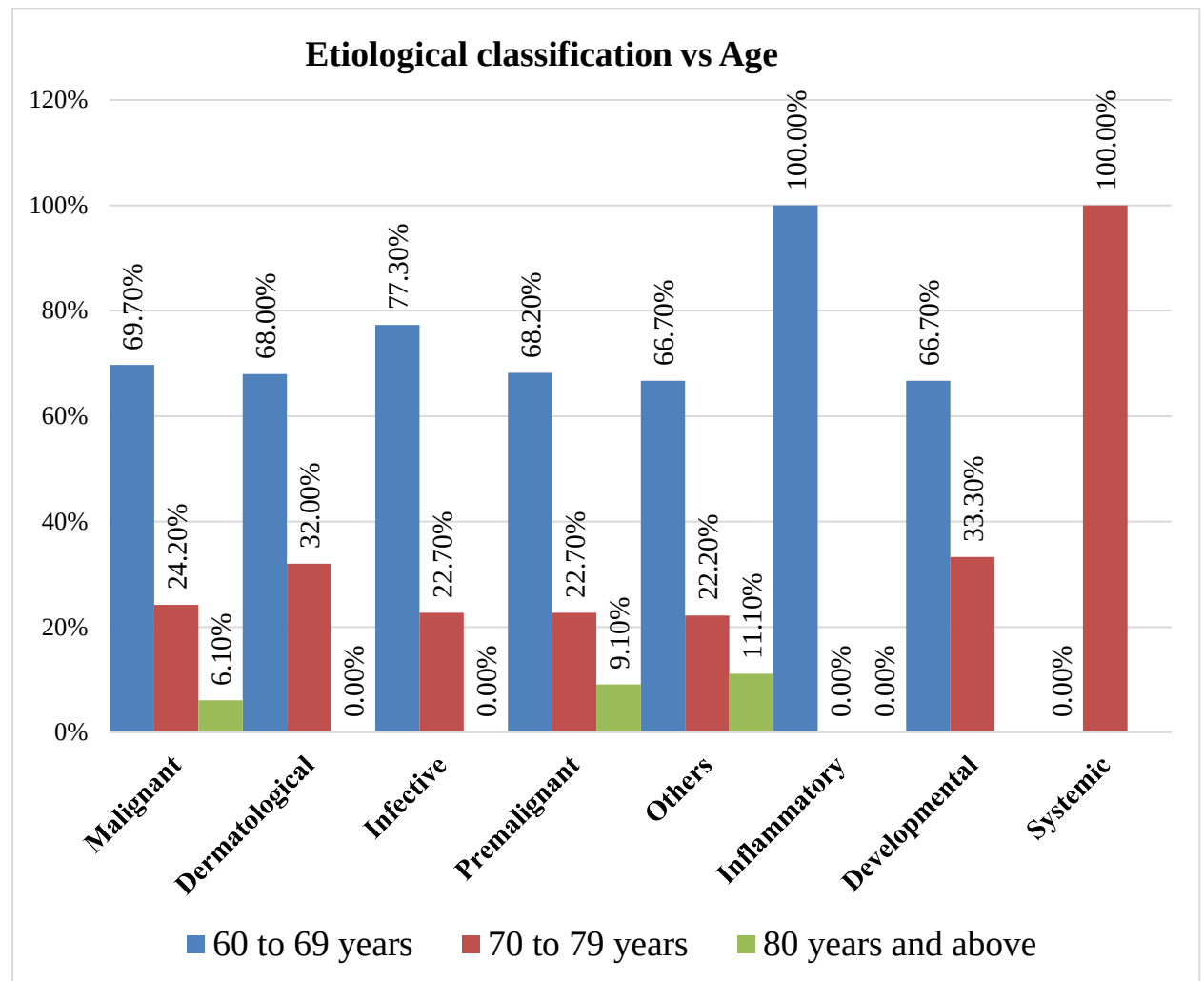
In the study among those with malignant lesions, majority of subjects were in the age group 60 to 69 years (69.7%), among dermatological lesions, majority 68% were in the age group 60 to 69 years, among infective lesions, premalignant lesions, other lesions, developmental lesions, inflammatory lesions majority were in the age group 60 to 69 years, among systemic lesions 100% were in the age group 70 to 79 years. There was no significant difference in etiological classification and age distribution.

Table 16: Age wise distribution of various etiologies in the study population

AGE						
Etiologies	60 to 69 years		70 to 79 years		80 years and above	
	Number	Percentage	Number	Percentage	Number	Percentage
Malignant	23	69.7%	8	24.2%	2	6.1%
Dermatological	17	68.0%	8	32.0%	0	0.0%
Infective	17	77.3%	5	22.7%	0	0.0%
Premalignant	15	68.2%	5	22.7%	2	9.1%
Others	12	66.7%	4	22.2%	2	11.1%
Inflammatory	6	100.0%	0	0.0%	0	0.0%
Developmental	2	66.7%	1	33.3%	0	0.0%
Systemic	0	0.0%	1	100.0%	0	0.0%

p value = 0.639

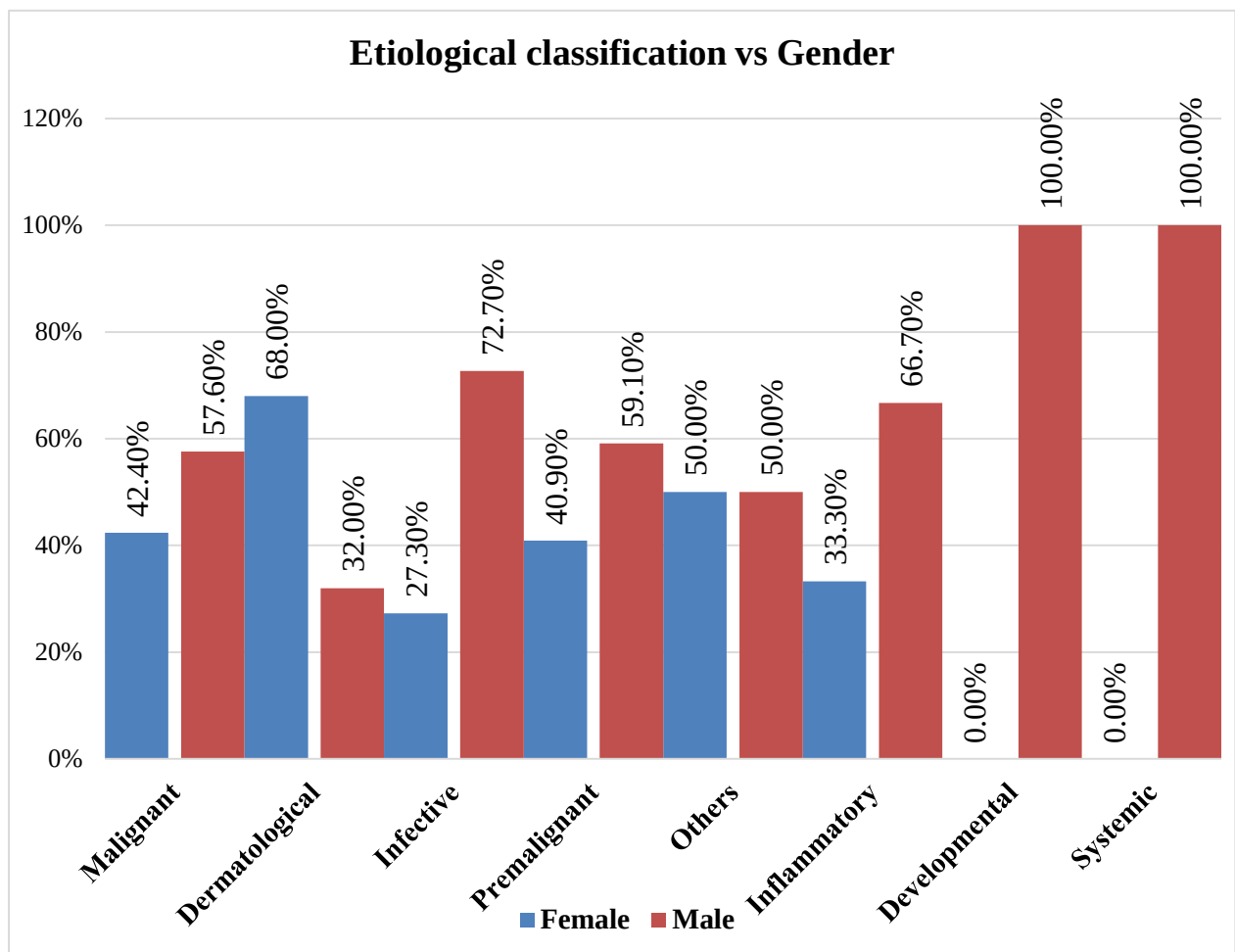
Graph 61: Age wise distribution of various etiologies in the study population



ASSOCIATION BETWEEN ETIOLOGY CLASSIFICATION AND GENDER

Malignant lesions, infective lesions, premalignant lesions, inflammatory lesions, developmental lesions and systemic lesions were common among males and dermatological lesions were common among female. There was no significant association between etiologies classification and gender.

Graph 72: Bar diagram showing gender wise distribution of etiologies among study population.



ASSOCIATION OF RISK FACTORS WITH VARIOUS ETIOLOGIES

Malignant and premalignant lesions were frequently associated with smoking, alcohol, other forms of tobacco use and betel nuts chewing. There was significant difference in oral lesions among smokers and alcoholics(p values were 0.019 and 0.001 respectively). With other risk factors, there was no significant difference in oral mucosal lesions.

Table 17: Association of risk factors with various etiologies

Risk factors	Malignant	Dermatologic	Infective	Premalignant	Others	Inflammatory	Developmental	Systemic	P value
	Number Percentage	Number Percentage	Number Percentage	Number Percentage	Number Percentage	Number Percentage	Number Percentage	Number Percentage	
Smoking	17 32.7%	3 5.8%	6 11.5%	11 21.2%	8 15.4%	4 7.7%	2 3.8%	1 1.9%	0.019*
Alcohol	12 52.2%	3 13.0%	1 4.3%	0 0%	5 21.7%	0 0%	1 4.3%	1 4.3%	0.001*
Tobacco	20 33.3%	7 11.7%	10 16.7%	14 23.3%	6 10.0%	2 3.3%	1 1.7%	0 0%	0.120
Betel nut	19 27.9%	12 17.6%	11 16.2%	16 23.5%	7 10.3%	2 2.9%	1 1.5%	0 0%	0.335
Dentures	1 6.2%	5 31.2%	1 6.2%	2 12.5%	6 37.5%	1 6.2%	0 0%	0 0%	0.061
Stress	7 38.9%	1 5.6%	6 33.3%	1 5.6%	3 16.7%	0 0%	0 0%	0 0%	0.179

SYSTEMIC COFACTORS ASSOCIATED WITH ORAL MUCOSAL LESIONS.

In the study 36.15% had Diabetes Mellitus, 17.69% had Hypertension, 0.8% were on Chemotherapy, Human Immunodeficiency Virus(HIV) infection, Hepatitis, Atopy and Tuberculosis.

Table 18: Systemic cofactors associated with oral mucosal lesions.

Systemic Cofactors	Number	Percentage
Nil	75	57.69%
Diabetes Mellitus	47	36.15%
Hypertension	23	17.69%
Chemotherapy	1	0.8%
HIV infection	1	0.8%
Hepatitis	1	0.8%
Atopy	1	0.8%
Tuberculosis	1	0.8%

ORAL CARCINOMA

- The most common clinical diagnosis the present study is oral carcinoma, its demographic data given in table 19.
- Age range of our study population was more than 60 years, with the highest prevalence seen in the age group of 60-69 years with 23 cases (70%).
- Oral carcinoma was frequently observed in males 19 (58%) cases in comparison to females with 15 (42%) cases.
- The buccal mucosa was predominantly involved in 28 (85%) cases. Followed by tongue in 4 (12%) cases and lips in 1 case (3%) respectively.
- Predominant risk factors associated with oral carcinoma were smoking in males with 17 cases, whereas in females use of other forms of tobacco with 9 cases (45%), followed by betel and areca nut chewing in 8(42%).

Table 19: Demographic and disease characteristics of oral carcinoma

	Male(%) n=19	Female(%) n=14	Total(%) n=33
Age group			
60-69 years	11	12	23 (70%)
70-79 years	7	1	8(24%)
80-89 years	1	1	2 (6%)
>90 years	0	0	0
Clinical Subtype			
Squamous cell carcinoma	18	14	33
Adenoid cystic carcinoma	1	0	1
Risk factors*			
Tobacco use	11	9	20 (61%)
Betel and areca nut	11	8	19 (58%)
Smoking	17	0	17 (45%)
Alcohol	9	3	12 (36%)
Stress	6	1	7 (21%)
Medical illness	2	1	3 (9%)
Dentures	0	1	1 (3%)
Site distribution*			
Buccal mucosa	15	13	28 (85%)
Tongue	3	1	4 (12%)
Lips	1	0	1 (3%)

* >1 risk factors or sites can be involved

ORAL CANDIDIASIS

- Oral candidiasis was the second most common clinical diagnosis the present study, its demographic data given in table 20.
- In present study, oral candidiasis was more frequently observed in males with 12 (75%) cases than in females with 4 (25%) cases.
- Age group of 60-69 years showed 11 (70%) cases followed by 70-79 years with 5 (31%).
- Hypertrophic type candidiasis was the most common subtype in 12 (75%) cases, followed by atrophic type 4 cases (25%).
- Tongue was the most common site affected in all 16 cases.
- Medical illness (75%) was the common underlying predisposing factor for oral candidiasis.

Table 20: Demographic and disease characteristics of Oral Candidiasis

	Male(%) n=12	Female(%) n=4	Total(%) n=16
Age Distribution			
60- 69years	3	8	11(69%)
70- 79years	1	4	5 (31%)
80-89 years	0	0	0
Above 90 years	0	0	0
Clinical types			
Hypertrophic type	10	2	12 (75%)
Atrophic type	2	2	4 (12%)
Risk factors*			
Medical illness	10	2	12(75%)
Smoking	4	0	4 (25%)
Betel and areca nut	3	7	10(63%)
Tobacco use	2	7	9(56%)
Alcohol	1	0	1 (6%)
Denture	0	0	0
Stress	0	0	0
Site distribution*			
Tongue	12	4	16(100%)
Buccal mucosa	4	1	4 (25%)
Hard palate	2	0	2(13%)
Labial mucosa	0	0	0
Lips	0	0	0

* >1 risk factors or sites can be involved.

ORAL LICHEN PLANUS

- In the present study, oral lichen planus was more frequently observed in males with 6 (60%) cases than in females with 4 (40%) cases (table 21).
- Age group of 60-69 years showed 5 (50%) cases followed by 70-79 years with 3 (30%).
- Reticular type of oral lichen planus was the predominant subtype in 7 (70%) cases, followed by atrophic type 2 cases (20%).
- Buccal mucosa was the most common site affected in 9 cases.
- Medical illness like diabetic mellitus (70%) was the common predisposing factor for oral lichen planus. Other frequently observed risk factors were betel nut chewing, use of other forms of tobacco and use of dentures.

Table 21: Demographic and disease characteristics of Oral Lichen Planus

	Male(%) n=6	Female(%) n=4	Total(%) n=10
Age group			
60years	2	1	3(30%)
61-65 years	3	1	4(40%)
66-70 years	1	2	3(30%)
71-75 years	0	0	0
76-80 years	0	0	0
Above 80 years	0	0	0
Subtype			
Reticular type	1	2	7 (70%)
Atrophic type	1	1	2 (20%)
Erosive -ulcerative	0	1	1 (10%)
Risk factors*			
Medical illness	4	3	7 (70%)
Betel and areca nut	3	2	5 (50%)
Tobacco Chewing	2	3	5 (50%)
Dentures	3	2	5 (50%)
Smoking	3	0	3 (30%)
Alcohol	2	1	3 (30%)
Stress	0	0	0
Site distribution*			
Buccal mucosa Lips	6	3	9 (90%)
Lips	1	2	3 (30%)
Labial mucosa	0	2	2 (20%)
Tongue	1	0	1 (10%)
Hard palate	0	0	0

* >1 risk factors or sites can be involved

Table 22: Dermatological conditions observed in study population

Dermatological condition	Number	Percentage
Lichen planus	10	8%
Vitiligo	8	6%
Pemphigus	4	3%
Psoriasis	2	2%
Steven Johnson Syndrome	1	1%
Systemic lupus erythematosus	1	1%
Discoid lupus erythematosus	1	1%

In our study, out of ten oral lichen planus cases, most common clinical type was reticular lichen planus (70%) and buccal mucosa was the common site involved.

Out of eight vitiligo cases with oral mucosal involvement observed common clinical type was mucosal vitiligo (6%) with a female predilection and lips as commonly involved site.

In vesiculobullous disorders, three cases were pemphigus vulgaris and one case was pemphigus foliaceus, presented with erosive and ulcerative oral mucosal lesions.

Less common dermatological conditions were two of psoriasis patients with fissured tongue, one case of Steven Johnson Syndrome with ulcerative

lesions over lips, labial mucosa, buccal mucosa and tongue, one female systemic lupus erythematosus case with oral ulcerative lesions and a female patient with ulcerative lesion over lower lips of discoid lupus erythematosus .

Others

Aphthous ulcer (n=8, 6%), herpes infection (5%), drug induced mucositis (5%), smokers melanosis (n=4, 3%), geographic tongue (2%), Fordyce spot (2%), cheilitis (2%), melanoplakia (2%), angina bullosa hemorrhagica (n=1, 1%).

CLINICAL PHOTOGRAPHS



Fig 2: Fordyce's Spots as yellowish spots on vermilion border of lips

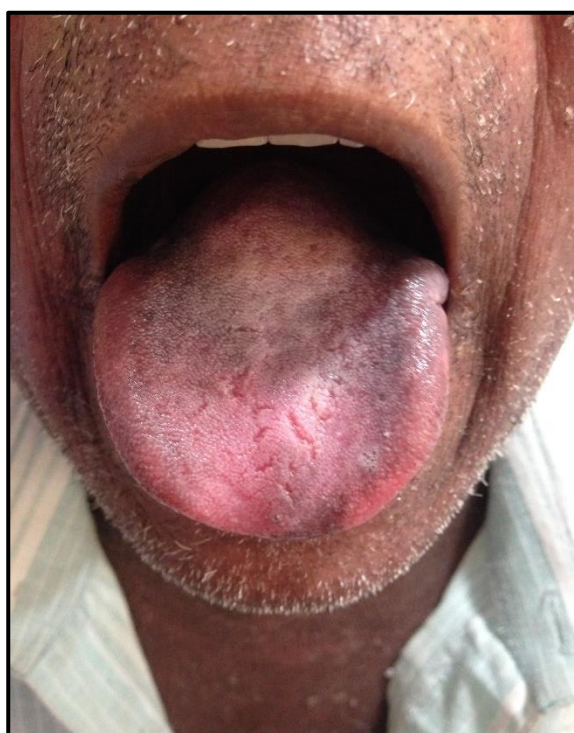


Fig 3: Nicotinic Stomatitis with pigmentation on dorsum of tongue



Fig 4: Vitiligo Vulgaris involving lips and labial mucosa

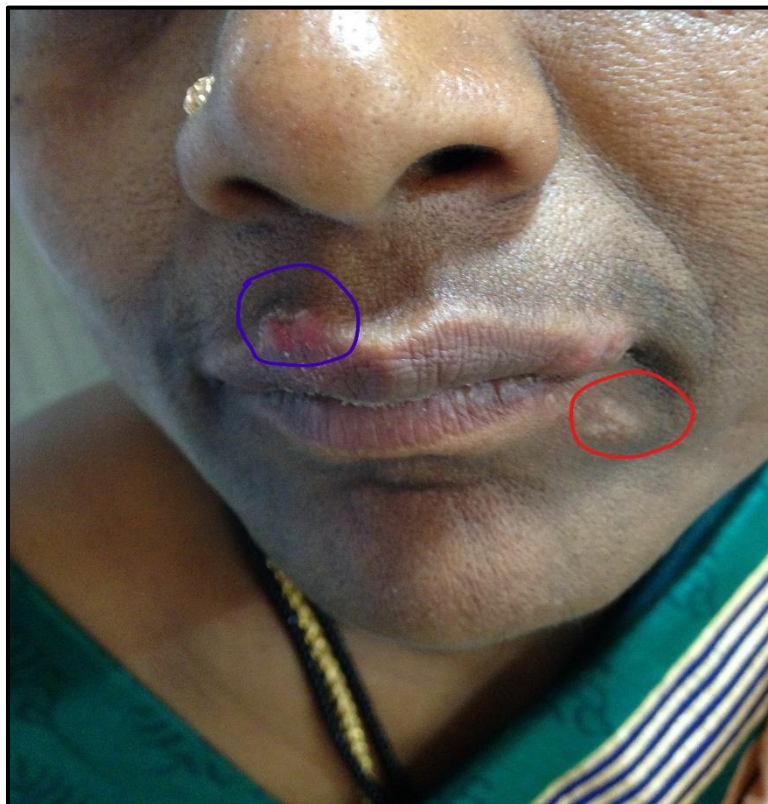


Fig 5: Herpes Labialis on vermilion border of lowerlips



Fig 6a: Reticular lichen planus on buccal mucosa

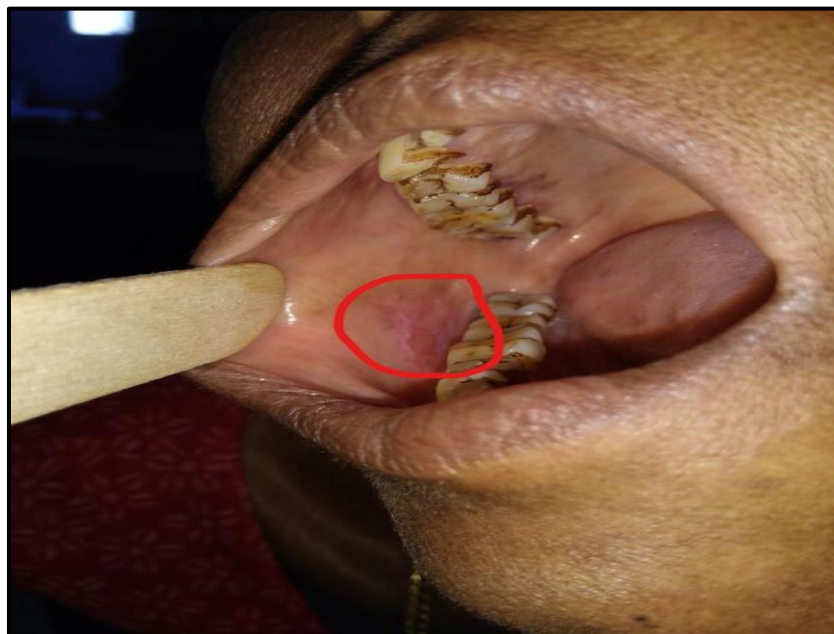


Fig 6b: Erosive Lichen Planus on buccal mucosa



Fig 7a: Homogenous Leukoplakia on buccal mucosa



Fig 7b: Speckled Leukoplakia on buccal mucosa



Fig 8: Erythroplakia on buccal mucosa

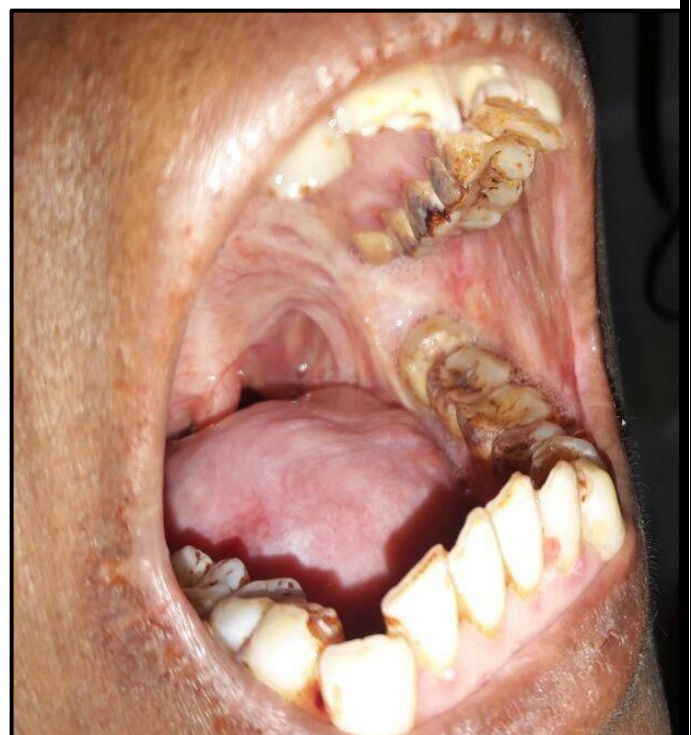


Fig 9a & 9b: Oral Submucous Fibrosis involving buccal mucosa and hard palate

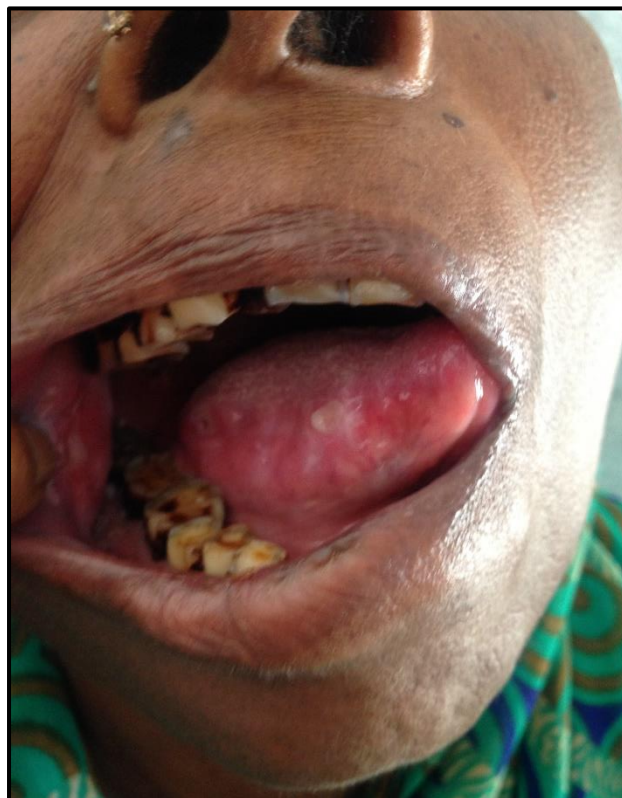
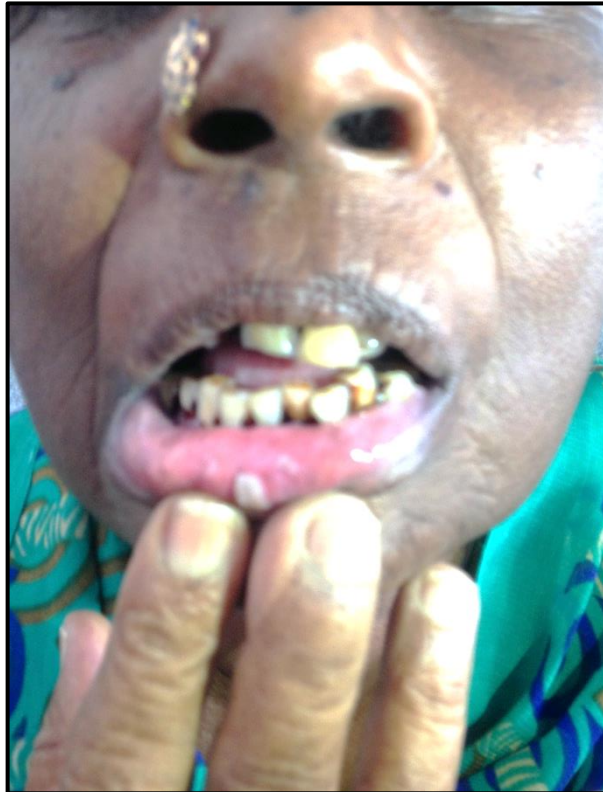


Fig 10a & 10b: Pemphigus Vulgaris case with flaccid bullae on lower labial mucosa and erosion on lateral aspect of tongue.



Fig 11: Discoid Lupus Erythematosus of lips



Fig 12a: Minor Aphthous ulcer on tongue



Fig 12b: Multiple Herpetiform aphthous ulcer coalescing on hard palate.



Fig 13a & 13b: Steven Johnson Syndrome with multiple erosive lesions on lips and buccal mucosa

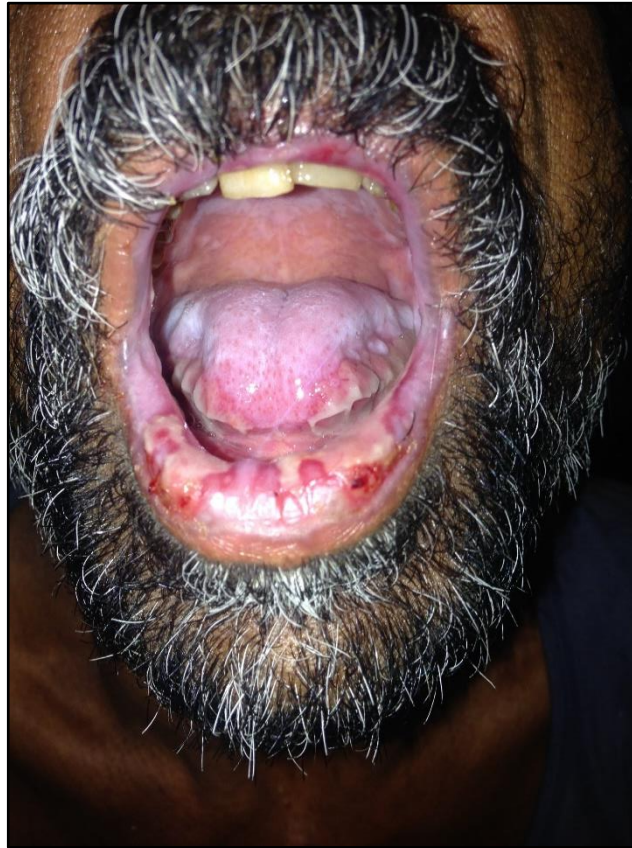


Fig 14: Drug induced mucositis causing multiple erosions on lips with oral candidiasis.



Fig15: Fissured Tongue

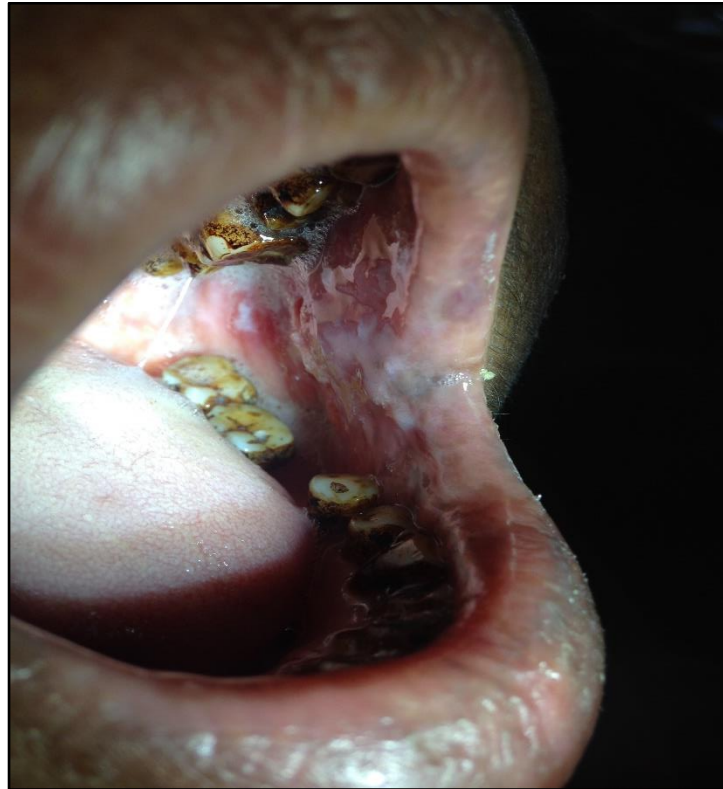


Fig 16a: Squamous cell carcinoma of buccal mucosa. Fig 16b: Cutaneous oozing lesion on cheek from the underlying carcinoma of buccal mucosa



Fig 17: Ulceroproliferative Squamous Cell Carcinoma of buccal mucosa

DISCUSSION

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DISCUSSION

Oral mucosal lesions are common findings representing a wide spectrum of conditions, ranging from benign physiological entities to dysplasia and squamous cell carcinoma.

Though the prevalence of oral lesions in general population has been documented based on clinical evaluation in other parts of the world like Turkey¹³⁷ and Yemen¹ limited information is available in rural or semi-urban population of India.^{138, 139}

The present study includes a total of 130 clinically diagnosed cases of oral mucosal lesions.

In our study after screening 5257 patients above 60years, 130 patients with oral mucosal lesions were enrolled for the study. In our study, the prevalence of oral mucosal lesions was 2.47% which was consistent to the prevalence in Turkish population (2.2%).¹³⁷ The prevalence rates of oral mucosal lesions varies with different geographical, risk habits, genetic factors and sociodemographic characteristics of the study populations.

Similar to few other studies,^{1,2} in the present study mean age of study population was 65.64 ± 6.1 years. Majority of subjects were in the age group 60- 69 years (70.8%), followed by 70- 79 years (24.6%). This can be because most of the individuals in their advancing age quit their addictions

due to other medical reasons, as a result the incidence of oral mucosal lesions will also decrease significantly. However above 70 age group (52%) showed the highest incidence in Bahia study.¹⁴⁰

In concordance with various other studies,^{1, 2} a male preponderance of 56.2% was seen in our study whereas similar study in elderly Venezuelan population,¹⁴¹ females were commonly affected than males. Sex differences in the occurrence of oral mucosal lesions might be attributed to the higher prevalence of deleterious oral habits among males in our study population.

In the present study, the predominant risk factors were betel quid chewers (52.3%), closely followed by use of other forms of tobacco (46.2%), smoking (40%) and alcohol (17.7%). Less common risk factors were ill fitting dentures (12.3%) and stress (13.8%). This is consistent with data reported by other studies.^{1, 2, 138} Most of the patients had more than one risk factors for the development of oral mucosal lesions. Smoking was the most common risk factor in males. Followed by use of other forms of tobacco and betel nut chewing. However in females, betel and areca nut chewing followed by other forms of tobacco usage and stress were the commonly associated risk factors elicited. A significant difference in smoking and alcohol as risk factors between males and females observed was consistent with other studies.¹⁴²

The present study showed bidi smoking was significant indicator for oral mucosal lesions such as oral carcinoma (59%), leukoplakia (54%), oral submucous fibrosis (36%) and smokers melanosis (4%) with duration and magnitude of habits had a significant effect in the development of oral lesions which is supported by other studies.^{2, 111}

Females were addicted to chewing habits more than smoking. Habitual betel and areca nut chewers had more prevalence (46%) of oral submucous fibrosis compared to others. During betel nut chewing, endothelial damage may be induced by areca nut components and leading to the pathogenesis of OSF, periodontitis, and endothelial dysplasia which was supported by the studies done in Chennai³ and China.¹¹¹ 60% females gave the history of eating supari (plain areca nut) and 49% females gave the history of using other forms of tobacco. Women in many rural areas believe that tobacco has many medicinal properties in keeping the mouth clean, getting rid of a foul smell, curing toothache, controlling morning sickness.¹⁴³

In the present study, among various etiologies encountered, 25.4% had malignant lesions, 19.2% had dermatological lesions, 16.9% were infective lesions and premalignant lesions, 13.8% had other lesions, 4.6% had inflammatory lesions, 2.3% had development lesions and 0.8% had systemic lesions.

In the study population, malignancy was observed in 25.4%, majority were diagnosed as squamous cell carcinoma (32 cases) and adenoid cystic carcinoma (one case). This finding was consistent with other studies.¹⁴⁴ The predominant age group affected was 61-69 years (70%), with a male preponderance (57.6%). The incidence of oral squamous cell carcinoma peaks between the fifth and seventh decades of life. With prolongation of life expectancy, however, the proportion of malignancy in elderly patients is also increasing. Buccal mucosa was the commonest site of involvement in the present study population (85%) which was consistent with done in a study done in Kerala.¹⁴⁵ Studies conducted elsewhere have shown the common risk factors associated with malignancy were use of different forms of tobacco and habits of chewing betel and areca nuts, which was similar when compared with present study.³

In the present study, total 25 cases of dermatological disorders (19.2%) were reported, which found higher than similar Indian study (4%).² Most frequent dermatological disorder was oral lichen planus, observed in 10 patients (7.7%), and most common clinical type was reticular type (70%) followed by atrophic type (20%) and erosive – ulcerative type (10%) which is consistent to similar studies.⁵⁶ Similar to other studies, buccal mucosa was the predominantly affected site (90%) in present study.⁵⁶ Cutaneous lesions

were hyperkeratotic flat topped papules and plaques with violaceous hue and dystrophic nail changes.

Vitiligo involving oral mucosa observed in eight cases (6%) with female predilection and common clinical type was mucosal vitiligo (75%). In all cases lips were observed as a common site of involvement which was consistent to similar Indian study.⁵⁰

Among four pemphigus cases, three cases were pemphigus vulgaris and one case was pemphigus foliaceus. Cutaneous lesions were flaccid bullae which ruptured to form erosive lesions. Whereas frequently observed oral mucosal lesions are erosive and ulcerative lesions, involving buccal mucosa, tongue and lips.¹⁴⁵

In our study, two patients with psoriasis showed fissured tongue which was consistent to earlier report.⁸⁶ Even though strong correlation suggested, these lesions are not pathognomonic feature of the disease.

One case of Steven Johnson Syndrome with ocular, oral, cutaneous and genital lesions were observed. Patient showed ulcerative lesions over lips, labial mucosa, buccal mucosa and tongue which is consistent to similar study.⁹⁹

One female systemic lupus erythematosus case with typical malar rash, ulcerative lesions over lips, labial mucosa and tongue was screened

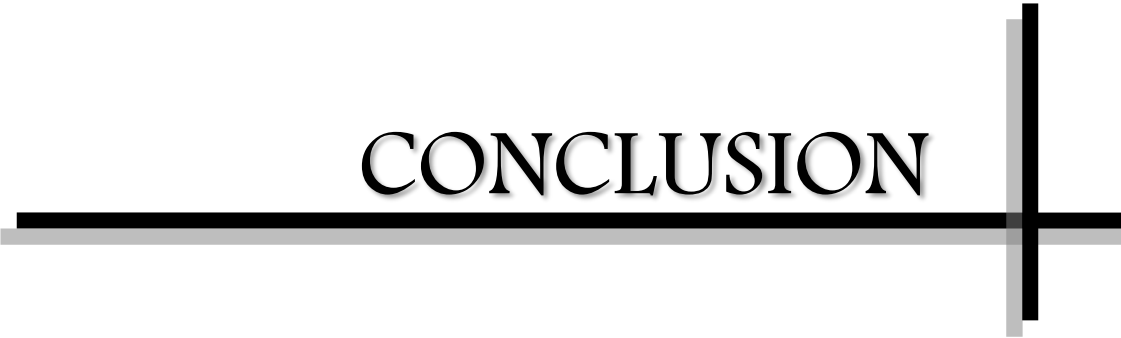
associated with joint pain, respiratory tract infection similar to earlier reports.^{90,94}

One 80 year old female patient with discoid lupus erythematosus seen in our study. Patient presented with ulcerative oral lesion over lower lips associated with burning sensation. No cutaneous lesions observed. Histopathology revealed hyperparakeratosis, focal areas of liquefaction degeneration of the basal layer.⁹⁴

Oral candidiasis, the second most common diagnosis in our study population and the common infective condition in elderly population. This can be because of their reduced salivary secretion, concurrent comorbidities like diabetics and immunosuppression caused by other medications.^{2,3}

Out of total 22 cases of premalignant conditions, leukoplakia was the most common etiology followed by oral submucous fibrosis. In our study, premalignant conditions showed significant association with smoking and other forms of tobacco with male preponderance. This result was supported by few other studies.^{3, 144, 145}

CONCLUSION

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CONCLUSION

- The present study brings to light various oral mucosal lesions in geriatric population, which also highlights the importance of early diagnosis of oral precancerous lesions before it develops into malignancy.
- The present study reveals the clinical types of oral mucosal lesions in geriatric population and also their distribution with possible etiological factors which will be valuable in planning future oral health studies.

SUMMARY

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SUMMARY

- The prevalence of oral health problems increases with age, highlighting the importance of oral health-related quality of life. Abuse of various oral carcinogens have been recognized as etiological factors for oral precancerous or cancerous lesions.
- A total of 130 cases above 60 years with oral mucosal lesions who presented to Dermatology OPD at R.L. Jalappa Hospital and Research centre, Tamaka, Kolar district, Karnataka during the study period from January 2016 - July 2017 were enrolled in this clinical study.
- In the present study, majority of the patients, were in the age group of 60-69 years (71%), followed by the age group of 70-79 years (24%) and less common were the age group of 60-69 year (5%).
- In the present study, males (56.2%) affected marginally more than females (43.8%).
- Buccal mucosa was the commonest site of involvement (58%) observed.
- In the present study, common risk factors associated with oral mucosal lesions were 52.3% were chewing betel nut, 46.2% were using tobacco, smoking 40% , alcohol intake 17.7%, 12.3% wearing dentures and 13.8% had stress.
- Smoking (52 cases) was the most common risk factor in males whereas, in females betel quid chewing followed by other forms of tobacco usage and stress were the commonly associated risk factors elicited.

- A total 130 conditions, classified into 8 various etiological categories. Malignancy (25.4%) was the most common etiology, followed by dermatological etiology (19.2%) and then premalignant and infective etiologies (16.9%). Aphthous ulcer (10%), inflammatory (4.6%), developmental (2.3%) and systemic etiologies (0.8%) were the uncommon observed etiologies.
- Among malignancy, squamous cell carcinoma was seen in 32 cases and adenoid cyst carcinoma in one.
- Among dermatological conditions, most common was oral lichen planus 8%, followed by vitiligo 6%, pemphigus 3% and psoriasis (2%). The least conditions were Steven Johnson syndrome, systemic lupus erythematosus and discoid lupus erythematosus.
- Among infective conditions, most observed were oral candidiasis (12.4%) and herpes simplex infections (5.4%).
- Among premalignant conditions, most common was leukoplakia (8.5%) followed by oral submucous fibrosis (7.7%).

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ANNEXURES

A decorative graphic consisting of a thick horizontal line and a thick vertical line intersecting at a right angle. The intersection is located to the right of the word 'ANNEXURES'. The horizontal line extends from the left edge of the page towards the center, and the vertical line extends from the bottom edge of the page upwards, crossing the horizontal line.

PROFORMA

Case number

Name:	Op Ip Number
Age & Sex:	Date:
Occupation:	RELIGION
Address:	Marital Status

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

1. Onset
2. Progression: slow/rapid
3. Site: Cheeks/tongue/lips/gingiva/hard palate/soft palate
4. Risk factors: Smoking/ alcohol/ chewing habits/ stress/ dentures

PAST HISTORY: similar illness/ treatment history

PERSONAL HISTORY:

Diet Appetite Sleep Bowel/Bladder habits

FAMILY HISTORY:

General physical examination:

Pallor/ Icterus/ Clubbing/ Cyanosis/ Lymphadenopathy/ Edema

Vitals: Pulse Blood pressure Respiratory rate Temperature

Cutaneous examination: Morphology and Distribution of lesions

Hair and nail examination

Systemic examination: CVS RS CNS GIT

INVESTIGATIONS:

1. Complete haemogram
2. Gram stain
3. KOH mount
4. Culture: Bacterial/Fungal
5. Skin biopsy:
6. Others if any:

FINAL DIAGNOSIS:

Remarks of the Guide

CONSENT FORM

I Mr. / Mrs./ Ms. _____ age _____years, resident of

Hereby giving consent to Dr. Jameema Corneli Peter, for performing the procedures related to the study as previously explained to me and any other procedures necessary or advisable to complete the study include the use of local anaesthesia.

I have completely understood the purpose of the procedure. I also agree to cooperative with him.

I have carefully understood the procedure and possible complications and agree to do it by my own free will and in complete consciousness without any influence.

I shall in no way hold the doctor responsible for any of the procedures or their consequences whatsoever.

Participant's signature/ thumb

Date:

Researcher's signature

KEY TO MASTER CHART

Gender

M	Male	F	Female
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Etiology

Develop	Developmental
Inflam	Inflammation
Inf	Infective
Derm	Dermatological
Syst	Systemic
PM	Premalignant
M	Malignant
O	Other miscellaneous

Systemic Cofactors

DM	Diabetes Mellitus
HTN	Hypertension
HIV	Human Immunodeficiency virus

Site of involvement

BM	Buccal Mucosa
T	Tongue
L	Lip
LM	Labial Mucosa
HP	Hard Palate

RISK FACTORS

S	Smoking
A	Alcohol
B	Betel nut
T	Tobacco
D	Dentures
St	Stress
N	Nil

CLINICAL DIAGNOSIS

Oral lichen planus	OLP
Oral candidiasis	OC
Herpes Labialis	HL
Vitiligo	V
Leukoplakia	L
Oral submucous fibrosis	OSF
Oral carcinoma	CA
Systemic lupus erythematosus	SLE
Discoid lupus erythematosus	DLE

MASTER CHART

SL NO:	AGE	GENDER	IP NO:	DIAGNOSIS	Etiology	Site	clinical Type	Comorbidities	Risk factors	Smoking	Alcohol	tobacco	betel nut	dentures	stress	Extraoral lesions
1	60yrs	M	232594	OC	Inf	T	hypertrophic type	DM, HTN	T, B	N	N	Y	Y	N	N	N
2	60yrs	F	294548	V	Derm	L	mucosal vitiligo	N	T, B	N	N	Y	Y	N	N	V
3	65yrs	F	332968	V	Derm	L	mucosal vitiligo	N	B	N	N	N	Y	N	N	N
4	75yrs	M	233054	OC and HL	Inf	T	hypertrophic type	atopy	S, T, B	Y	N	Y	Y	N	N	N
5	65yrs	M	469537	OC	Inf	BM, T, HP	atrophic type	DM,HTN	S,A,T,B	Y	Y	Y	Y	N	N	N
6	62yrs	M	306285	OC	Inf	T	hypertrophic type	DM	N	N	N	N	N	N	N	N
7	65yrs	F	194923	OC	Inf	T	hypertrophic type	DM, HTN	T, B	N	N	Y	Y	N	N	drug eruption
8	70yrs	F	308363	OLP	Derm	L, BM	reticular type	N	T, B	N	N	Y	Y	N	N	N
9	65yrs	F	260679	OC	Inf	T	atrophic type	N	B	N	N	N	Y	N	N	N
10	60yrs	F	365594	cheilitis	Inflam	L	granulomatous cheilitis	DM	B, D	N	N	N	Y	Y	N	N
11	70yrs	M	314557	L	PM	BM, HP	reticular, homogenous	N	S, T, B, D	Y	N	Y	Y	Y	N	N
12	67yrs	F	418411	OSF	PM	BM	OSF	DM	B	N	N	N	Y	N	N	N
13	62yrs	M	349744	OC	Inf	T	hypertrophic type	DM, HTN	T,B	N	N	Y	Y	N	N	N
14	60yrs	M	297356	OLP	Derm	BM	reticular type	N	D	N	N	N	N	Y	N	cut LP
15	70yrs	M	265949	fissured tongue	others	T	fissured tongue	DM	N	N	N	N	N	N	N	N
16	64yrs	M	368209	aphthous	others	HP	ulcerative lesion	DM	S, A, D	Y	Y	N	N	Y	N	N
17	64yrs	F	284072	fissured tongue	others	T	fissured tongue	TB	N	N	N	N	N	N	N	N
18	83yrs	M	288210	OSF	PM	BM, LM, L	OSF	N	T, B	N	N	Y	Y	N	N	N
19	73yrs	M	2530	CA	M	BM	SCC	N	A, St	N	Y	N	N	N	Y	N
20	75yrs	F	306550	V	Derm	LM, L	mucosal vitiligo	N	B	N	N	N	Y	N	N	vitiligo
21	65yrs	M	263941	aphthous	others	LM	ulcerative lesion	HIV	S, A, D	Y	Y	N	N	N	N	N
22	64yrs	M	405796	CA	M	BM	SCC	N	S, T, B	Y	N	Y	Y	N	N	N
23	70yrs	M	332260	fordyce spots	Develop	L	fordyce spot	DM	S, T, B	Y	N	Y	Y	N	N	psoriasis
24	66yrs	M	352854	L	PM	BM	homogenous	HTN	S, T, B, St	Y	N	Y	Y	N	Y	N
25	60yrs	F	386050	aphthous ulcer	others	T, LM	ulcerative lesions	N	S, T, B	Y	N	Y	Y	N	N	N
26	60yrs	F	307040	perioral dermatitis	Derm	LM, T	erosive lesion	DM	B	N	N	N	Y	N	N	N
27	76yrs	F	302544	L	PM	BM	homogenous	N	T,B	N	N	Y	Y	N	N	N
28	60yrs	F	268855	HL	Inf	L	Herpes labialis	DM	D, St	N	N	N	N	Y	Y	N
29	63yrs	M	345197	OLP	Derm	BM	reticular type	DM	A, T, B, D	N	Y	Y	Y	Y	N	N
30	70yrs	F	344725	L	PM	BM, HP	homogenous	N	T, B	N	N	Y	Y	N	N	N
31	75yrs	M	409660	induced mu	others	T, LM	ulcerative lesion	DM, HTN	St	N	N	N	N	N	Y	psoriasis
32	60yrs	M	258570	OC	Inf	BM, T, HP	hypertrophic type	N	N	N	N	N	N	N	N	N
33	70yrs	F	296791	OC	Inf	T, BM	atrophic type	N	N	N	N	N	N	N	N	N
34	60yrs	F	296928	V	Derm	L, LM	mucosal vitiligo	N	N	N	N	N	N	N	N	vitiligo vulgaris
35	65yrs	M	294408	OSF	PM	LM, BM	OSF	DM, HTN	S, T, B	Y	N	Y	Y	N	N	N
36	60yrs	M	294774	HL	Inf	L	Herpes labialis	DM,HTN	St	N	N	N	N	N	Y	herpes
37	60yrs	F	416986	aphthous ulcer	others	LM	ulcerative lesion	DM, HTN	T, B	N	N	Y	Y	N	N	N
38	62yrs	M	307363	OLP	Derm	BM	reticular type	DM	S, D	Y	N	N	N	Y	N	cut LP
39	60yrs	F	196179	L	PM	BM	homogenous	HTN	T, B	N	N	Y	Y	Y	N	N
40	80yrs	M	414870	aphthous	others	T, LM	ulcerative lesion	HTN	S, T, B	Y	N	Y	Y	Y	N	N
41	62yrs	M	443736	CA	M	BM	SCC	N	S, T, B	Y	N	Y	Y	N	N	N

MASTER CHART

42	70yrs	F	202425	CA	M	L	SCC	N	T, B	N	N	Y	Y	N	N	N
43	60yrs	F	248438	V	Derm	L, LM	mucosal vitiligo	N	B	N	N	N	Y	N	N	N
44	60yrs	F	269707	CA	M	BM	SCC	N	T, B	N	N	Y	Y	N	N	N
45	62yrs	M	472655	V	Derm	L	mucosal vitiligo	N	N	N	N	N	N	N	N	N
46	61yrs	F	366401	CA	M	BM	SCC	N	T, B	N	N	Y	Y	N	N	N
47	60yrs	F	406574	CA	M	BM	SCC	N	T,B	N	N	Y	Y	N	N	N
48	60yrs	F	220793	cheilitis	Inflam	L	Actinic cheilitis	DM	T,B	N	N	Y	Y	N	N	N
49	70yrs	F	172187	nduced mu	others	BM, LM	ulcerative lesion	DM	N	N	N	N	N	N	N	N
50	60yrs	F	344924	L	PM	BM	homogenous	N	T, B	N	N	Y	Y	N	N	N
51	60yrs	M	415506	HL	Inf	L	Herpes labialis	DM	S, T,B, St	Y	N	Y	Y	N	Y	N
52	70yrs	F	391982	phigus vulg	Derm	T	erosive lesion	DM	T, B, St	N	N	Y	Y	N	Y	Pemphigus vulgaris
53	60yrs	M	380158	V	Derm	L, BM	vitiligo vulgaris	DM	N	N	N	N	N	N	N	vitiligo
54	72yrs	M	344130	OC	Inf	T, BM	atrophic type	N	S	Y	N	N	N	N	N	N
55	80yrs	F	389381	CA	M	BM	SCC	N	T, B, St	N	N	Y	Y	N	Y	cheek swelling
56	65yrs	F	380616	L	PM	BM	homogenous	N	T	N	N	Y	N	N	N	N
57	65yrs	M	412647	sured tong	others	T	fissured tongue	N	S,A	Y	Y	N	N	N	N	psoriasis
58	65yrs	F	414794	HL	Inf	L	Herpes labialis	N	St	N	N	N	N	N	Y	N
59	60yrs	F	467795	CA	M	BM	SCC	N	N	N	N	N	N	N	N	N
60	62yrs	M	472655	OLP	Derm	BM	reticular type	DM	T, B	N	N	Y	Y	N	N	N
61	62yrs	F	467068	CA	M	BM	SCC	N	T, B	N	N	Y	Y	N	N	N
62	60yrs	F	466235	OSF	PM	BM, LM, L	OSF	N	B	N	N	N	Y	N	N	N
63	68yrs	M	452928	OLP	Derm	T, BM	reticular type	DM	S, A	Y	Y	N	N	N	N	N
64	61yrs	F	465643	CA	M	BM	SCC	N	T	N	N	Y	N	N	N	N
65	60yrs	M	449693	CA	M	BM	SCC	N	S,A,T,B	Y	Y	Y	Y	N	N	N
66	80yrs	M	476157	CA	M	BM	SCC	N	S,A, St	Y	Y	N	N	N	Y	N
67	60yrs	M	469771	CA	M	T	SCC	N		Y	N	Y	Y	N	N	N
68	65yrs	M	424992	OSF	PM	BM	OSF	DM		N	N	Y	Y	N	N	N
69	65yrs	M	454966	CA	M	BM	SCC	DM		N	N	Y	Y	N	Y	N
70	73yrs	M	460869	CA	M	BM	SCC	N		Y	N	N	N	N	Y	N
71	75yrs	M	442442	CA	M	T	SCC	N		Y	N	Y	Y	N	N	N
72	75yrs	F	418348	phigus vulg	Derm	T, BM	erosive lesion	DM, HTN		N	N	N	N	N	N	erythroderma
73	60yrs	M	264896	ordyce spo	Develop	L	fordyce spot	DM		Y	N	N	N	N	N	N
74	64yrs	M	264896	OC	Inf	T	hypertrophic type	DM, HTN		N	N	Y	Y	N	N	drug eruption
75	60yrs	F	379421	CA	M	BM	SCC	N		N	N	Y	Y	N	N	N
76	62yrs	M	415851	HL	Inf	L	Herpes labialis	DM, HTN		Y	N	N	N	N	Y	N
77	62yrs	M	443736	CA	M	BM	SCC	N		Y	N	Y	Y	N	N	N
78	65yrs	M	356126	rythroplaki	PM	BM	speckled erythroplakia	N		Y	N	N	N	N	N	N
79	62yrs	M	377949	ker's melan	Inflam	HP	smokers melanosis	N		y	N	Y	N	N	N	N
80	60yrs	F	245376	DLE	Derm	L	erosive lesion	N		N	N	N	N	N	N	N
81	70yrs	M	439589	CA	M	BM	SCC	N		Y	N	Y	Y	N	Y	N
82	60YRS	M	466344	CA	M	BM	SCC	N		Y	N	Y	Y	N	N	N

MASTER CHART

83	72yrs	M	445204	CA	M	T	adenoid cystic ca	N		Y	N	Y	Y	N	N	N
84	60yrs	F	446371	CA	M	BM	SCC ulceroproliferative	DM		N	N	Y	Y	Y	N	N
85	60yrs	F	368154	OLP	Derm	lower L	actinic lichen planus	DM,HTN		N	N	N	N	Y	N	N
86	60yrs	M	348500	L	PM	BM	homogenous	N		Y	N	N	N	N	N	N
87	62yrs	M	331293	phthous ulc	others	T, BM	ulcerative lesion	DM		Y	Y	Y	Y	Y	N	N
88	73YRS	M	347598	OC	Inf	T	hypertrophic type	DM		N	N	N	N	N	N	N
89	70yrs	F	434390	graphic ton	others	T	geographic tongue	N		N	N	N	N	N	N	psoriasis
90	75yrs	M	480856	g induced m	Inf, others	T, BM	hypertrophic type	DM		N	N	N	N	N	N	drug induced mucositis
91	75yrs	M	409650	L	PM	BM	homogenous	N		Y	N	N	N	N	N	N
92	62yrs	F	475241	phthous ulc	others	BM	ulcerative lesion	N		N	N	Y	Y	N	N	N
93	60yrs	F	483966	nduced mu	others	T, BM	erosive lesion	DM		N	N	N	N	Y	Y	FDE
94	60yrs	M	299176	ker's melar	Inflam	HP	smokers melanosis	N		y	N	N	N	N	N	N
95	62yrs	M	461615	OC	Inf	T	hypertrophic type	DM, HTN		Y	N	Y	Y	N	N	N
96	68yrs	F	482312	CA	M	BM	SCC	N		N	Y	N	N	N	N	N
97	70yrs	M	475406	jaundice	Syst	HP	jaundice	HTN		Y	Y	N	N	N	N	N
98	65yrs	M	443782	L	PM	BM	homogenous	N		Y	N	N	N	N	N	N
99	63yrs	M	481608	HL	Inf	L	Herpes labialis	N		N	N	N	N	N	Y	N
100	60yrs	M	326258	ker's melar	Inflam	HP	smokers melanosis	N		y	N	N	N	N	N	N
101	68yrs	M	227502	graphic ton	others	T	geographic tongue	DM,HTN		Y	N	N	N	N	N	psoriasis
102	75YRS	M	463449	L	PM	BM	homogenous	N		Y	N	N	N	N	N	N
103	65yrs	M	227578	CA	M	BM	SCC	N		Y	Y	N	N	N	N	N
104	65yrs	M	473387	CA	M	BM	SCC	DM		Y	Y	N	N	N	Y	N
105	60yrs	F	448324	CA	M	T	SCC	N		N	Y	N	N	N	N	N
106	60yrs	M	434890	CA	M	BM	SCC	N		Y	Y	N	N	N	N	N
107	60YRS	F	469073	nduced mu	others	T, BM	ulcerative lesion	DM		N	N	N	N	Y	Y	FDE
108	60yrs	F	361922	OC	Inf	T	hypertrophic type	DM, HTN		N	N	Y	Y	N	N	N
109	60yrs	M	432921	OSF	PM	BM, LM, L	OSF	N		Y	N	Y	Y	N	N	N
110	68yrs	F	431648	CA	M	BM	SCC	N		N	N	N	N	N	N	cheek swelling
111	62yrs	M	459712	CA	M	BM	SCC	N		Y	Y	N	N	N	N	N
112	74yrs	M	471286	CA	M	BM	SCC	N		Y	Y	N	N	N	N	N
113	62yrs	F	456540	CA	M	BM	SCC	N		N	Y	N	N	N	N	N
114	61yrd	F	479998	OLP	Derm	BM	erosive lesion	DM, HTN		N	N	Y	Y	N	N	N
115	70yrs	F	481382	SLE	Derm	LM	erosive lesion	N		N	N	N	N	N	N	MALAR RASH
116	60yrs	M	482309	OSF	PM	BM, LM, L	OSF	N		Y	N	N	Y	N	N	N
117	70yrs	F	482304	SJS	Derm	L, LM, T	erosive lesion	N		N	N	N	N	N	N	SJS
118	65yrs	F	481370	OSF	PM	BM, LM, L	OSF	N		N	N	Y	Y	N	N	N
119	86yrs	F	482306	OSF	PM	BM, LM, L	OSF	N		N	N	Y	Y	N	N	N
120	63yrs	M	481379	ker's melar	Inflam	HP	smokers melanosis	N		y	N	N	N	N	N	N
121	70yrs	M	482313	OLP	Derm	BM	atrophic type	N		Y	N	N	N	N	N	N
122	69yrs	F	482300	V	Derm	L, BM	vitiligo vulgaris	DM		N	N	N	N	N	N	vitiligo

MASTER CHART

123	68yrs	F	461171	nduced mu	others	T, BM	ulcerative lesion	DM		N	N	N	Y	Y	N	Breast carcinoma
124	78yrs	F	374623	OLP	Derm	BM	reticular lichen planus	DM,HTN		N	Y	N	Y	Y	N	cut LP
125	64YRS	M	305233	melanoplaki	Develop	T	melanoplakia	DM,HTN		N	Y	N	N	N	N	N
126	82YRS	M	228000	phthous ulc	others	T	ulcerative lesion	N		Y	Y	Y	Y	N	N	N
127	62YRS	F	242192	ophigus vulg	Derm	T, BM	erosive lesion	N		N	N	Y	Y	N	N	Pemphigus vulgaris
128	70YRS	M	153714	CA	M	BM	SCC	N		Y	Y	Y	Y	N	N	N
129	60YRS	M	455495	OC	Inf	T	hypertrophic type	DM, HTN		N	N	Y	Y	N	N	herpes zoster
130	65YRS	M	471118	OSF	PM	BM, LM, L	OSF	N		Y	N	Y	Y	N	N	N